UNIVERSAL
LIBRARY
OU_172975
UNIVERSAL
LIBRARY

172975

TAYLOR'S
PRACTICE OF MEDICINE

First Edition	1890
Second Edition	1891
Third Edition	1893
Fourth Edition	1895
Fifth Edition	1898
Sixth Edition	1901
Seventh Edition	1904
Eighth Edition	1908
Ninth Edition	1911
Tenth Edition	1914
Eleventh Edition	1918
Twelfth Edition	1922
Thirteenth Edition	1925
Fourteenth Edition	1930
Fifteenth Edition	1936

Printed in Great Britain

LIST OF CONTRIBUTORS

General Medicine.	E. P. POULTON, M.A., D.M. Oxon., F.R.C.P Lond., Physician to Guy's Hospital, Consulting Physician to the London County Council, correspondant (Hon. Causa) de la Société de Thérapeutique de Paris, formerly Clinical Examiner in Medicine, Oxford University, Examiner in Medicine for the Conjoint Board, and Associate Examiner in Medicine, University of London.
Diseases of the Nervous System.	C. P. SYMONDS, M.A., D.M. Oxon., F.R.C.P. Lond., Physician in Charge of the Neurological Department, Guy's Hospital, Physician to Outpatients at the National Hospital for Nervous Diseases, Queen Square, Consulting Neurologist to the Royal Air Force, Neurologist to the Central London Throat, Nose and Ear Hospital.
Diseases of the Skin (Dermatoses).	H. W. BARBER, M.A., M.B. Camb., F.R.C.P. Lond., Physician in Charge of Skin Department, Guy's Hospital, Corresponding Member of the French, American and Vienna Dermatological Societies.
Mental Diseases.	R. D. GILLESPIE, M.D. Glas., F.R.C.P. Lond., D.P.M. Lond., Physician and Lecturer for Psychological Medicine, Guy's Hospital, Examiner in Psychological Medicine, Royal College of Physicians and University of London, Corresponding Member of the American Psychiatric Associations.
Diseases of the Tropics.	N. HAMILTON FAIRLEY, O.B.E., M.D. D.Sc. Melb., F.R.C.P. Lond., Assistant Physician and Director of Pathology, Hospital for Tropical Diseases, Lecturer in Clinical Medicine and Applied Pathology, London School of Hygiene and Tropical Medicine, Lecturer in Tropical Medicine, Westminster Hospital Medical School, Hon. Member of the American Society of Tropical Medicine, Corresponding Member of the Belgian Society of Tropical Medicine.
Diseases of the Nose, Throat and Ear.	W. M. MOLLISON, C.B.E., M.Ch. Camb., F.R.C.S., Eng., Surgeon to the Ear and Throat Department, Guy's Hospital.

PREFACE TO THE FIFTEENTH EDITION

It is six years since the last edition of Taylor's Medicine was published and during this time there has been steady progress throughout the range of medicine. In the present edition Dr. Symonds, Dr. Barber and Dr. Gillespie have again been responsible for their respective sections of the book. The biggest change is in the section on Diseases of the Tropics, which has been almost entirely rewritten by Dr. N. Hamilton Fairley, who kindly consented to join us. It has been placed at the end of the book and, as it is as complete as is compatible with the number of pages that can be allowed in a text-book of general medicine, the subject appears as an organic whole, so that this section may be looked upon as an addendum to the rest of the book. Of course some overlapping is unavoidable ; the diseases in this country due to worms are of more importance in the tropics and the variety of worms met with there is so large that this part of medicine is bound to be described among the tropical diseases. Attention may be drawn to articles on bites and stings, including snake bite, and to a section on tropical skin diseases.

The next important alteration is that the diseases of the larynx and tonsils, which have hitherto been described in different parts of the book, are now grouped together in a new section on Diseases of the Nose, Throat and Ear (from the medical aspect), which includes short articles on sinusitis and on the ear. Mr. W. M. Mollison has very kindly co-operated by revising and adding to this part of the subject.

Infectious Diseases have now been arranged on an ætiological basis beginning with those due to ultra-filterable viruses, then those due to bacteria, fungi, spirochætes, protozoa, helminths and other metazoa. This order applies not only to the Infectious Diseases, but to Infections of the Skin and Tropical Diseases. Throughout this book the lettering of the headings has been simplified. In order to save space it has been considered desirable in the case of those rare diseases which are dealt with in quite a short paragraph, not to use headings of the same importance as for the common diseases, a description of which often occupies many pages. Consequently while for these latter diseases the headings are in capitals as hitherto and stand out in the middle of the page, for the former black italics are used and these are placed at the side of the page so that the continuity of the text is not broken. This has been pointed out, as otherwise these small black italic headings might be regarded as sub-headings of the more important diseases ; but this is not the case.

The articles on the following subjects are new or have been considerably altered or added to ; in the introduction, diet in infancy, dosage, remedial exercises, climate and natural waters ; among the infectious diseases, variola minor, acute poliomyelitis, glandular fever, influenza, scarlet fever, tuberculosis in childhood, syphilis and poisoning by arsenobenzol, sporotrichosis and other uncommon mycotic diseases ; among the respiratory disorders, dry bronchiectasis, pulmonary œdema, pneumonia, including the typing of pneumococci and treatment with serum and the oxygen tent, pulmonary abscess, bronchoscopy, anthracosis, silicosis, asbestosis, epituberculosis, the Mantoux test, and empyema ; among the circulatory diseases, the size of the heart, the new alkaloids of digitalis, cardiac compensation and its failure, rheumatic fever, the prognosis of heart

disease, chronic constrictive pericarditis, prognosis of aortic aneurysm; among the alimentary diseases, congenital pyloric stenosis, diarrhœa in infants, cœliac disease, liver function, fatty liver; among the blood diseases, the Arneth count as simplified by Schilling, anhæmopoietic anæmias of adults and children, simple achlorhydric anæmia, pernicious anæmia, agranulocytosis, hæmolytic anæmias, Lederer's anæmia, purpura, hæmophilia, acidosis and alkalosis, Hodgkin's disease and rare diseases of the spleen, including Gaucher's and other diseases; among the diseases of metabolism and internal secretion, basal metabolism, diet tables arranged on a new plan (to be published in full in a special monograph), hypoglycæmia, the parathyroids, the pituitary, including Cushing's syndrome, the suprarenals, the gonads and obesity; among the diseases of the urinary organs, new methods of examination and of testing renal function, reaction of the urine, hydronephrosis.

The rheumatic diseases have now been brought together and new matter added, especially in relation to morbid anatomy and to spondylitis. The articles on beri-beri, rickets, renal dwarfism and poisoning by means of carbon monoxide have been altered. In the diseases of the nervous system the anatomical parts, which were previously scattered through the section with consequent overlapping, have now been brought together as an introduction, entitled "Applied Anatomy and Physiology"; cerebral tumour has been rewritten. Among the mental diseases Dr. Gillespie is now responsible for the psychoneuroses, while there is a new article on psychological principles. Among the skin diseases there may be mentioned new articles on eczematoid streptococcal eruption of the scalp, erythema annulare centrifugum, granuloma annulare, pustular psoriasis, parapsoriasis, keratosis pilaris atrophicans, acanthosis nigricans, while alopecia has been reclassified. This list provides a conspectus of the chief advances of medicine in the period; but there are of course many other smaller alterations and additions throughout the book and no trouble has been spared in attempting the task of keeping the book up to date. There are sixty-nine more pages. Certain articles like typhus and sprue have been transferred to the tropical section so that it is difficult to compare the lengths of the various sections in the two editions. Broadly speaking, the length of the sections on "Internal Medicine" and mental diseases remains the same as before; the section on nervous diseases is ten pages shorter. The section on skin diseases is twenty-one pages longer, while the tropical section has been about doubled.

A number of the older plates have been replaced and the total number is now seventy-one as against sixty-four previously. The text-figures have been increased to 104.

It is my pleasant duty to thank many friends for help in different parts of the book. Professor R. T. Leiper has kindly read through the section on helminths and made suggestions. I should like to thank Dr. A. C. Hampson, for help in the children's diseases, Mr. V. E. Lloyd, for looking through the article on syphilis, Miss Angove, Sister in charge of the Massage Department of Guy's Hospital, and Mr. J. Rivers, who has again made the Index and helped in numerous ways.

E. P. POULTON

25 Upper Wimpole Street,
London, W.1.

PREFACE TO THE TWELFTH EDITION

Sir Frederick Taylor's "Practice of Medicine" has for thirty years held one of the foremost places as a text-book for students and practitioners, and it remains a splendid monument to the industry and knowledge of its author. To one whose lot it is to carry on the work there might well come a feeling of trepidation at the thought of following in the footsteps of such a leader.

Nevertheless, it was not a task that could be avoided, and in undertaking it my first thought was to try and find out what special features the book possessed that made it appeal to such a wide circle of readers. The completeness of the book seemed the most important—the fact that in a single volume the whole of medicine was represented, including such a speciality as Diseases of the Skin, a subject which is often omitted from text-books on medicine. Again, the book contained a detailed account of the method of examining the various systems of the body, so that it can be truly said that a student who read this book required no other during his course of study in the medical wards and out-patient department. It was evident that the main scope of the book must remain unchanged; but this very fact created a difficulty, because the range of medicine has increased so much of late that it is almost beyond the powers of a single individual to cover the whole ground himself. Sir Frederick Taylor and Sir William Osler will perhaps have been the last to have made the attempt. At the same time a text-book is apt to lose in continuity if there are too many writers, and so it was decided that, while I must myself revise the greater part of the work, two other authors should be asked to take in hand the sections dealing with the two definite specialities in medicine.

E. P. POULTON

15, Cavendish Place, W. 1.
June, 1922.

CONTENTS

PAGE

INTRODUCTION 1

INFECTIOUS DISEASES . . . . . 10—119

Nature of infection, 10; immunity, 13; anaphylasxis, 15; pyrexia, 17; ***diseases due to ultra-filterable viruses or of unknown origin,*** measles, 24; rubella, 27; small-pox, 28; vaccination, 33; chicken-pox, 34; mumps, 36; influenza, 37; acute poliomyelitis, 40; psittacosis, 45; foot and mouth disease, 45; glandular fever, 45; ***rickettsia,*** trench fever, 46; ***bacteria,*** streptococcal infections, 47; scarlet fever, 48; septicæmia, 53; erysipelas, 54; staphylococcal infections, 56; pneumococcal infections, 56; gonococcal infections, 57; cerebro-spinal fever, 59; diphtheria, 63; whooping-cough, 69; typhoid fever, 71; tuberculosis, 83; paratyphoid fevers, 84; glanders, 91; anthrax, 92; tetanus, 94; gas gangrene, 98; ***mycoses,*** actinomycosis, 99; sporotrichosis, 101; blastomycosis, 102; torulosis, aspergillosis, 103; ***spirochæta,*** syphilis, 104; congenital syphilis, 114; poisoning by arseno-benzol, 117.

DISEASES OF THE ORGANS OF RESPIRATION . . . 120—194

Examination of the chest, 120; tracheitis and specific infections, 127; new growths, obstruction, 128; bronchitis, 130; bronchiectasis, 135; hay fever and asthma, the allergic state, 138; obstruction, 144; emphysema of the lungs, 145; collapse, 148; œdema, 149; pneumonia, 150; Friedländer pneumonia, broncho-pneumonia, 157; abscess, 159; fibroid lung, 160; gangrene, 162; pulmonary tuberculosis, 163; syphilis, poisoning by irritant gases, 176; pulmonary embolism and thrombosis, 177; intra-thoracic neoplasms, 179; pleurisy and empyema, 182; hydrothorax, hæmothorax, chylothorax, 189; pneumothorax, 190; diaphragmatic hernia, 192; mediastinitis, 193.

DISEASES OF THE NOSE, THROAT AND EAR (*from the medical aspect*) 195—215

Coryza, 195; chronic rhinitis, 197; sinusitis, 197; epistaxis, 197; tonsillitis, 198; Vincent's angina, 201; pharyngeal tonsils, 201; lingual tonsils, 202; chronic pharyngitis, 202; retropharyngeal abscess, 202; laryngitis, 203; tubercle, 205; syphilis, 206; tumours, foreign bodies, 207; paralysis of laryngeal muscles, 208; spasm of the glottis, 211; congenital laryngeal stridor, anæsthesia, 212; the ear, 213; otitis media, 214.

DISEASES OF THE ORGANS OF CIRCULATION . . . 216—317

Examination of the heart, 216; capacity for effort, 223; X-rays, 224; radial pulse, 226; venous pulse, 229; ***abnormalities of cardiac action,*** 230; sinus irregularity, 232; heart-block and Adams-Stokes syndrome, 232; premature beats, 235; frequent action, 238; paroxysmal tachycardia, 239; auricular flutter, 241; auricular fibrillation, 242; pulsus alternans, infrequent action, 247; ventricular fibrillation, ***diseases of the heart,*** compensation, 248; hypertrophy, 248; dilatation, 250; failure of compensation, 252; myocarditis, myocardial degeneration, 253; rupture, aneurysm of the heart, 256; new growths and parasites, rheumatic fever, 257; chorea, 264; endocarditis, chronic endocarditis, 266; aortic stenosis, aortic regurgitation, 268; mitral disease, 270; mitral stenosis, 272; right-sided valvular disease, diagnosis, prognosis, and prevention of valvular disease, 273; treatment of chronic cardiac disease, 276; malignant endocarditis, 280;

DISEASES OF THE ORGANS OF CIRCULATION—*continued*

PAGE

effort syndrome, 283; congenital malformations, 286; pericarditis, 288; adherent pericardium, 291; chronic constrictive pericarditis, hydropericardium, 292; pneumohydropericardium, hæmopericardium, angina pectoris, 293; ***diseases of the blood vessels,*** infective arteritis, 297; chronic arterial degenerations, 298; arteriosclerosis, 300; high arterial pressure, 301; intermittent claudication, 304; erythromelalgia, 305; aneurysm, 306; congenital coarctation of the aorta, Raynaud's disease, 310; phlebitis, 311; thrombosis and embolism, 312; angeio-neurotic œdema, 316.

DISEASES OF THE ORGANS OF DIGESTION . . . 318—421

Examination of the abdomen, 318; the acute abdomen, 320; stomatitis, oral sepsis, 321; thrush, 323; obstruction of the œsophagus, 324; achalasia, 325; diverticula, 326; ***diseases of the stomach and duodenum,*** examination of the stomach, X-rays, 327; test meals, 328; dyspepsia, 332; aerophagy, 338; gastroptosis, 339; hysterical vomiting, cyclical vomiting, 341; acute dilatation of the stomach and duodenum, gastritis, 342; peptic ulcer, 344; gastro-jejunal and jejunal ulcers, 350; chronic dilatation, 351; hour-glass contraction, 352; congenital hypertrophic stenosis, carcinoma, 353; benign tumours, 356; ***diseases of the intestine,*** constipation, 356; alimentary toxæmia, 359; diarrhœa, 361; hæmorrhage, colic, 362; enteritis, 363; food-poisoning, cœliac disease, 367; phlegmenous enteritis, colitis, 368; appendicitis, 371; diverticulosis, 374; tubercle, new growths, and syphilis, 376; intestinal obstruction, 377; intussusception, 380; Hirschsprung's disease, 382; ***diseases of the liver,*** liver function and functional tests, 383; jaundice, 384; ascites, 388; liver abscess, 390; common infective hepatic jaundice, 390; acute necrosis of the liver, 391; cirrhosis, 393; syphilis, and ulcers, 397; new growths, 398; fatty liver, 398; perihepatitis, 401; pylephlebitis, 402; functional test of the biliary apparatus, 403; cholecystitis, 404; gall stones, 405; suppurative cholangitis, 407; functional tests of the pancreas, 408; acute pancreatitis, 410; chronic pancreatitis, 411; calculi, 412; neoplasms and cysts, acute peritonitis, 413; subphrenic abscess, 416; chronic peritonitis, tuberculous peritonitis, 417; peritoneal effusions, new growths, 419.

DISEASES OF THE BLOOD, SPLEEN, AND LYMPHATIC SYSTEM 422—458

Examination of the blood, 422; anhæmopoietic (deficiency) anæmias, 429; chlorosis, 430; simple achlorhydric anæmia, 431; pernicious anæmia, 432; agranulocytosis, 435; anhæmopoietic anæmias of childhood, hæmolytic anæmias, acholuric jaundice, 436; Lederer's anæmia, splenic anæmia, 437; leukæmia, 438; chloroma, polycythæmia rubra, erythræmia, 442; erythrocytosis, hæmoglobinæmia, 443; paroxysmal hæmoglobinuria, 444; methæmoglobinæmia and sulphæmoglobinæmia, purpura, 445; hæmophilia, 448; blood transfusion, 449; reaction of the blood and acidosis, 450; diseases of the spleen, 453; Gaucher's disease, Niemann-Pick's disease, Hand-Christian's disease, diseases of the lymphatic system, 455; Hodgkin's disease, 456.

DISEASES OF METABOLISM AND INTERNAL SECRETION . 459—504

The basal metabolism, 459; diabetes mellitus, 460; diet tables, 474; hypoglycæmia, 479; the thyroid gland, goitre, exophthalmic goitre, 482; myxœdema, 485; cretinism, 487; the parathyroid glands, hyperparathyroidism, 488; tetany, 488; the thymus gland, 490; the suprarenal capsules, 491; Addison's disease, 492; tumours, 493; the pituitary gland, 494; acromegaly, 495; hypopituarism, basophil adenoma, 496; diabetes insipidus, 497; the pineal gland, the gonads, the female organs, 498; eunuchism, eunuchoidism, 499; hyper- and hypo-genitalism, 500; obesity, 500; infantilism, 503; glycogen disease (in Appendix), 504.

PAGE

DISEASES OF THE URINARY ORGANS . . . . . 505—553

Examination of the kidney and bladder, 505; examination of the urine, 506; reaction, 508; albuminuria, 510; hæmaturia, casts, 513; estimation of the renal functions, 515; Bright's disease, 517; acute nephritis, 520; sub-acute glomerulo-tubal nephritis, 525; chronic glomerulo-tubal nephritis, 528; arteriosclerotic kidney, 532; bacteriuria and bacilluria, 534; pyelo-nephritis (pyelitis), 535; metastatic nephritis, perinephritis and perinephric abscess, 538; tuberculosis, 539; hydronephrosis, 541; new growths, 544; cystic disease, 545; movable kidney, 546; calculus, 547; functional albuminuria, 551.

DISEASES INVOLVING BONES, JOINTS AND FASCIÆ . . 554—568

Infective arthritis, the rheumatic diseases, fibrositis, 554; rheumatoid arthritis and osteo-arthritis, 556; gout, 561; hypertrophic pulmonary osteo-arthropathy, 565; achondroplasia, osteogenesis imperfecta, 566; osteitis deformans, 567.

DISEASES DUE TO CERTAIN DEFICIENCIES IN DIET . 569—583

Accessory food factors, 569; beri-beri, 570; epidemic dropsy, 572; pellagra, 573; scurvy, 574; rickets, 577; osteomalacia, 581.

SOME CHRONIC INTOXICATIONS . . . . . 584—591

Alcoholism, delirium tremens, 584; carbon monoxide poisoning, 586; lead poisoning, 587; mercurial poisoning, 590; arsenical poisoning, 591; manganese poisoning, 591.

DISEASES OF THE NERVOUS AND MUSCULAR SYSTEMS . 592—763

Applied anatomy and physiology, 593; blood supply of the central nervous system, 605; cervical sympathetic fibres, cerebro-spinal fluid, 606; lesions of peripheral nerves and nerve roots, lesions of the spinal cord, 607; lesions of the brain, 609; clinical examination of the nervous system, 617; ***diseases of the nerves***, 633; olfactory, optic, 634; third, fourth and sixth, 635; fifth, 636; facial, 637; auditory and vestibular, 638; glosso-pharyngeal, vagus, 640; spinal accessory, hypoglossal, 641; upper cervical, 642; phrenic, posterior thoracic, circumflex, 643; musculo-spiral, ulnar, 644; median, brachial plexus, 645; cervical ribs, 647; sciatic, popliteal, 648; sciatica, 649; meralgia paræsthetica, multiple neuritis, 651; localised muscular spasm, hiccup, ***diseases of the spinal cord***, 655; compression, 656; tumours, 661; myelitis, 662; hæmorrhage, 666; disseminated sclerosis, 667; syringomyelia, 672; tabes dorsalis, 675; subacute combined degeneration, 681; Friedreich's ataxia, 684; peroneal muscular atrophy, 685; motor neuron disease, 686; Landry's paralysis, 688; senile paraplegia, 689; ***meningitis***, suppurative, 690; syphilitic, 692; pachymeningitis interna hæmorrhagica, 693; spinal meningitis, 694; ***diseases of the brain***, cerebral hæmorrhage, 695; cerebral embolism and thrombosis, 698; chronic cerebral softening, 701; thrombosis of cerebral sinuses, 702; sub-arachnoid hæmorrhage, 703; encephalitis, 704; encephalitis lethargica, 705; abscess, 711; cerebral contusion, 712; infantile cerebral diplegia, 715; amaurotic family iodicy, 716; cerebro-macular degeneration, Schilder's encephalitis, cerebellar atrophy, 717; hepato-lenticular degeneration, paralysis agitans, 718; tumours, 721; chronic hydrocephalus, 732; general paralysis of the insane, 735; Huntington's chorea, 737; epilepsy, 738; infantile convulsions, 745; migraine, 746; myoclonus, 749; paramyoclonus multiplex, the tics, 750; spasmodic torticollis, 751; writers' cramp and allied neuroses, 752; neuralgia, trigeminal neuralgia, 754; ***diseases of the muscles***, muscular atrophy, 755; progressive muscular dystrophy, 756; Thomsen's disease, myotonia atrophica, 759; amyotonia congenita, family periodic paralysis, 760; myasthenia gravis, 761; other disorders of muscle, 762.

PAGE

MENTAL DISEASES . . . . . 764—823

Psychological principles, 764; classification, 768; methods of psychiatric examination, 770; the psychoneuroses, anxiety neurosis, 777; hysteria, 785; affective reaction types, the manic-depressive psychoses, 793; involutional melancholia, 797; schizophrenic reaction types (dementia præcox), 799; paranoia, 804; paraphrenia, organic reaction types, 806; infective exhaustive psychoses, 807; presbyophrenia, Alzheimer's disease, 808; psychopathic reaction types, 809; mental deficiency, 810; microcephalic amentia, 812; Mongolian aments, sclerotic amentia, idiots savants, 813; ***legal relationships***, lunacy certification, 914; mental deficiency, testamentary capacity, criminal responsibility, 820.

DISEASES OF THE SKIN (DERMATOSES) . . . . . 824—983

Primary lesions, 824; ***diseases caused by infective organisms—ultra-filterable viruses***, 825; molluscum contagiosum, warts, 826; herpes simplex, 827; herpes zoster, 829; ***bacterial diseases***, 832; streptococcal infections, impetigo contagiosa, 833; ecthyma, dermatitis gangrenosa infantum, 836; intertrigo, 837; streptococcal fissure, 838; relapsing streptococcal lymphangitis, eczematoid streptococcal eruption of the scalp, 839; napkin rash, 840; staphylococcal infections, 841; staphylococcal pustule, 842; miliaria rubra, 843; boils, 844; carbuncle, pemphigus neonatorum, 846; multiple abscesses of infants, 847; sycosis coccogenica, 848; sycosis nuchæ, acne necrotica, 850; hidradenitis, 851; granuloma pyogenicum, dermatitis infectiosa eczematoides, 852; acrodermatitis continua, 853; seborrhœic state and associated infections, 854; pityriasis simplex, 859; comedo, acne vulgaris, 860; seborrhœic dermatitis, 862; tuberculosis, lupus vulgaris, 864; lupus verrucosus, 868; the tuberculides, 869; sarcoids, 874; soft sore, 875; rhinoscleroma, 877; ***diseases due to fungi***, favus, ringworm, 878; trichophytides, microsporides, epidermophytides, favides, 884; tinea versicolor, 885; erythrasma, lepothrix, 886; oidiomycoses, 887; ***spirochætal diseases***, venereal warts, ***metazoal diseases***, 888; pediculus capitis, pediculus vestimentorum, 889; pediculus pubis, 890; scabies, 891; ***diseases classified according to their morphology***, the erythemas, 893; erythema multiforme, 894; erythema annulare centrifugum, granuloma annulare, 896; erythema nodosum, 897; erythema pernio, 899; erythema ab igne, 900; lupus erythematosus, 901; rosacea, 904; urticaria, 906; urticaria pigmentosa, 910; pruritus, 911; prurigo, 912; prurigo simplex acutus, 916; prurigo of Hebra, 918; prurigo of Besnier, 919; prurigo nodularis, 922; summer prurigo, 923; hydroa vaccinoforme, summer prurigo (Hutchinson), 924; light sensitiveness, 925; prurigo hiemalis, dermatitis herpetiformis, 927; dermatitis venenata and toxic eruptions, 929; eruptions caused by drugs ingested, 930; eruptions caused by drugs applied externally, traumatic and solar dermatitis, 931; eczema, 932; erythemato-squamous eruptions, pityriasis rosea, 940; psoriasis, 941; the erythrodermias, 946; pityriasis rubra, premycosic erythrodermia, 947; leukæmic erythrodermia, pityriasis rubra pilaris, 948; papular eruptions, lichen planus, 949; lichen nitidus, 953; parapsoriasis, parakeratosis variegata, 955; vesicular eruptions, cheiropompholyx, 956; bullous eruptions, pemphigus, pemphigus acutus malignus, pemphigus vulgaris, 958; pemphigus foliaceus, pemphigus vegetans, epidermolysis bullosa, 960; hyperkeratoses of the skin, callosites and corns, 961; keratosis, keratosis pilaris, keratosis pilaris atrophicans, keratosis follicularis, 962; cornu cutaneum, ichthyosis, 963; atrophic and dystrophic conditions of the skin, sclerodermia, 964; sclerema neonatorum, atrophodermia neuritica, striæ et maculæ atrophicæ, 965; xerodermia pigmentosa, alterations of pigment, 966; lentigo, chloasma uterinum, 967; ochronosis, albinism, vitiligo, 968; acanthosis nigricans, 969; affections of the sweat glands, anomalies of secretion, 970; miliaria, affections of the sebaceous glands, milium, adenoma sebaceum, sebaceous cysts, 971; affections of the hair and hair follicles, alopecia,

PAGE

DISEASES OF THE SKIN (DERMATOSES)—*continued*

972; alopecia symptomatica, 973; calvities, 974; alopecia areata, 976; new growths in the skin, fibroma molluscum, Recklinghausen's disease, cheloid, myoma, neuroma, lymphangeioma, xanthoma, 981; mycosis fungoides, 982.

DISEASES OF THE TROPICS . . . . . 985—1114

Introduction, 985; clinical examination, 986; special therapy, 987; heat stroke and other maladies, 988; food poisoning, and diet deficiencies, 990; tropical macrocytic anæmia, 991; tropical dysfunction of the gastro-intestinal tract, tropical sprue, 992; ***infectious diseases of the tropics—filterable viruses,*** 995; hydrophobia, 996; yellow fever, 998; dengue, 1001; sandfly fever, 1002; climatic bubo, 1003; ***rickettsial diseases,*** 1004; louse typhus, 1005; Rocky Mountain fever, 1007; tick typhus, 1008; Japanese river fever, ***bacterial diseases,*** bacillary dysentery, 1009; cholera, 1013; leprosy, 1016; undulant fever, 1022; tularæmia, 1025; oroya fever, 1026; tropical myositis, 1027; ***mycoses,*** 1028; moniliasis, rhinosporidiosis, maduramycosis, 1028; coccidioides, 1029; ***spirochætal diseases,*** yaws, 1030; goundou, gangosa, 1031; juxta-articular nodes, 1032; louse relapsing fever, 1033; tick relapsing fever, 1034; Weil's disease, 1035; Japanese, seven-day fever, rat-bite fever, 1038; ***protozoal diseases,*** malaria, 1039; blackwater fever, 1046; kala-azar, 1049; oriental sore, American dermal leishmaniasis, 1052; African trypanosomiasis, 1053; South American trypanosomiasis, amœbic dysentery, 1056; amœbic hepatitis, 1059; ciliate dysentery, flagellate diarrhœa, giardiasis, 1063; ***helminthic diseases,*** trematodes, fascioliasis, 1064; paramphistomiasis, 1065; clonorchiasis, paragonimiasis, 1066; vesical schistosomiasis, 1067; intestinal, 1070; Asiatic, 1071; heterophyidiasis, cestodes, Tænia solium, 1072; Tænia saginata, Dipylidium caninum, Diphyllobothrium latum, 1073; Sparganum mansoni, S. proliferum, cysticercosis, 1074; echinococcosis, 1076; hydatid of the liver, 1078; of lung, 1080; of brain, renal, Hymenolepis nana, 1081; nematodes, strongyloidiasis, 1082; filaria bancrofti, 1083; F. perstans, 1084; F. ozzardi, Loa loa, 1085; onchocerciasis, 1086; dracontiasis, 1088; trichiniasis, 1089; œsophagostomiasis, 1090; ancylostomiasis, 1091; ascariasis, 1093; trichuriasis, oxyuriasis, 1094; ***diseases due to larvæ,*** myiasis, 1095; tongue-worms, ***bites and stings,*** 1097; mites, 1098; ticks, spiders, 1099; scorpions, centipedes, biting leeches, 1100; snake bite, 1101; poisonous fishes, 1104; ***tropical skin diseases,*** chigger disease, craw-craw, 1105; veldt sore, tropical ulcer, 1106; pemphigus contagiosus, tinea, 1107; ***tropical diseases of unknown origin,*** ainum, big heel, onyalai, 1109; chiufa, chappa, mossy foot, 1110; ulcerating granuloma, 1111.

INDEX 1115

PLATES

PLATE		FACING PAGE
1.	Radiograms of Bronchiectasis after Lipiodol. (a.) Saccular; (b.) Fusiform (Glove Finger) Types	136
2.	Radiogram showing A. Normal Chest after Lipiodol; B. Carcinoma of the Bronchus	137
3.	Radiograms showing Wedge-shaped Infiltration in Lobar Pneumonia with Gradual Resolution	152
4.	A. Photograph of an Oxygen Tent; B. Radiogram of Broncho-pneumonia in a Child	156
5.	Radiograms of Abscess of Lung in Vertical and Lateral Positions	159
6.	Radiograms showing Advanced Phthisis with Cavitation at the Right Apex; B. Pleural Effusion	168
7.	A. Radiogram showing Phthisis with Cavity at Right Apex. B. Same Patient after Induction of Pneumothorax	170
8.	Radiogram showing Pleural Effusion with Resolution	186
9.	Radiograms showing A. Hydro-pneumothorax; B. Diaphragmatic Hernia	192
10.	Graphic Registration of Cardiac Murmurs	220
11.	Radiograms showing Mitral Stenosis	224
12.	Radiograms showing A. Aortic Regurgitation; B. Pure Pulmonary Stenosis	225
13.	Radiograms showing Attempted Expiration and Inspiration with Breath held	252
14.	(Coloured) Illustration of the Retina in Arteriosclerosis and Parenchymatous Nephritis	303
15.	Radiograms showing A. Saccular Aneurysm of Aorta; B. Hodgkin's Disease	308
16.	Figs. 1, 2, 3.—Radiograms of Normal Teeth	321
	Figs. 4, 5, 6.—Radiograms of Teeth showing Early Pyorrhœa Alveolaris	321
	Figs. 7, 8, 9.—Radiograms of Teeth showing Advanced Pyorrhœa Alveolaris	321
	Figs. 10, 11, 12.—Radiograms of Teeth showing Apical Root Abscesses	321
17.	Radiogram of Œsophagus showing Carcinomatous Stricture	324
18.	A. Radiogram showing Œsophageal Diverticulum	325
	B. Radiogram showing Dilatation of the Œsophagus with Spasm in Heartburn	325
19.	Radiogram showing Dilatation of the Œsophagus with Achalasia of the Cardia.	326
20.	Radiogram showing Normal Œsophagus filled with Barium	326
21.	Radiogram of Elongated Stomach	340
22.	Radiogram of Hypertonic Stomach	340
23.	Radiograms showing A. Diverticulum at Lower End of Œsophagus; B. Gastric Ulcer	346
24–25.	Radiograms of Duodenal Cap with Ulceration	348
26.	Radiogram of Dilated Stomach from Pyloric Stenosis	351
27.	Radiogram of Stomach with Hour-glass Contraction and Ulceration	352
28.	A. Radiogram of Stomach with Carcinoma; B. Leather Bottle Stomach	355
29.	Radiograms showing A. Ulcerative Colitis; B. Large Intestine showing Diverticula in the Descending Colon	370
30.	Radiograms showing Carcinoma of the Transverse Colon	377
31.	Cholecystography. A. Normal Gall-bladder; B. Gall-bladder containing Pigment Gall-stones	403

PLATE		FACING PAGE
32.	A. Radiogram showing Gas which has escaped through a Perforated Peptic Ulcer; B. Cholecystography	407
33.	(Coloured) Illustration of Nucleated Red Cells	423
34.	(Coloured) Illustration of Normal Leucocytes	424
35.	(Coloured) Illustration of Abnormal Blood Cells	425
36.	(Coloured) Illustrations. A. A Patient with Polycythæmia Rubra; B. Reticulocytes; C. Punctate Basophilia	433
37.	Nomogram for calculating Basal Metabolism	460
38.	Progeria	494
39.	Intravenous Pyelography; A. Normal Pelvis; B. Left Renal Tuberculosis	505
40.	Retrograde Pyelography. A. Left Normal; B. Right Hydronephrosis	506
41.	Radiograms of Renal Calculi	550
42.	Radiograms of Hand in Rheumatoid Arthritis (with Normal)	558
43.	Radiograms of Pelvis and Hips. A. Right Hip Joint shows Osteo-arthritis; B. (for comparison), Left Hip Joint shows Tuberculosis	559
44.	Radiograms of the Hands in Gout	564
45.	Radiograms showing Osteitis Deformans affecting the Skull, Humerus, Femur and Pelvis	567
46–49.	Radiograms of the Arms and Legs in Rickets	580
50.	(Coloured) Illustrations of Normal Optic Disc, Papilloedema, Primary and Secondary Optic Atrophy	634
51.	Sections of Spinal Cord showing Degeneration of Fibre Tracts in Complete Transverse Lesion	656
52.	Radiograms after Lipiodol Injection	659
53.	Sections of Spinal Cord in Disseminated Sclerosis	668
54.	Sections of Spinal Cord in Tabes Dorsalis	675
55.	Sections of Spinal Cord showing Conditions found in Motor Neurone Disease, Subacute Combined Degeneration and Friedreich's Ataxia	682
56.	Radiograms of Sella Turcica. A. Enlargement in Acromegaly; B. Flattening by Pressure from above	728
57.	Radiograms of Sella Turcica. A. Normal; B. Small; from a case of Hypopituitarism	728
58.	(Coloured) A. Impetigo Contagiosa; B. Lupus Vulgaris; C. Pemphigus Neonatorum; D. Molluscum Contagiosum	833
59.	(Coloured) A. Scabies; B. Pediculosis Corporis; C. Alopecia Areata; D. Tinea Tonsurans	878
60.	(Coloured) Lupus Erythematosus	901
61.	A. Herpes Zoster; B. Bromide Eruption; C. Premycosic Erythrodermia; D. Prurigo Nodularis; E. Pityriasis Rubra Pilaris; F. Psoriasis of the Nails	922
62.	(Coloured) Pityriasis Rosea	940
63.	(Coloured) A. Psoriasis of Knee; B. Pityriasis Rosea	942
64.	(Coloured) A. Pustular Psoriasis of the Feet; B. Lichen Planus	945
65.	A. & B. Fibroma Molluscum (Von Recklinghausen's Disease); C. Vitiligo	968
66.	(Coloured) Pigments in Blackwater Fever	1047
67.	(Coloured) Illustrations of A. Malarial Parasites; B. Trypanosomes; C. Leishman-Donovan Bodies	053
68.	(Coloured) Illustrations of Various Worms	1066
69.	(Coloured) Cystoscopic Pictures of Vesical Schistosomiasis	1068
70.	Radiograms of Cysticercosis	1075
71.	Radiogram of Porocephalus Infection	1097

THE PRACTICE OF MEDICINE

INTRODUCTION

A THOROUGH knowledge of every disease requires an acquaintance with several separate branches of study, which are as follows :—

Ætiology, the study of its causes in general. *Pathology*, the study of its causes within the body, and the processes resulting therefrom. *Morbid Anatomy*, the alterations in the structures caused by it. *Symptoms*, the indications—subjective on the part of the patient, and objective to the physician (usually called *physical signs*)—by which we arrive at a knowledge of what is wrong. *Diagnosis*, the method of distinguishing from one another the diseases that may have symptoms more or less nearly alike. *Prognosis*, the art of foretelling the course, duration, and termination of any given case. Finally, the *Prevention* of disease (prophylaxis), and the *Treatment* of disease when it occurs, both of which are the chief aims of the study of the science and art of medicine.

Ætiology. The causes of disease are commonly divided into *predisposing* and *exciting*, but no broad line can be drawn between them. A predisposing cause may be in operation for a great length of time without the disease being produced, whereas the exciting cause is usually only of short duration; but conditions which act as predisposing causes at one time may act as exciting causes at another. *Ætiology* strictly covers the whole of the causation of disease, but it is perhaps more often applied to the remoter causes and to those conditions which are constantly associated with a disease, although we are unable to say how they influence its occurrence. The relations to disease of age, sex, climate, hygienic surroundings, food, and preceding illnesses are commonly considered under this heading. On the other hand, changes taking place in the body, immediately preceding or causing the disease, are considered rather as pathological processes than ætiological factors.

Pathology is sometimes used to signify the study of diseased structures, but it is better limited to the study of diseased processes—that is, practically, the influence which the causes of disease have upon the function and structures of the body; while **morbid anatomy** or **pathological anatomy** describes in detail the diseased structures themselves.

Symptomatology is the study of the symptoms of any disease, and associated with this and with its morbid anatomy we have to consider what have been called **complications** and **sequelæ.** Emphasis has with perfect right been recently laid on the study of the early symptoms of disease, so that treatment may be carried out in the earliest stage.

Complications are certain lesions or symptoms which are the result of the original disease, but only occur from time to time, and are not regarded as a necessary part of the disease; thus abscesses are a complication of enteric fever, hæmoptysis a common complication of pulmonary tuberculosis, parotitis a very rare complication of pneumonia. But the term is applied somewhat arbitrarily; for instance, in enteric fever rose spots and diarrhœa are not universally present, and yet they are regarded as part of the disease, and never as complications. We must regard in a different light the case where one disease occurs at the same time as another, but, as far as our own knowledge goes, is quite independent of it; the complication may seem to be purely accidental, yet the

primary disease may have disposed the individual, in some way not hitherto ascertained, towards the acquirement of the second. Two common cases are (1) the complication of any slight or severe local disorder by an infectious disease, such as scarlet fever, caught by contact; (2) the termination of some chronic nervous disease, like hemiplegia or locomotor ataxy, by pneumonia or bronchitis.

A sequela is a symptom or lesion appearing or persisting after the original disease has subsided.

Diagnosis is the recognition of diseases by certain symptoms, physical signs or facts in the history of the cases which, taken together, indicate that the patient is suffering from a particular ailment. By *differential diagnosis* is meant a knowledge, in any given disease, of all the other diseases which most clearly resemble it and the points of difference upon which reliance may be placed to distinguish it.

If two complaints are likely to be confounded together, and one is much more serious than the other, a wrong decision that the less serious is present is dangerous for the patient, since his undiagnosed complaint may progress to a fatal point without proper treatment. On the other hand, a wrong decision that the more serious is present may cause the physician to alarm the patient unnecessarily and ultimately bring discredit upon himself. Especially is it desirable in the case of the commoner, temporary, and more curable complaints to bear in mind the possibility of their being simulated by rarer and more dangerous diseases. The confusion of angina pectoris with various forms of chronic indigestion and of appendicitis with acute indigestion are instances which too often occur. Probability is an important element in diagnosis. In exceptional instances a disease may present a physical sign, symptom, or indication which is not caused by any other known condition. Such a sign or symptom is said to be *pathognomonic* of the disease in question. As a matter of fact, there are very few *pathognomonic symptoms.*

It will have been gathered from the remarks on diseases that by diagnosis we shall always aim at finding out the *primary* lesion; thus we must not be content with calling any pain rheumatism or neuralgia, but we must try to find out whether such pain is caused by pressure on a nerve, by inflammation of a nerve, or by degeneration of nerve tracts. But in many cases the patient suffers from numerous symptoms: pain, cough, sickness, dropsy, albuminuria, and others. As a rule, we should try to see how far all these conditions may be due to one single primary lesion, such as valvular disease of the heart or granular disease of the kidney; but we must not forget that frequently two or more independent lesions co-exist, and produce a complex arrangement of symptoms.

Prognosis. Successful prognosis requires a thorough acquaintance with the natural history of every disease, with the extent to which the disease is influenced by age, sex, and other ætiological factors, and a careful judgment on the variations of the patient from day to day.

The questions that arise in prognosis are such as these: Will the patient recover? Will he recover completely or be left with any organ damaged? Will he ever have the disease again? If it is a fatal disease, how long will he live?

In the early days of a disease the question of recovery can only be answered by a consideration of the percentage mortality as shown by statistics. As the case proceeds the rapidity or severity of the symptoms, the conditions of the circulation, the ability to take food, and the integrity of the nervous system are the points which have most bearing on one's opinion. In practice, prognosis is often of the greatest importance for the physician's credit, and a hasty conclusion which turns out wrong is often remembered against him more than any want of success in treatment.

When in this volume it is stated that the prognosis of any disease is favourable,

this means, not that it is never fatal, but that *most* cases recover ; if any particular symptom or complication renders the prognosis *less* favourable, this means that the percentage mortality of cases with such complication is greater than it was before or without the complication.

Prevention. The *prevention* or *prophylaxis* of disease may be looked at from two points of view : (1) that of the community, and in this connection it is known as the study of *hygiene* or *public health*, and involves all measures by which the community endeavours to ward off all external influences adverse to health ; (2) that of the individual, by which the body itself may be prepared against the operation of the causes of disease, partly by judgment in matters of diet, exercise, clothing, etc., and partly by such special treatment in relation to particular diseases as is effected by the injection of typhoid and plague vaccines in the bacterial infections, and vaccination against small-pox and antirabic inoculations in the filterable virus diseases. For efficient prevention in this sense it is essential to recognise the very beginnings of disease, so that remedies may be applied before the disease becomes established and irremediable structural alterations in organs have taken place. For this purpose the early symptoms exhibited by patients require special study. Prevention of this kind is of growing importance in medicine, and it will be considered in detail in the appropriate places.

Treatment. In this we should aim first at the removal of the cause where this is possible ; if not, we may succeed in neutralising its influence. One or other of these methods may suffice to cure all the symptoms and troubles of the patients ; but though the numbers of specific remedies are steadily increasing with the progress of research we are still in most cases called upon to deal directly with the symptoms, using remedies that have no influence upon the underlying disease. We must, when doing this, never forget that such symptoms hold a position secondary in importance to that of the disease which causes them. Lastly, we must in all cases counteract the tendency to death, which may, indeed, be the natural course of the disease, or may arise rather as an accident from some infrequent complication. As an example we may take phthisis, which is due primarily to the invasion of the lung by the tubercle bacillus. The removal of this, when once it has obtained a footing, cannot be directly effected. Its influence can be neutralised by the best hygienic surroundings, by fresh, bracing air, and by special climates which enable the body to resist the action of the bacillus. In the meanwhile there are numerous symptoms—cough, expectoration, pain, sweating, diarrhœa—which will diminish as the condition of the lung improves, and which can be also controlled by suitable medicines. In addition serious complications may arise, especially hæmoptysis, or spitting of blood, by which life is directly threatened, and such a death may be averted by proper therapeutic means. A short account of the various methods of treatment may be given here.

Rest. In many diseases, *e.g.*, acute infections, rest is the most valuable method of general treatment we possess. The presence of pain is one of its most important indications, as was pointed out by Hilton in his book " Rest and Pain." The subject of rest will be constantly referred to throughout this book.

Diet. Food consists of proteins, fats and carbohydrates, and the proportions of these substances may have to be altered in certain cases. The proportion of carbohydrate to fat is important in diabetes. Again, flesh foods contain purin substances which may be harmful in gout, and strict moderation must be exercised, whereas in sprue, cœliac disease and idiopathic steatorrhœa high protein, low fat, and low carbohydrate diets are indicated. Patients confined to bed require less food than persons taking active exercise ; in febrile states more food will be needed than when the temperature is normal, because the energy output is greater ; at the same time, it must be taken in an easily digestible form, and the latter applies to various gastro-intestinal diseases. The diet must

be arranged so that it contains sufficient of the various *accessory food substances*, or *vitamins*, the presence of which are essential to life.

Artificial Feeding in Infancy. It is not possible to deal with this subject adequately in a general text-book, and the following should be regarded only as a summary.

The food requirements of a normal infant depend on age, weight and individual idiosyncrasies. It is usually best to consider the age and weight first, and later to modify the feeds according to the individual needs, which vary greatly in different infants, according to vigour, temperament and power of digestion of various constituents. The nervous, restless, wakeful child requires more food to support its increased metabolism in order to leave a sufficient margin for proper growth. Frequency of feeding varies with the capacity of the stomach and the rate at which it empties: as far as possible it should be assured that the stomach is empty before the next feed is given: it is impossible to fix an arbitrary rule. Increase in weight must be carefully watched. Usually three-hourly feeding is satisfactory up to the age of three months, after which the interval may be increased to four hours. Many infants thrive on four-hourly feeding in the early months, in which case the longer interval is desirable as being more likely to ensure emptying of the stomach.

From the point of view of growth, protein is the most important constituent of the food, but fat is important, partly on account of the fat-soluble vitamins. Sugar is a valuable means of meeting calorie requirements, but tolerance to both sugar and fat varies greatly in different infants.

In working out a first *trial* feed, it is usually best to consider what the weight of the child should be for its age, taking account of the birth-weight, rather than basing calculations on the actual weight. If the child's weight is very much less than the "forecast" weight, there would be a great risk of intolerance to a sudden increase in food, and it is better to start at a lower level, increasing the intake every few days till a satisfactory rate of growth is obtained, and decreasing if there are any signs of intolerance. Using the "forecast weight" as a basis, the average requirements for the twenty-four hours may be taken as:

Total fluid, in ounces	= weight in pounds	× 3 (in early months).
		× 2 (in later months).
Milk, in ounces	= weight in pounds	× 1·75.
Total calories required	= weight in pounds	× 45.

Whole cow's milk provides approximately 21 calories per ounce. The remainder of the calorie requirement is furnished by sugar. A level teaspoonful of cane sugar supplies about 15 calories; of lactose or dextrimaltose, about 10 calories. It should be noted that rather more than half the calorie value of the milk is provided by the fat, and that if for any reason the fat content is reduced by skimming it will be necessary to increase the amount of other constituents in the feeds, usually by increasing the proportion of milk to water: it is dangerous to use an excess of carbohydrate. If the capacity of the infant's stomach is small it may be necessary to increase the proportion of milk to water: in this case the milk may be rendered more digestible by adding two minims of lactic acid to each ounce of milk: in adding this, the milk must be kept constantly stirred to secure an even emulsion.

It is often possible, on a first examination, to recognise the type of infant who will require considerable modification of the above formula.

When an infant has been seriously underfed, increases must be slow, but sufficiently rapid to allow for the increased demands of growth and to stimulate the powers of digestion.

It is often convenient to use one of the forms of dried milk. In evaporation, approximately $\frac{7}{8}$ of the weight of the milk is lost.

In all cases of artificial feeding it is desirable to give additional quantities of

vitamin C. At the age of three months, a daily allowance of one tablespoonful of orange juice, diluted with an equal quantity of water, may be given between feeds, and the amount gradually increased up to 2 oz. If this is not tolerated, tomato juice forms a good substitute. If the percentage of fat has been decreased, vitamins A and D should be given in concentrated form.

Climate is generally described as "tonic" or "bracing," and on the other hand as "relaxing" or, if this word has unpleasant associations, as "sedative." From the point of view of clear thinking the use of these words might well be discontinued. A "bracing" climate means a climate of marked cooling power. Leonard Hill's observations with his kata-thermometer show that cooling power depends on three factors: temperature, humidity, and the movement of air. Hence a bracing climate must mean one possessing a cool, dry, breezy atmosphere, while a relaxing atmosphere will be hot, moist, and still. British spas, with the possible exception of Bath, belong to the former category, and this is an advantage, because at the end of the cure, which usually lasts three months, the patient can go straight back to his ordinary occupation. British seaside resorts have a wonderful variety of climate. In the South-West they approximate to the French and Italian Riviera, but as there are usually more clouds in the sky the fall in temperature at night is less marked; the days are not so hot and the nights are not so cold. The resorts in the East and North-West are cool, while those in the South-East may be regarded as intermediate.

England possesses no mountain climate, and if such is required patients must go to Switzerland, or farther afield to the High Tatra in the Carpathians. The action of such a climate is due to the reduced pressure of oxygen, which appears to stimulate the production of adrenaline, causing a rise of blood sugar, an increase in the formed elements of the blood which are at first pressed out of the spleen; there is an increase of glutathione, the ferment first prepared *in vitro* by Sir Gowland Hopkins; and certain substances appear in the serum, known as hæmopoietins, which have the property of hastening the regeneration of blood after hæmorrhage. A point of some interest is the rise of serum calcium, which means that the sympathetic becomes less excitable and the thyroid less active. This fact was discovered empirically a number of years ago when an exophthalmic goitre patient, sent from Vienna to the High Tatra, did remarkably well; the mountain climate is now recognized to be of value in this disease, and insured patients are sent to the Tatra. No patient with cardiac insufficiency should be sent to the mountains; but it has long been known that patients with phthisis and surgical tuberculosis do well there. The deficiency of oxygen must clearly be a responsible factor, since among other things this stimulates the production of red cells and counteracts the anæmia.

What is meant by "fresh air" in the treatment of phthisis in this country? "Fresh air" does not mean air with an unusually large amount of oxygen in it, because the percentage of oxygen is much the same in the country as in the town. "Fresh air" treatment of phthisis in this country must mean treatment by cold, since this has been found to increase the metabolism of the resting subject, and patients who live out of doors all the time have better appetites and eat more food to provide fuel for their increased metabolism. The three general factors in treatment that can be supplied by the tuberculosis sanatoria of this country are fresh air with its increased cooling power, rest, and good food. A fourth factor—diminished oxygen supply—is only present in the mountains. *Sunlight*, an antiseptic agent and elaborator of vitamin D in the skin, is a fifth factor suitable for surgical tuberculosis and septic states, but this is not given in phthisis, since it causes hæmoptysis from congestion of the lungs—at least, that is the Swiss experience.

Drugs. No specific drugs are available for the bacterial and filterable virus infections, but a large number are known which cure protozoal and helminthic diseases. Quinine, atebrin and plasmoquine in malaria, emetine in amœbic

dysentery and abscess of the liver, salvarsan in the spirochætal diseases like syphilis, yaws, relapsing fever and rat-bite fever, Bayer 205 and tryparsamide in sleeping sickness, and pentavalent antimony compounds, like neostibosan in kala-azar, may be cited as a few examples. Many of the intestinal helminths can be cured by specific remedies, and trivalent antimony preparations, like tartar emetic and fouadin, are effective in eradicating bilharzia parasites from the portal system of man. The British Pharmacopœia gives the official list of drugs which are required in treatment, but fresh drugs are constantly being introduced, and older drugs not now in the Pharmacopœia may still be of service. Besides the older methods of administration by the mouth and rectum, and through the skin by means of ointments and by medicated baths, drugs are now introduced by hypodermic, intramuscular, intravenous, and intraspinal injection, and also by *ionisation* or *cataphoresis*. In this method ionisable salts, of which one or both of the component elements are efficient drugs, are applied to the skin; and, by means of a galvanic current, one or other of the ions is driven into the tissues, and exerts the desired effect.

Dosage. Full details of adult dosage are given in the Pharmacopœia; but the problem arises as to the correct proportions to be given to children or undersized adults. Again, in carrying out the "sugar tolerance test" or "urea output test," what dose of sugar or urea should be given to a child? Unless there is any idiosyncrasy in the case of children it is best to calculate dosage as proportional to $\frac{2}{3}$ power of the body weight. If a man of 10 stone (140 lb.) requires the full dose, then the following proportional doses have been calculated according to this rule:—

Weight (lb.)	180	160	140	120	100	80	60	55	50	45	40	35
Dose ...	1·18	1·1	1·0	0·9	0·8	0·69	0·57	0·53	0·5	0·47	0·43	0·4

Organo-therapy or *Opotherapy.* As special forms of drugs, which can be given internally or *per rectum*, or by subcutaneous injection, must be mentioned the extracts of various organs of animals (thyroid, suprarenal gland, pituitary body, insulin) which may be made to supply defects in the corresponding organs in the human subject.

Antitoxic and Antibacterial Sera. These are of great value in some infectious bacterial diseases—for instance, in diphtheria. They consist of the serum of an animal which has been rendered immune to the particular disease; and the serum contains anti-bodies which will neutralise the disease in the human patient (*see* p. 14). They are standardised by careful experiments upon animals. They may be injected subcutaneously, or into the muscles, or into the veins, or within the theca of the spinal column.

Bacterial Vaccines. A vaccine is a solution containing up to several million dead bacteria of the same species as those of the disease requiring treatment, and preferably cultivated from material obtained from the patient to be treated. The injection of these bacteria in gradually increasing amounts increases the anti-bodies in the patient's serum, raising the immunity.

Heat. Besides the local application of warmth for purposes of stimulation or counter-irritation, and of heat for its destructive effects (cautery), *radiant heat*, by means of incandescent electric lights or *infra-red* radiation is employed for the local treatment of rheumatic joints and allied conditions.

Diathermy is a more recent method of applying heat locally. The heat is produced by continuously maintained high frequency currents, and in this form it penetrates more deeply into the part, *e.g.* a joint, than any heat, that can be borne, supplied by sources external to the limb.

Finsen Light. This light treatment of lupus and rodent ulcers consists in directing an intense light upon the diseased part for specific periods of time. The light consists of violet and ultra-violet rays, and is produced by an arc-light from which the heat rays are cut off.

Roentgen Rays or X-rays. The powerful effects of these rays are well known, both for good and evil. Constantly playing upon the unprotected skin, as in the case of X-ray operators, they have caused intense and incurable dermatitis, leading on to carcinoma. Death has also been caused by their destructive action on the blood-forming organs, producing *aplastic anæmia*. Used with proper precautions for limited periods, they modify the growth of cells in the body, and have been of value in the treatment of rodent ulcer, carcinoma, Hodgkin's disease, leukæmia, syringomyelia, ringworm, and other affections. In deep X-ray therapy the less penetrating rays are filtered off and the more penetrating rays alone used. Structures lying deep inside the body, *e.g.* the uterus, affected with carcinoma, can be reached by the rays and, by varying the direction from which the rays come, in other words the portal of entry, the skin is saved.

Radium. The rays emanating from this substance have powerful effects on all living tissues and especially on cancer cells.

Electricity. The chief uses of this force have been in the treatment of paralysis and other nervous diseases. Muscles which cannot be stimulated by the will can be made to contract by electric stimulation, so long as their nutrition is normal and they are not the subject of atrophy. This contraction, effected at stated intervals, maintains the circulation of blood and lymph in the muscles, and facilitates the return to health. Such contractions can be effected by the faradic or by interruption of the continuous current. Many painful neuralgic affections are benefited by a continuous current of electricity. Another application of electricity now often used is that of high-frequency currents. These are currents of high potential, perhaps 10,000 volts, alternately positive and negative, and changing their sign about every millionth part of a second. They are consequently too rapid to stimulate sensory nerves or motor nerves or muscles, which can only respond to stimuli of about $\frac{1}{1000}$ second duration; nevertheless they have certain effects upon the tissues, which are claimed to be increased cellular activity, changes in the vascular system, and inhibition, *i.e.* diminished susceptibility of the neuromuscular system to ordinary stimuli.

Massage. By massage is meant the manipulation of the soft tissues of the body and limbs by an operator, aiming at assisting the circulation of the blood and lymph to the part, thus stimulating metabolism which is normally produced in the healthy person by active exercise. By its use adhesions round stiff joints are loosened and relaxation more easily obtained. It is valuable as an introduction to normal activity applied to muscles which, owing to injury or prolonged illness, are weak and wasted. In severe nervous strain and in some nervous disorders it is a means of obtaining relaxation of the whole body, and in others it tends to prevent excessive wasting. It will materially lessen the feeling of fatigue in the convalescent period and enable progressive muscular work to be introduced more quickly. To obtain the quickest result the limbs about to be manipulated should be thoroughly warm and relaxed.

In *effleurage* the surface is stroked in an upward or centripetal direction. The hand of the operator should be relaxed and kept in close contact with the skin of the patient; the movement is performed rhythmically by alternate hands, slowly if lymphatic drainage is required and more or less quickly for the venous return. *Petrissage* includes all forms of muscle manipulation. The hands of the operator are placed firmly in contact with the part under manipulation and the muscles are alternately squeezed and relaxed, care being taken to prevent any slipping of the hand on the skin. *Friction* consists of a small circular movement performed by the thumb or finger on areas, for dispersing local tenderness and adhesion. *Vibrations* are fine intermittent movements performed by the fingers or hand, used chiefly over nerves and in cases of persistent flatulence. *Tapotement* includes various forms of *tapping*, *hacking* and *pounding*, a percussion movement

performed with the ulnar surface of the fingers and hand, the closed hand or the heel of the hand, producing local hyperæmia.

Massage movements are mainly centripetal: the hands of the operator should be soft, dry and relaxed. Oil, ointment or liniments should not be used unless specially ordered by the physician.

Passive Movements. This form of treatment is applied to the joints. They may be classified under two headings: *Manipulation*, in which the joint is passively moved in its full range in every direction by an operator, relaxation of the patient being first obtained with or without an anæsthetic, and *continuous traction*, which is obtained by manually drawing the surfaces of the joints apart for a prolonged period, or by some form of weight extension.

The duration of massage is determined by the area of the body to be treated. A limb in which there is acute traumatic swelling or in which there is a diminished blood supply requires five to fifteen minutes, three times a day. The whole body cannot be properly manipulated under forty-five minutes. Massage should only be ordered in those cases in which active work cannot be introduced, and if ordered should only be continued for the period that activity is not possible.

Swedish remedial exercises, Nauheim treatment, Frankel's precision movements and others are various systems of graduated active movements in which the muscles of the body are forced to work, under the direction of the physician or medical gymnast, with the object of providing a daily amount of exercise either locally or generally. Their value is to work up gradually through controlled muscular contraction the joints, the heart, the muscles, the organs of digestion and excretion; or, as in the case of precision movements, re-establish the function of co-ordination through the nervous system.

This system of work is the only method of restoring the normal function of the muscular system, and massage should only be employed as an introduction to active work. The amount of active work at each treatment should be regulated by the pulse rate charted on a morning and evening chart. In severe debility the pulse may be raised six to 10 beats after each treatment, provided it returns to normal after two minutes' rest; and in more chronic cases may be raised twenty to thirty beats after exercise, returning to normal after three minutes' rest. A gradually rising pulse may result if the active movements are too rapidly progressed.

As an adjunct to massage and active muscle work, in some conditions various forms of baths have their value in that they increase the action of the skin, and thoroughly warm the part under treatment. For a local part, whirlpool baths or paraffin wax baths will be found the most useful. For the whole body, foam baths are most effective, and can be used in the patient's own home.

Natural Waters. The drinking or application, by baths or douches, of natural waters is one of the very earliest treatments in medicine. To avail themselves of this treatment patients must visit the *Spa*, because waters after coming up from the earth often rapidly age, losing their physical and biophysical properties. Mineral springs come either from relatively superficial geological strata, when they are known as *vadose*, or from deep down in the earth through faults in the strata, when they are warm or hot. When the temperature is 93° F. the body neither gains nor loses heat when immersed; this is the point of thermal indifference. Such waters are called *thermal*, or if the temperature is much higher *hyperthermal*. In subthermal or cold baths the temperature is much lower, *e.g.* 68° F., when the loss of heat from the body is increased five-fold by immersion.

Classified according to their mineral content, waters in the first place may be hyper- or hypo-tonic according to the concentration; in the second place, according to their nature, they may be *alkaline*, when they contain metals, such as sodium, potassium, magnesium, calcium or carbonates, borates or silicates; *saline* containing sulphates, chlorides, nitrates or phosphates; *acid* containing hydrochloric or sulphuric acid—these are usually volcanic; *ferruginous* or *chalybeate*, containing

iron; *sulphur* or *sulphuretted* containing sulphides. Then there are qualifying substances present in small amounts in various waters, such as arsenic, carbon dioxide, nitrogen, iodides, bromides and radioactive substances. The treatment by waters, whether mineral or ordinary tap water, is *hydrotherapy* and this science is called *medical hydrology* Finally, mention must be made of the *peloids*, or muds, which are used for external application; these may be alluvial or volcanic, or consist of peat.

Baths and Douches. By these means heat and cold and mechanical effects may be produced, and so the vasomotor system and the circulation may be affected both locally and generally. Immersion baths, like the ordinary household bath, may be combined with under-current douching with water at a different temperature directed to a special part. In "Massage sous l'eau" streams of water are directed on the patient while massage is applied. Alternate hot and cold douches, the hot air bath, vapour or steam bath, foam bath, whirlpool bath, paraffin wax bath, are different methods used at any institution for physical medicine. The mineral waters at the Spa are also commonly employed for baths; special mention may be made of carbon dioxide baths for circulatory disorders, with waters containing the gas coming out of solution; these may be made artificially. Hot baths are valuable for promoting diaphoresis or sweating.

INFECTIOUS DISEASES

NATURE OF INFECTION

Action of Virus in the Recipient. The virus, or causal agent of the disease, enters the system by the respiratory tract (scarlet fever, small-pox), the throat (diphtheria), the alimentary canal (enteric fever, cholera), the genital mucous membranes (gonorrhœa, syphilis), by the bites of insects (malaria, yellow fever, sleeping sickness), or by coarser lesions of the skin (syphilis, hydrophobia).

If the organism is virulent and the individual susceptible, the entry of the virus is followed by a period of *incubation*, during which no changes are manifest, and which varies generally from two or three to twenty-five days, being constant within limits for each particular disease. During the period of incubation the organisms are developing and multiplying, and elaborating the poisonous products to which for the most part the different symptoms and effects of an infectious disease are due. The micro-organisms are sometimes confined to the seat of inoculation or invasion, while their poisons or toxins alone are diffused through the system (*toxæmia*). Another rather old-fashioned term for this condition is *sapræmia*, which however implies that there is a rather extensive area of necrosing tissue, *e.g.* in the uterus, from which toxins are absorbed. Again, the micro-organisms may gain an entrance from some primary focus into the blood stream, remaining there alive, so that living bacteriological cultures may be obtained from samples of blood. Such a condition is called a *septicæmia*. In the last stages of the disease these organisms may be actively multiplying in the blood stream; but ordinarily there is a balance between the rate at which the organisms enter the circulation and the ability of the blood to deal with them by means of its various immunity reactions. In fact, there may be so few organisms present that the bacteriological examination is negative; consequently a negative result does not necessarily exclude a septicæmia.

When a septicæmia is present the micro-organisms may become impacted in different parts of the circulatory system, and thus form fresh foci of disease in the form of metastatic abscesses in different parts of the body. This condition is called *pyæmia*. But metastatic abscesses or pyæmia may arise independently of a septicæmia by minute fragments of clot, etc., containing micro-organisms becoming detached from the primary focus, being washed into the blood stream, and being disseminated throughout the body. The position of the primary infective focus determines to some extent in what organs the abscesses will be situated, owing to the direction of the blood stream, as follows: (1) Where the lesion is situated in the peripheral systemic circulation, *e.g.* in acute osteomyelitis, abscesses or septic infarcts occur primarily in the lung. However, certain minute emboli will succeed in traversing the pulmonary circulation, so that further abscesses may be found in the heart muscle and in other organs. (2) Where the primary focus is in the lung, *e.g.* in chronic bronchiectasis, or in the heart, *e.g.* in infective endocarditis, abscesses or infarcts will occur primarily in the brain and other organs of the systemic circulation. (3) In *portal pyæmia* the primary lesion is some form of ulceration of the parts which drain their blood into the portal vein, *e.g.* an appendix abscess; and secondary abscesses form in the liver, with or without a suppurative pylephlebitis (*see* Pylephlebitis).

Transmission of Infectious Diseases. This is really a branch of Public Health, but a brief notice of it cannot be excluded from a work like this. The infectious diseases having been defined as those in which a virus, or micro-organism, is introduced into the body, it must be here stated that the virus is derived, first, from other human beings ill of the disease directly or indirectly, as in scarlatina, measles, and many others; or, secondly, from animals, as in rabies, anthrax, foot-and-mouth disease; or, thirdly, from the soil or other source independent, as far as is known, of the previous participation of other men or animals in the process, as in tetanus. In many cases, as in scarlet fever and diphtheria, the secretion from the respiratory mucous membrane, in the form of droplets of sputum, is the means by which the poison is conveyed; in others, as in cholera or enteric fever, the fæcal discharges; and in others, as in syphilis and glanders, the pus from sores. Increasing importance attaches to the fact that the organisms may persist in the individual for months or years after convalescence is complete, and thus may be the cause of infection in others. This happens in typhoid fever, diphtheria, cholera, cerebro-spinal fever and poliomyelitis, and the persons conveying the infection are called *carriers*.

In an increasing number of diseases it is becoming evident that the virus or micro-organism is conveyed from the sick to the healthy by means of biting or sucking insects, which either take up the infecting agent in blood from the patient's skin and discharge the virus by puncture into the skin of a new host, or discharge on to the healthy skin fæces which subsequently get rubbed into punctures, or otherwise infect it. Thus malaria, yellow fever, and filariasis are conveyed by mosquitoes; sleeping sickness by tsetse flies; typhus by lice; relapsing fever by lice and a similar disease in Africa by ticks; plague by fleas; while the common house fly may possibly have a share in the transmission of cholera, typhoid, infantile diarrhœa, ophthalmia, and some other diseases. In some cases the virus, or micro-organism, undergoes development in the body of the insect.

Mixed Infections. Some of the more familiar instances of mixed infections are the co-existence in the same person of scarlatina with diphtheria, of scarlet fever with whooping-cough, of scarlet fever with chicken-pox, of diphtheria with measles, of whooping-cough with broncho-pneumonia, of tubercle with lobar pneumonia; but the most important and frequent, perhaps, is the secondary invasion of the body in a great number of infectious diseases by the pus-forming organisms, *Staphylococcus pyogenes aureus* and *Streptococcus pyogenes*, leading to suppurative lesions, septicæmia, and pyæmia as complications or sequels of the original disease.

Prevention of Infection. There are three ways by which the transmission of infectious diseases from one person to another, or others, may be prevented. One is by separating the sick from the healthy (*isolation*). Another is by destroying the virus in the sick person, or in whatever clothes, books, room or furniture he may contaminate, or in whatever excreta may pass from him (*disinfection*). If insects are a factor in the contagion, they should be exterminated if possible or, at least, prevented from contact with the sick. The third method is by so modifying the condition of the possible recipient that he becomes insusceptible to the influence of the virus, even if brought into contact with it (*production of immunity; immunisation*).

Isolation. The patient should be placed in a separate room, if possible on a separate floor of the house, which may be screened off by a sheet wetted with a solution of carbolic acid (1 in 40). Thorough ventilation must be as far as possible maintained, as the dilution of the poison by a constant influx of fresh air is a most important part of the process. All unnecessary furniture, curtains and carpets, clothes, etc., to which contagion may adhere, should be removed from the room. The attendants should be, as far as possible, those who are protected by a previous illness; and it should be remembered that their clothes

may convey the disease as they pass from the sick-room to other parts of the house, unless such over-clothing is changed before coming into contact with others. Only such books, papers, or toys should be allowed in the sick-room as may be afterwards burned. Food utensils should be disinfected by being heated in water to the boil.

Quarantine. The quarantine period for persons who have been in contact with patients suffering from an infectious disease is regarded as two days longer than the maximum incubation period which is stated in the description of each disease ; but in the case of diphtheria all exposed persons are in quarantine until shown by bacteriological examinations not to be carriers.

In the case of the infected person himself isolation from susceptible or unprotected persons should be maintained as long as the patient is believed to be infectious. Every case must be taken on its merits ; thus in mild uncomplicated scarlet fever four weeks will suffice, or if anti-scarlet fever serum has been used as little as three weeks may suffice. The Medical Officers of Schools Association has adopted the following as the shortest times which should elapse between the appearance of the rash or other commencement and the return of the patient to his home or school : In rubella, seven days, provided there is no persistence of nasal or other symptoms ; in measles, not less than ten days from the appearance of the rash, convalescence being satisfactorily established ; in mumps, two weeks, including one clear week from the subsidence of all swelling ; in diphtheria, four weeks, providing all discharges have ceased and no specific bacilli can be found in the nasal or pharyngeal mucus ; in pertussis, two weeks free from onset of spasmodic cough or whoop, or in case of persistent whooping four weeks from this date ; in scarlatina, four weeks, provided convalescence is completed and there is no sore throat, discharge from ear or nose, suppurating gland, or eczematous patch, but there should be two weeks' extra convalescence before return to school. In small-pox and varicella, all scabs should have fallen off, and all sores should be healed, particular attention being paid to the scalp.

Disinfection. *Disinfection of the Excreta.* Fæces or urine, *e.g.* in enteric fever, should be covered with lysol (1 in 50), and allowed to stand for at least one hour before being emptied down a W.C. Sputum should be treated similarly, or it may be burnt or boiled.

Disinfection of the Clothing. Linen may be disinfected by soaking in 1 in 50 solution of lysol for one hour ; it may then be wrung out and sent to the laundry. If stained with albuminous matter it should be soaked in water before being put into lysol. Many local authorities remove clothing and bedding, etc., and return it after disinfection by steam ; this is the only reliable method for bedding and clothes, etc. Woollen clothes must be exposed to a dry heat of 180° or 200°, and this is best done in special ovens constructed for the purpose, now in possession of the local sanitary authorities.

Disinfection of the Patient. During the illness it is important to prevent discharges from the patient drying, and so being spread about as dust. All secretions, etc., are wiped away with moist swabs, which are put in some antiseptic solution. The mattress and pillow are protected by mackintosh or jaconette. After the patient has recovered, and before he mixes with his friends, he should have several warm baths and be rubbed with carbolic soap.

Disinfection of the Room. After the patient has left the room in which he has been ill it requires to be thoroughly disinfected before it is occupied by others. In most cases prolonged ventilation, with the scrubbing of the floor with soap and water, is sufficient. Articles that will not stand boiling may be often disinfected sufficiently by exposure to fresh air and sunlight. Where a gaseous disinfectant is required moist *formalin* vapour or *sulphurous acid gas* may be used.

In using formalin, a special apparatus (the Alformant lamp or Lingner's glycoformal apparatus) is required ; the room must be securely sealed and exposed to the vapour for at least four hours.

Sulphurous acid gas is obtained by burning sulphur. Three pounds of sulphur should be used for every 1,000 cubic feet of space in the room; it is placed in one or more earthenware vessels or pipkins, and each should rest on two or three bricks in a large pan of water. The chinks of the windows should be pasted up with slips of brown paper; the sulphur should be set alight, and the door should be closed and pasted up in the same way as the windows. After twenty-four hours the room may be entered, and the windows should be thrown wide open. Sulphur has the disadvantage of tarnishing metal work, and injuring pianos, sewing machines, etc., and these should be removed before the fumigation. After gaseous disinfection the wall paper should be stripped off and burned, the floor and woodwork thoroughly scrubbed with soap and water.

Notification of Infectious Diseases. The diseases specified for notification in the Infectious Disease (Notification) Act, 1889, are small-pox, cholera, diphtheria, membranous croup, erysipelas, scarlatina or scarlet fever, typhus, typhoid, enteric, relapsing, continued or puerperal fevers. The diseases generally notifiable under regulations of the Local Government Board and Ministry of Health are plague, cerebro-spinal fever, acute poliomyelitis, acute encephalitis lethargica, acute polioencephalitis, tuberculosis, ophthalmia neonatorum, dysentery, malaria (but not if induced for therapeutic reasons, unless patient is liable to relapse after discharge from hospital), acute primary pneumonia, acute influenzal pneumonia, and puerperal pyrexia. The following diseases are notifiable in particular districts either under (*a*) orders made by local authorities extending the Infectious Disease (Notification) Act, 1889, to the disease; (*b*) local Acts; or (*c*) special regulations made by the Minister: anthrax, glanders and hydrophobia, chicken-pox, whooping-cough, epidemic or summer diarrhœa of infants or zymotic enteritis, measles and German measles, pemphigus neonatorum, acute rheumatism in children under sixteen.

Immunity. Persons who are insusceptible to a particular disease are said to be immune.

Acquired immunity is that which is imparted in one or more ways to individuals previously susceptible. The most common cause of immunity towards an infectious disease is the fact that the individual has already had the disease. There are relatively few exceptions to the rule that scarlet fever, small-pox, chicken-pox, measles, and other such illnesses do not occur a second time in the same patient.

In contradistinction to this accidentally acquired immunity is *artificial immunity*, or the immunity intentionally or purposely acquired by the inoculation of the individual with some substance related to the virus or micro-organism which causes the disease. Artificial immunity may be *active* or *passive*.

In *active immunity* the body cells or fluids are themselves stimulated by the inoculation to the production of substances which will neutralise the injecting agent or its toxins. The substance injected may be the micro-organisms in *living culture*, weakened in virulence or *attenuated*; or it may be the same micro-organisms in their full virulence, but in very small amount; or it may be the dead organisms; or it may be the bacterial products or toxins of the disease without the organisms.

In *passive* or *indirect immunity* the neutralising, and therefore protecting, substance is not provided by the body cells or fluids, but is supplied from without. In diphtheria, for example, a susceptible animal, for instance the horse, is gradually rendered immune by successive injections of increasing quantities of the culture fluid of the diphtheria bacillus, which contains the toxins but not the organism itself. When the animal is at length completely insusceptible, its blood serum is found to have the power of neutralising the influence of diphtheria cultures inoculated into animals; and hence this serum contains a substance (*anti-toxin*) which antagonises the toxin of the diphtheria bacillus. The serum is standardised by experiment upon animals. The unit adopted by Ehrlich is the

amount which, when mixed with a hundred times the fatal dose of toxin, protects a guinea-pig of 250 grammes weight from death within four days.

If on the other hand the animal has been rendered immune by injections of certain bacteria, it is *antibacterial* or *antimicrobic*. In either case the effect of the injection has been to produce *anti-substances* in the horse's serum which operate in the blood of the animal (man) to be protected ; and the materials injected for the purpose of modifying the serum are therefore called *antigens*. *Antitoxic sera* have been employed as cures ; that is, the serum of immunised animals has been injected in order to neutralise the toxins of organisms already in the body, and causing symptoms (*serum therapeutics*), as, for instance, in diphtheria, tetanus and pneumonia. Specific antivenenes against venomous snakes are prepared by immunising horses with the venom, and when given intravenously often save life. The viperine antivenenes are also injected locally in the vicinity of the bite.

An important factor in protection from bacterial invasion is the process known as *phagocytosis*, or the destruction of the bacteria by the leucocytes and other cells of the body. The chief *phagocytes* are the monocytes and polymorphonuclear leucocytes, endothelial cells, and some tissue cells ; they are attracted to the bacilli, and this attraction is called *chemiotaxis*. Polymorphonuclear leucocytes and eosinophils are classed as *microphages* ; monocytes, endothelial cells, connective tissue cells, and other large cells are classed as *macrophages*. The former are more powerful in dealing with the bacteria of acute disease, the latter with those of chronic infections.

Anti-bodies. It has been shown that the entrance into the body of toxins, whether contained in the bacteria (*endotoxins*) or produced from bacteria (*exotoxins*), will cause the formation of *antitoxins*. This is only one instance of a large group of similar occurrences, for the injection not only of bacteria and toxins, but of cells, blood corpuscles, ferments, and other bodies, will cause the formation of *anti-bodies* or *anti-substances*—that is, of substances which act adversely to, and destroy, the bacteria, cells, and other substances which have been injected. The anti-bodies which result from infection are formed in the spleen, lymph glands, and bone marrow, by leucocytes or by endothelial cells, or by both.

Agglutinins form another group of anti-substances the development of which is stimulated by bacterial infection, or even by injection of the red corpuscles of another animal (*hæmagglutinins*). If in certain diseases (enteric fever, Mediterranean fever, dysentery, cholera) the blood serum of a patient or convalescent is mixed with cultures of the organism of the same disease, in a short time the bacilli are seen under the microscope to lose all active movements, and to become densely aggregated together (*agglutination*, or *clumping*). The same effect may be obvious to the naked eye if the serum and a culture fluid be mixed in a test-tube, when after a time precipitation of the bacilli takes place, leaving the upper part of the fluid clear (*sedimentation*). These facts form the basis of the diagnostic method known as *Widal's test* (*see* Enteric Fever). The action of agglutinins is not absolutely specific. Thus the typhoid agglutinin will clump not only the *Bacillus typhosus*, but also the paratyphoid bacilli and the *Bacillus coli*. The results vary with the time employed and with the extent of dilution of the serum. Agglutinins may also be obtained artificially, for the blood of an animal inoculated with sublethal doses of a given bacillus will acquire *agglutinative* properties towards the bacillus which has been injected (Bordet-Durham reaction).

Precipitins are similar substances, developed in the serum of animals which have been inoculated with bacterial culture fluids, albumose, milk, etc. The serum containing them precipitates the corresponding culture fluid, or a solution of the corresponding organic substance which has been used for inoculation.

The actions of *anti-bodies* in regard to bacteria, blood corpuscles, leucocytes, kidney cells, and other animal cells are known as *bacteriolysis*, *hæmolysis*, or *cytolysis*. They are for the most part specific ; that is, if certain bacteria are inoculated into an animal the serum subsequently has a destructive

effect on the same kind of bacteria only; if rabbit's blood corpuscles are injected into a guinea-pig, the guinea-pig's serum will afterwards dissolve (or lake) rabbit's blood outside the body; if liver cells are inoculated, the serum will dissolve liver cells, and so on. These different forms of cytolysis and hæmolysis are dependent not only upon the anti-body produced in the process (also known as *immune body*), but they also require the assistance of an enzyme which exists normally in the serum, and has been called the *complement*. Its presence is shown by the fact that the blood-dissolving power of a hæmolytic guinea-pig's serum may be neutralised by a temperature of 55° to 60° C., which destroys the complement; but it can be restored by the addition of serum from a healthy guinea-pig. The complement is probably a product of the leucocyte, and is identical with the *cytase* of Metchnikoff and the *alexine* of Buchner.

The facts connected with hæmolysis and the action of the complement are utilised in some important diagnostic methods (*see* Syphilis).

Another element in the protective power of the blood is the existence of *opsonins*, bodies which act on the bacteria so that they are more readily digested by the leucocytes (*opsono*, I cater for, or prepare food). The opsonic power of the serum is measured by the number of bacilli which the phagocytic leucocytes can take up (Wright and Douglas).

Anaphylaxis. In close relation to immunity and the operation of toxins are the phenomena known under the name of *anaphylaxis*, or *supersensitiveness*. This was discovered by Richet in 1902. He had injected a dog with a small dose of a poisonous protein from a sea-anemone, with the production of evanescent symptoms. Some weeks later he injected a second dose, expecting to find that some degree of immunity had been established, but instead there was a violent intoxication, and the dog succumbed. The name "anaphylaxis" means the opposite of immunity or "phylaxis." The explanation is as follows: Any foreign protein (antigen) injected into an animal causes the production of anti-bodies, which have the nature of *precipitins*. While these remain in the blood they produce immunity by precipitating further doses of the antigen. But after a time they largely disappear from the blood and enter the tissues. At this stage there will not be enough anti-body in the blood to precipitate the antigen, if injected, and so the latter will invade the tissues; but here the meeting of the two produces a violent reaction, viz. anaphylactic shock (**1**). This is proved by making an animal anaphylactic to horse serum, removing its uterus, washing it carefully free from blood and treating it with horse serum. A maximal contraction is obtained; but the uterus does not contract if other sera are used instead of horse serum. The reaction is thus specific. From what has been said it follows that though the animal shortly after an injection of antigen is not anaphylactic, its blood as soon as it contains anti-bodies is potentially anaphylactic, and if this blood is injected into a second animal the latter becomes passively anaphylactic or passively sensitised fifteen to eighteen hours later when the injected anti-body reaches the tissue cells. Further, it has been shown that the anti-body disappears from the blood *pari passu* as the animal becomes passively anaphylactic. Again, an animal may be treated with successive doses of antigen at frequent short intervals, so that the blood becomes crowded with anti-bodies and a high degree of active immunity is produced. Such an animal will not suffer from anaphylactic shock if a fresh dose of antigen is administered because there are sufficient anti-bodies in the blood to neutralise the antigen, although it may be proved that the tissues themselves also contain anti-bodies. It is this method that is used when a patient with hay fever is treated with small but gradually increasing doses of pollen, so that when subject to a large dose in the hay fever season no attack follows. There is another method of arresting anaphylaxis when it is once established. It is to give the animal a non-fatal anaphylactic shock which automatically gets rid of the anti-bodies from the

tissues, so that a refractory period of some duration follows before the anti-bodies become again stored in the tissues. This refractory state has been called anti-anaphylaxis.

Anaphylactic shock is always attended by more or less collapse of the animal, with fall of body temperature: but the main symptoms vary in different animals. Thus in the guinea-pig violent respiratory efforts are seen, and the smooth muscles of the bronchioles are found to be in extreme contraction. In the rabbit respirations are increased and death is due to right-sided heart failure, the result of increased resistance in the pulmonary circuit due to constriction of the pulmonary arterioles. In the dog the liver becomes greatly engorged. It is of interest to observe that there is a very great similarity between these reactions and those due to poisoning these animals by histamine. This suggests that it is the sudden breakdown of protein molecules with liberation of toxic amino-acids that is directly responsible for anaphylactic shock, a breakdown which is caused by the reaction of antigen and anti-body in the cells. The importance of anaphylaxis in relation to the clinical group of allergic diseases is dealt with on p. 138.

When an immunised serum is used for the treatment of diphtheria or other disease the patient sometimes (in about 7 per cent. of the cases) suffers from toxic symptoms, which develop in from seven to twelve days, and are due to the serum injected, and not to the anti-bodies in it. They consist of urticarial swelling at the site of injection, with swelling of the associated lymphatic glands; spread of the eruption—urticarial, circinate, morbilliform or scarlatiniform—to the rest of the body; glandular swelling in other parts; œdema of the face, body or glottis; pains in the joints; slight pyrexia; and occasionally albuminuria, jaundice, diarrhœa or bronchitis. Leucopenia of the polymorphonuclear cells also occurs following a leucocytosis in the stage of incubation. This is known as "serum disease." The symptoms pass off in a day or two. It has been suggested that serum disease is a true anaphylactic phenomenon, the antigen being present in sufficient amount not only to produce anti-bodies which enter the cells, but to enter the cells itself, with resulting anaphylactic shock.

Symptoms similar to those of serum disease are still more likely to occur after a second injection of serum, and are then certainly anaphylactic. The anaphylaxis requires from six to twelve days for its development; hence a second injection before the period of six days usually produces no result. If the interval between the two injections is from twelve days to six or eight weeks (sometimes six months), two types of reaction may occur: (1) the *immediate reaction*, in which symptoms occur *shortly after* the second injection or within twenty-four hours, and pass off quickly, the general symptoms in twenty-four hours, the local in two or three days. These symptoms are œdema at the site of injection, pyrexia, swelling of glands, urticaria, œdema of the face and leucopenia. Occasionally serious symptoms (so-called *anaphylactic shock*) may occur within half an hour of the injection. The patient complains of difficulty in breathing, the chest becomes expanded and rigid, the face becomes congested, and the mucous membranes are cyanosed. Relief comes in from fifteen to thirty minutes. Patients have died in the attack. (2) The *accelerated* reaction, which comes on four to eight days after the second injection. It is called *accelerated* because it comes on sooner than the symptoms which follow a *single* injection. The symptoms are similar to those which occur after a single large dose (serum disease), but are generally more acute, passing off in twelve to eighteen hours.

The danger of the occurrence of anaphylactic shock should not prevent the administration of serum if it is indicated on therapeutic grounds. It is impossible to tell if a patient has become sensitised by a previous dose of serum; but if it is thought that such may be the case, he must be *desensitised* if the second injection is made. The best plan is to inject ½ or 1 c.c. of the serum five or six hours before the chief injection is to be made. If greater rapidity is desirable,

such a preliminary injection may be followed in five or ten minutes by a rather larger one, and so on at similar intervals with increasing doses until the whole has been given. The treatment of anaphylactic shock consists in intravenous or intramuscular injections of pituitary extract, atropine or adrenin, while pure oxygen is also administered in a rapid stream through a mask or funnel held as close as possible to the patient's face. Chloral hydrate may also be given.

The Prausnitz-Küstner reaction depends on a local passive sensitisation. The serum of an egg-sensitive person, for example, is injected intradermally into a normal person. Then if the normal person eats an egg a wheal appears at the site of injection, or this occurs if a dilute solution of egg is injected at the site.

PYREXIA

The terms *fever* and *pyrexia* are not always used in the same sense, pyrexia being sometimes limited to the mere fact that the body temperature is elevated, while by fever is understood the rise of temperature together with all the other bodily disturbances which usually accompany it.

Registration of Temperature. The temperature of the body is taken for ordinary clinical purposes by means of the clinical mercurial thermometer, which is a "maximum" thermometer. The bulb of the instrument may be placed in the axilla, the groin, the mouth, or the rectum.

In the two former situations it is necessary to see that there is complete contact of the skin with the bulb, and it must remain there sufficiently long for the surface of the skin to attain the temperature of the body generally; from one to three or five minutes suffice, according to the sensitiveness of the thermometer. In the mouth the bulb should be placed under the tongue, and the stem must be grasped by the lips. When the rectal temperature is taken, the bulb is introduced for $1\frac{1}{2}$ inches. The result can be depended on, but it is obviously a method that is not always convenient.

Range of Temperature. In health, with the subject at rest in bed, the *mouth* temperature varies from about 97° F. in the early morning up to 98·4° F. in the middle of the afternoon. The *rectal* temperature varies between about 98° and 99·5° F. under the same conditions. Muscular exercise may raise the rectal temperature by 2° F., while the mouth temperature remains the same or actually becomes lower. This is because the sweating and increased respiration tend to cool the mouth. The rectal temperature, on the other hand, approximates more closely to the internal temperature of the body. The temperature of the urine as discharged from the meatus is always slightly above the rectal temperature. The temperature of the axilla is about the same as that of the mouth, being somewhere intermediate between the skin and body temperature.

In a pyrexial disease the temperature ranges from 93·3° (35·5° C.), or even lower, to 110° or 111° (43·8° C.). Temperatures of 116° and 122° have been recorded, but considerable doubt attaches to their genuineness. The temperature is usually lower in the morning and higher in the evening; the lowest point is commonly reached about midnight or 2 A.M., and the highest from 4 to 6 P.M. It may be *continuous*, *remittent*, or *intermittent* as shown in Fig. 1. Occasionally the reverse obtains: the temperature is highest in the morning, lowest in the evening—*typus inversus*. The pulse and respiration rise and fall with the temperature, and the general discomfort of the patient varies in the same manner.

Pathology. The maintenance of the temperature of the body at its normal standard is dependent upon two factors, *Heat production* or *Thermogenesis* and *Heat loss* or *Thermolysis*. In fever there is increased heat production; this shows itself in the fact that the respiratory exchange (intake of O_2 and output of CO_2) is increased. During a malarial rigor the heat production has been found to

increase by 200 per cent., while the heat loss remains the same. During this time, about an hour perhaps, the body temperature is rising. When the high temperature is established the heat production falls to about 80 per cent. above normal, while the heat loss increases to cause a balance. In other fevers, unaccompanied by rigor, during the rise of temperature, both the heat production and heat loss rise step by step, the former being, of course, greater than the latter. When a high temperature is established, the heat production depends on the temperature and is about the same for all fevers, increasing by 7·2 per cent. for each degree F. Curiously enough, the amount of the rise is about the same as that of chemical reactions *in vitro* (**4**). The regulation of temperature is a probable function of the central nervous system as shown by the excessively high or low temperatures that may occur in some diseases of the brain and spinal cord, but it is also a function of the thyroid-adrenal apparatus. Heat production takes place in the organs of the body, particularly the skeletal muscles (*see* Diseases of Thyroid and of Suprarenal Capsules). Heat loss occurs to the extent of 87 per cent. from the skin by radiation, convection, conduction, and evaporation, to the extent of about 10 per cent. from the lungs, and to the extent of about 2 per cent. from the urine and fæces. The nerve apparatus concerned is chiefly the vasomotor system, by which the circulation through the skin is affected. If the

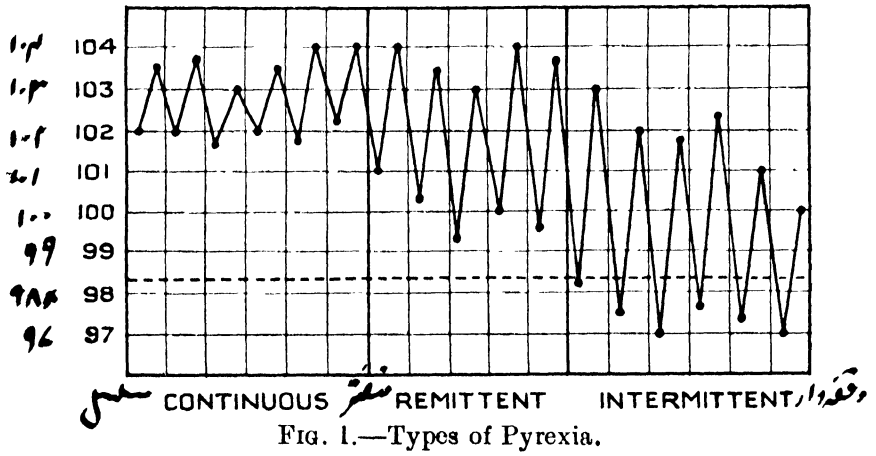


FIG. 1.—Types of Pyrexia.

skin becomes hot, the vessels dilate, so that the warm blood comes to the surface of the body. Sweating enormously increases the heat loss owing to the evaporation that occurs. With high fever respiration is quickened, and the loss of heat from the pulmonary surface is proportionately increased. A common result of pyrexia is a wastage of the body tissues, with increased nitrogen excretion in the urine. This may be partly due to the poisonous action of toxins on the body cells ; but the nitrogen loss can be largely prevented by administering sufficient amounts of non-nitrogenous foods, especially carbohydrates. The body can then utilise these and so spare its own proteins. A high body temperature artificially produced in a normal subject does not cause a breakdown of body proteins if there are sufficient non-nitrogenous foodstuffs available (**5**).

Morbid Anatomy. Certain anatomical changes, probably chiefly due to bacterial infection, are common to nearly all deaths in high fever. The red corpuscles are diminished, and leucocytosis is common. Small petechiæ or hæmorrhages are found under the serous membranes of the pleura and pericardium. The solid organs—liver, spleen, and kidneys—are large and soft, and the kidneys and liver show, under the microscope, cloudy swelling with some granular change or fatty degeneration in their secreting cells. In hyperpyrexia the cells of the central nervous system stain diffusely, and Nissl's granules are absent. The lipoids in the cortex of the suprarenals are discharged.

The muscles may be soft and friable, or may show the degeneration which was first described by Zenker, and is now regarded as a coagulative necrosis. In this condition the muscular fibres are converted into a homogeneous, colourless, waxy-looking material, forming cylinders, which break up into fragments, and finally crumble into a granular detritus; it is sometimes accompanied by hæmorrhage. This change is most common in the abductors of the thighs, in the recti abdominis, in the diaphragm, and in the muscles of the tongue.

Symptoms. Pyrexia or fever is accompanied by many other disturbances besides elevation of temperature. These are in part a direct result of the high temperature; but in all cases of its production by disease toxins are circulating in the body, and they are probably the cause of certain disturbances.

Skin. It is hot to the touch, sometimes intensely so, and generally dry, but it may be moist, usually when the temperature is falling. In some diseases profuse sweats may occur, which sometimes perceptibly, sometimes scarcely at all, reduce the temperature. Such perspirations may cause an eruption of sudamina or miliaria. The colour of the skin over the body is generally normal, unless there are eruptions, such as miliaria, or the specific rashes of scarlatina, measles, typhus, and others. But the face is often flushed especially at the commencement of a fever; often the cheeks and lips are flushed, and the face is elsewhere pale; later on, with a failing circulation, the face becomes deeply congested or livid, and the extremities show the same change. The petechiæ and subcutaneous hæmorrhages which occur in the most malignant forms of infectious disorder (small-pox, typhus, measles, scarlatina) result, no doubt, from the action of virulent toxins upon the capillary walls.

Alimentary System. The tongue becomes furred; generally at first the fur is white, and the tongue is still moist; then the tongue becomes dry: the fur peels from the edges or tip, and shows the bright red tongue beneath. Later on the tongue becomes very dry, stiff, hard, dirty brown in colour, fissured on the surface, and caked with dried remains of saliva, food, and sometimes blood mixed with epithelium, which are allowed to accumulate in the passive state of the organs of mastication. In this stage also the gums are covered with a similar collection, which is called *sordes*. Loss of appetite, or anorexia, is one of the first signs of fever; sometimes sickness is present, and in all cases digestion is feeble. The bowels are usually constipated. The spleen is often slightly, in certain diseases very much, enlarged and tender.

Circulation. The heart's action is quickened, at first excited, then feebler. The pulse ranges from eighty to 120 or more. It is at first full, bounding and firm; it soon becomes softer and dicrotic. In later stages, as the heart becomes more feeble, it is quick, very small, very compressible, running or flickering.

Respiration. This is quickened in proportion to the pulse and the rise of temperature; it may rise to thirty or forty in the minute. When the illness has lasted some time, the bases of the lungs become congested (hypostatic congestion).

Kidneys. In consequence of the loss of aqueous vapour through the skin and lungs the urine in fever is scanty; and, as a direct result of this, it is high-coloured and deposits a brick-red sediment of urates on cooling. In severe febrile illnesses there may be a small quantity of albumin.

Nervous System. Headache is common at the commencement of pyrexia; there is also a heavy feeling, dulness, or disinclination to think or make any mental effort; after a time the patient not only does not wish to, but cannot, exert the intellect; he becomes drowsy, and when he drops off to sleep, begins to talk. Later on he is delirious without really sleeping, and the delirium may be muttering, and is occasionally maniacal, the patient getting out of bed, struggling with his nurses or attendants, or jumping out of the window. In the last stages there is profound unconsciousness or coma. In the earlier stage of coma the patient frequently picks with his fingers at the bedclothes, or catches

at imaginary objects in the air in front of him. The disturbance of the muscular system shows itself in general bodily weakness, tremor of tongue or limbs when they are moved, and twitching of the muscles (*subsultus tendinum*), while the relaxation of the sphincter ani allows the uncontrolled passage (incontinence) of fæces, and the diminished visceral sensations lead to retention of urine and dangerous distension of the bladder.

Course of Pyrexia. In many cases of fever a very definite course may be recognised. The rise of temperature at the beginning may be entirely unnoticed; but often there is a sensation of cold—it may be a mere chilly feeling, or he shivers, and finally he may have a definite *rigor*. This is an attack of shivering, in which the patient trembles all over, his teeth chatter, he feels intensely cold, his face is pinched, and the nose, ears and finger tips are livid. But though the surface is cold, the internal parts are hot, and the thermometer will show that the temperature is constantly rising from the first. The rigor may last from a few minutes to half an hour, an hour, or more. In young children rigors do not generally occur, but their place is sometimes taken by a convulsion. The second stage of the fever is the *fastigium*, in which the skin is hot and the various phenomena already recorded are present. The third stage is that of *defervescence* or decline, which occurs either by *crisis* or *lysis*. In *crisis* there is a rapid fall of temperature to the normal within twelve to thirty-six hours; it is sometimes accompanied by profuse sweating, sometimes by diarrhœa (critical sweat or diarrhœa). In *lysis* the temperature falls more slowly, taking three or four days to reach normal. For some days after a pyrexia the temperature may be unusually low (subnormal), *e.g.* 97° or 96° in the morning, and from this time the period of *convalescence* commences. Rigor, fastigium, and crisis occur typically in some forms of malaria, and may then all be completed within a period of six to twelve hours.

Prolonged Pyrexia. While we recognise that the duration of a pyrexia is determined mostly by the infection with which it is associated, and may therefore be from a few hours to several months, it may be useful here to mention the diseases which are most commonly found to be the causes of a pyrexia prolonged for several weeks or months. They are the following: typhoid and paratyphoid fevers, undulant fever, malarial fevers,, kala-azar, trypanosomiasis, amœbic abscess of the liver, tuberculosis, septicæmia, pyelonephritis, malignant endocarditis, pernicious anæmia, leukæmia. Among less common conditions are syphilis, cirrhosis of the liver, Hodgkin's disease and malignant growths.

Subnormal Temperatures. The subject of abnormally low temperatures cannot properly be separated from the consideration of pyrexia, and the following list of the causes of subnormal temperatures may be found useful: (1) Direct withdrawal of heat from the body, as in case of exposure of unconscious or drunken persons in very cold atmospheres, or of immersion in very cold water. (2) Loss of great quantities of fluid from the body, as in severe diarrhœa, cholera, enteritis, or profuse hæmorrhage. (3) Conditions of cachexia and inanition, such as carcinoma of the various parts of the alimentary canal, severe diabetes, pernicious anæmia, convalescence from febrile affections, and many chronic mental diseases. (4) Various diseases of the central nervous system, the onset of cerebral hæmorrhage and embolism, some cases of cerebral tumour, and general paralysis of the insane. (5) The shock that may follow intestinal strangulation, perforations of the intestine, and surgical operations. (6) Extensive skin affections, such as universal eczema, and large burns. (7) Poisoning by phosphorus, atropine, morphine, carbolic acid, and alcohol; uræmia and diabetic coma.

General Treatment of Diseases attended with Pyrexia. The treatment will vary with the cause, and the length of the fever. The following applies particularly to a long case. The patient should be at absolute rest in bed, in a thoroughly ventilated, plainly furnished apartment, from which all hangings,

mirrors, striking pictures, or other objects likely to excite him in the event of his becoming delirious have been removed. The bed pan and urine bottle should be used so as to avoid exertion. He should be watched day and night, preferably by trained nurses, and should be kept scrupulously clean by sponging with tepid water daily. He should also be kept cool, the amount of clothes being lessened if the fever is very high. A distinct lowering of temperature may be sometimes effected in this way, a point to be remembered all the more as the tendency of the patient's friends is to heap clothes upon him to prevent his "catching cold." The extremities, however, must be carefully watched, and specially covered or warmed if necessary.

At the present day there is not the same tendency as previously to restrict the amount of food allowed the patient. Pyrexia is associated with increased metabolism, so that 2,000 calories or more may be allowed an adult if the pyrexia is long continued. It is essential that the diet should be easily digested, and it should be to the liking of the patient. It should be given in rather small amounts at frequent intervals, six to eight times in the day. Milk (2 or 3 pints in the day) will form an important element in the diet, and lactose, sugar or extract of malt may be added, so as to increase the calorie value. In cases where milk disagrees, or is felt to load the stomach, or is rejected, it may be citrated (sod. cit. gr. ii to 1 oz.), mixed with half its bulk, or an equal quantity, of barley water or soda water; or it may be peptonised or predigested by warming for a little time with liquor pancreaticus. Plenty of fluid should be taken—water, lemonade, weak tea, barley water, also toast water, etc., and to many of these sugar may be added. Arrowroot, cornflour, blanc-mange, custards, junkets, milk puddings, mashed potatoes and other vegetables, bread and butter, milk chocolate, eggs raw or lightly scrambled, may be allowed, and fish and minced chicken if the patient can tolerate them. Fruit, fresh and stewed, *e.g.* apples, grapes, plums, are often much appreciated; but pips, skins and excessive fibre should be avoided; this can be done in the case of oranges, raspberries, currants, etc., by giving the fruit juice. It must be remembered that beef tea, mutton broth, chicken broth, and veal broth, although they may act excellently in stimulating the appetite, have practically no value as foods.

Frequent attention to the mouth is necessary, since the accumulation therein of secretions and sordes is likely to be followed by parotitis and other complications. The mouth should be washed out after each feeding, or more frequently, according to the amount of the secretions, with an antiseptic solution, such as a solution of thymol in water or 2 per cent. boric acid.

When the intensity of the toxæmia reaches a certain point, and the patient's organic sensations are dulled, the bladder should be carefully watched, to provide against retention of urine. Fulness and dulness on percussion above the pubes are the signs of a full bladder, and the mere statement of the attendants that the patient is passing his urine must not be accepted as a proof that no urine is being retained. The frequent involuntary discharge of small quantities of urine is, indeed, the result of the bladder being already distended; and even the discharge of larger quantities at the request of the nurse may still leave a pint or more in the bladder, which will be revealed on manual examination. The catheter must be kept in place as long as the disability persists. Care must be taken to prevent bed-sores.

In some cases of pyrexia the temperature has been directly dealt with by methods known as *antipyretic*. It must be distinctly understood that such treatment will not lessen the duration of the illness; that in many illnesses the temperature will of itself fall in a few hours, that is, in the early morning; that in temperate climates there is very rarely any danger that it will rise to a height which can be directly fatal; and that any considerable lowering of the temperature by artificial means falsifies to a certain extent the information which the temperature gives to the physician as to the course of the disease. But most

important of all, pyrexia is to be looked upon as a defensive mechanism on the part of the body against the infecting micro-organisms, and hence it should not be interfered with without careful consideration. However, it is possible to have too much of a good thing, and in very long continued fever, such as typhoid, the pyrexia may eventually act deleteriously on nerve cells and other tissues, so that the application of external cold in the form of baths not only often increases the comfort of the patient during the time that each successive dose or application is in operation, but diminishes the headache, delirium, or stupor and improves the pulse. It is claimed that the mortality of typhoid has been improved by 5 or 6 per cent. by such means. Care must be taken to avoid collapse of the patient.

Antipyretic methods may be divided into three groups :

Milder Refrigerants. These are the ordinary saline remedies —citrate of potassium (10 to 30 grains), liq. ammonii acetatis (½ ounce), dilute acids—which were formerly given in every fever, but have very little influence.

Stronger Antipyretic Drugs. These drugs are very little employed at the present time for their purely antipyretic action. If one of them is given in a single dose to a patient with a temperature of 103° or 104°, the temperature falls within two or three hours to normal or even lower, but it rises again in six or seven hours to a height not much different, if at all, from what it would have reached had no antipyretic been given. The following have been most often employed : quinine sulphate, 20 to 30 grains ; salicin, 30 grains ; salicylic acid, 20 grains ; antipyrin (phenazone), 15 grains ; antifebrin (acetanilide), 2 to 5 grains ; phenacetin, 5 to 10 grains. The last three are the most certain in their antipyretic action, but in doses beyond the limit stated these drugs are apt, especially the last two, to cause alarming cyanosis and collapse.

External Application of Cold. This may be done in several ways : the cold bath ; the wet pack ; sponging ; ice applications ; Leiter's coils. Though more troublesome than the administration of drugs, its use can be better controlled, and there is less risk of harm to the patient.

Hydrotherapy. This has been largely used in the treatment of enteric fever. The temperature is taken every three hours, and whenever it is found at any of these periodical observations to be 102° F. or higher, the patient is placed in a bath of a temperature of 70° F., in which he remains for ten or fifteen minutes, according to its effect upon him. He is then removed, lightly dried, and replaced in bed. The temperature will then be generally found to have fallen to 99°, 98°, or even lower. The system is open to modifications : the observations may be made less frequently, the bath may be only used when the body heat is 102·5°, or 103°, or 103·5°, and the temperature of the bath may be as low as 60° or as high as 80° or 90°. Sometimes the patient is put in the bath at a temperature of 90°, and ice is then introduced to bring down the heat to 75° or 70°. It is obvious that the greater the number of baths, and the lower their temperature, the greater will be their effect upon the mean body heat. Continuous immersion has been also successfully employed.

Wet Pack. A sheet is wrung out of ice-cold water and wrapped round the patient for ten or fifteen minutes, the application being made under the same conditions of bodily temperature as are directed for the bath.

Sponging. The body is uncovered and sponged over with cold or ice-cold water for from seven to ten or fifteen minutes. This method is not generally so effective as the two former ; the temperature commonly falls from one and a half to two degrees.

Ice-bags. These may be placed on the chest or abdomen for varying periods, or hung within a cradle placed over the patient. The application of an ice-bag to the head is often a good method of relieving headache.

Stimulants. In all febrile illnesses a stage may be reached when the heart's action and the nervous system are so profoundly affected that some kind

of artificial stimulation is required; but although the signs indicative of such a stage are, as a rule, severe in proportion to the elevation of the temperature, they are due not so much to the fever itself as to the toxins which circulate in the blood, and are themselves the cause of the pyrexia. The results of such cardiac failure and nervous prostration are quick and feeble pulse, inaudible first sound of the heart, irregular action of the heart, cyanosis, congestion and œdema of the bases of the lungs, dry tremulous tongue, muscular tremor, sleeplessness, and delirium.

The simplest method of stimulation, and one long in vogue, is the administration of alcohol in the form of brandy or whisky; the quantity may be from 2 to 6 or 8 ounces in the twenty-four hours. But the larger amounts must not be continued for many days; and especially in prolonged illnesses, like typhoid fever, the effects of this drug must be carefully watched, since an excessive amount will keep up a quick pulse and a drowsy muttering delirium, deceptively like the very condition for which it was originally given. If the delirium assumes a maniacal form, it is very likely to be aggravated by alcohol.

In more recent times there has been an increasing tendency to prefer other modes of stimulation, which may often be used with success. Such are the following: the internal administration of spirit ammon. aromat. in doses of 30 minims or tincture of digitalis 15 or 20 minims three times a day; the intramuscular injection of the double salt of caffein and sodium salicylate or of caffein and sodium benzoate in the dose of 5 grains for an adult; the intramuscular injection of camphor in 10 or 15 or 20 per cent. solution in olive oil (or oil of sesame), the dose of camphor for an adult being from 3 to 5 grains; the intramuscular injection of adrenalin (5 to 10 minims of the 1 in 1,000 solution). In any case the result of each dose will be the guide to the time at which the next should be given.

Insomnia. The following remarks are applicable generally, and not only to pyrexia.

There is now available a fairly wide variety of useful hypnotics. The principal hypnotics may be grouped as follows:

(1) Bromide salts, especially potassium and ammonium bromide (10 to 30 grains).

(2) Chloral hydrate (10 to 30 grains) and its ally, chloralamide or chloral formamide (10 to 60 grains).

(3) The barbituric acid group: Barbitone (veronal) (5 to 10 grains), medinal (sodium barbitone) (5 to 15 grains), dial (1½ grains), allonal (2 to 4 tablets), luminal (2 to 5 grains), etc.

(4) A group also derived from urea, but without a carbon ring in the nucleus: adalin and bromural (5 to 15 grains).

(5) The sulphone group: sulphonal (20 to 40 grains) and methylsulphonal (trional) (10 to 20 grains).

(6) Paraldehyde (1 to 2 drams).

(7) Hyoscine hydrobromide ($\frac{1}{100}$ grain).

(8) Opium and its derivatives, *e.g.*, morphia, heroin ($\frac{1}{25}$ to $\frac{1}{8}$ grain) and pantopon ($\frac{1}{8}$ to $\frac{1}{2}$ grain).

When sleeplessness is due to pain, an analgesic like aspirin (5 to 15 grains), pyramidon (5 to 8 grains) or veramon (5 grains) may be tried along with a dose of one of the first six groups. But the only effective hypnotics when there is much pain are opium or its derivatives. Opium may be given by mouth as Dover's powder (10 to 15 grains), or, if a more rapid effect is desired, subcutaneously as morphine ($\frac{1}{6}$ to $\frac{1}{2}$ grain). When insomnia complicates a febrile illness, a drug of the first six groups may be tried, and chloral or paraldehyde are in fact to be preferred to bromides or the barbituric or sulphone series, as the latter are apt to produce in these circumstances a certain amount of dulling and sometimes actual mental confusion, while not succeeding very well in producing sleep. In severe

prolonged febrile illness, such as a streptococcal septicæmia, morphine is the most satisfactory hypnotic.

In pneumonia, morphine is mainly used in the first five days, but after the fifth day is contra-indicated (respiratory depression), when paraldehyde may be substituted. A mixture of chloral and digitalis may be used instead from the beginning. In acute bronchitis, opium is usually contra-indicated; but when the sleeplessness is due to cough, and there is not too much secretion, morphine, heroin or dionin is permissible (and also in the insomnia from cough in chronic phthisis).

In the dyspnœa of heart disease, opium " acts like a charm " and so greatly promotes sleep. In other causes of insomnia in cardiac disease (apart from dyspnœa), chloral is valuable, and has not the dangerous depressant cardiac effect that it is alleged to have. Paraldehyde should however be used instead when myocardial degeneration is suspected.

In delirium, when chloral and paraldehyde have failed, and when there is much restlessness endangering the patient, hyoscine hydrobromide ($\frac{1}{100}$ grain) may be given hypodermically and repeated with care if necessary, but in smaller doses ($\frac{1}{150}$), and a second dose should not be given within two hours of the first.

In insomnia due to anxiety or other mental cause the barbituric acid group is particularly useful. These drugs have to be given with special care in elderly people in whom the tendency to a cumulative effect is greater. When these fail, and sleep is urgently required in mental conditions, chloral (often given with bromide) and paraldehyde may have to be resorted to. Continuous tub treatment, if properly given, may make hypnotics unnecessary, but it requires special equipment and a trained attendant. The cold wet pack for young, robust, excited patients, or a warm wet pack for excited patients of any age if in good physical condition, are especially valuable in insomnia associated with much restlessness in mental disorders.

The bromides are sedative rather than hypnotic, but may suffice in mild recent insomnia. They are also helpful if taken over a long period in the over-anxious individual. The cumulative action, including the tendency to produce acne, has to be watched.

Convalescence. After a short febrile attack, such as influenza, the patient may be allowed to get up after the temperature has been down for twenty-four hours. After long attacks the patient may be helped on to a couch for a few hours after the temperature has been down for two or three days. The time up is gradually increased. The next stage is to allow the patient to get up himself and to sit on a chair. After a week or ten days he may be allowed to walk about the room, then to go downstairs. Walking outdoors and climbing stairs may be allowed after two or three weeks. It is customary to prescribe a tonic during convalescence, such as iron or cod-liver oil, malt extract, or a mixture containing acid hydrochlor. dil. 10 minims, tr. nucis vom. 10 minims and Infus. gent. ad 1 oz. a.c.

Diseases caused by ultra-filterable viruses or of unknown origin.

MEASLES

(*Morbilli*)

Measles is a contagious febrile disease, characterised by an eruption of pink or red spots and catarrh of the respiratory mucous membranes.

Ætiology. In civilised communities its spread is determined by circumstances very similar to those influencing scarlatina. It occurs in epidemics, which attack the young rather than the old, chiefly because nearly all the older members of the community have had the disease when young, and are thereby protected from a second infection; but infants up to six months are either

insusceptible or get the disease in a mild form (**48**). In large towns it is almost continuously present, spreading from point to point in the form of limited outbreaks, which subside, and are succeeded by others in different places; but where introduced among populations that have never been visited by the disease, or have been entirely free from it for years, it attacks the majority of the people, young and old alike, in one great and often destructive epidemic. This was the case in the Faroe Islands in 1846.

Infection is due to an unknown virus which is present in the secretions from the nose and throat. Experimentally the disease has been transmitted by inoculation from this source. Infection is spread from inhalation of droplets of saliva projected into the air by talking and coughing during the catarrhal stage of the disease; the virus also adheres to clothes, toys and other articles, though with much less tenacity than does the contagion of scarlatina.

Morbid Anatomy. This depends on the complication causing death, since uncomplicated measles is so rarely fatal.

Symptoms and Course. The period of *incubation* in measles is usually eight to sixteen days (limits—six to twenty) (**12**). The disease commences with pyrexia and catarrhal symptoms: the temperature rises perhaps to 102°; the child loses appetite, is drowsy and unwell; there may be at first vomiting or chills, or, in children, convulsions. With this the conjunctivæ becomes suffused; the eyes water; there is a mucous discharge from the nose, and cough as a result of bronchial secretion. The catarrhal symptoms continue, but the temperature frequently falls after the first day, and continues at a lower level for another day or two, when it again rises. Occasionally in this early period there is a so-called prodromal rash, which may be like that of scarlatina, or urticarial, or like the true measles rash. It lasts only twenty-four or thirty-six hours.

The characteristic eruption appears most commonly on the fourth day, but it may be as early as the third. It is first seen on the face, at the roots of the hair, on the forehead, temple, or behind the ears, and it subsequently spreads to the neck, trunk, and limbs. It consists of pink spots, round, oval, or irregularly shaped, slightly raised above the surface, running together into irregular groups, which may have a somewhat crescentic shape, and leave some intervening area of skin unaffected. In colour, it is generally darker red, or more purple than that of scarlatina; but a distinction may be difficult, especially if the spots are uniformly distributed and do not coalesce. Occasionally a few petechiæ occur in the darkest part of the eruption, and in other cases a few vesicles may form in the centres of some papules. It comes out most fully on the face, giving it a blotchy, swollen appearance, and though less abundant on the extremities, it may form continuous patches of infiltration on the back and arms. It takes from one to three days to reach its height, and then rapidly declines, mostly beginning to fade first where it first appeared. It commonly leaves some mottling of brown or yellowish-brown colour, which lasts for some days; while petechiæ leave still more pronounced stains. It is also succeeded by slight desquamation in minute branny scales, but never in the large flakes seen in scarlatina.

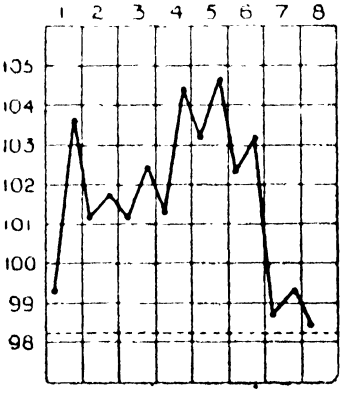


FIG. 2. — Temperature in Measles. (*After Strümpell.*)

If the temperature has fallen in the prodromal stage, it rises again, with the appearance of the rash, to 102°, 103°, or even higher, and, reaching a maximum in two, three, or four days, falls generally rather suddenly as the rash begins to fade, and may reach the normal in about thirty-six hours. The catarrh continues throughout the eruptive stage; it may extend

into the frontal sinuses and cause headache. There is more or less general bronchitis, indicated by cough, expectoration of mucus, and diffused rhonchi; and the larynx may be implicated, as shown by hoarseness, croupy cough, and in occasional cases by stridulous breathing. Even before the appearance of the rash the palate often shows abnormal redness, diffused or in patches, and almost invariably the lesions known as *Filatow's* or *Koplik's spots*. These are small, raised, white or opal dots, the size of a small pin's head, generally on a reddened base. They are seen best on the buccal mucous membrane opposite the premolar teeth of the lower jaw, and to a less extent opposite the other teeth. These appear two or three days before the eruption. The tongue is usually furred, and the fungiform papillæ are prominent. After the subsidence of the fever the return to normal appetite and sleep is generally rapid.

Complications and Sequelæ.[1] The most important complications are those connected with the respiratory organs, and it is to them that the majority of the deaths in connection with measles are due. Inflammation of the lungs is of frequent occurrence, and has generally been attributed to an extension of the bronchitis, which is common in all cases of the disease. But the pneumonia may be lobular or lobar in its distribution, and it may present in one case the features of a *broncho-pneumonia* (*16·2*), and in another case those of a lobar or pneumococcal pneumonia. The *laryngitis* (*2·7*) may be so severe as to threaten asphyxia, and may be accompanied with the formation of membrane; in some such cases it is a true diphtheria; in others it is caused by pyogenic organisms. Other complications are conjunctivitis (*1·3*), keratitis (*·3*) or iritis, stomatitis (*1·7*) and parotitis, inflammation of the Eustachian tube, *otitis* (*8·3*), diarrhœa or dysentery from enteritis of the small or large intestine respectively, albuminuria (*3·3*), and intestinal hæmorrhage. Gangrene of the mouth, called *cancrum oris*, or *noma*, occurs occasionally (*·9*), and gangrene of the vulva, also called noma, more rarely. The encephalitis of measles is described later.

Varieties. Measles without eruption and measles without catarrh have both been described; but it is doubtful if the former occurs, and some cases of the latter may really have been instances of rubella or German measles (*see* p. 27). In either case, the disease is mild. Of the severer or malignant forms *hæmorrhagic* measles is an example, in which bleeding takes place from mucous membranes, and the eruption becomes *purpuric*. Other severe forms are merely characterised by intense fever, dark or livid rash, often imperfectly developed, rapid and feeble pulse, prostration, delirium, dry brown tongue, and a generally typhoid condition.

Diagnosis. A confusion with *scarlatina* and *rubella* is most likely to occur (*see* p. 27). In *typhus* the rash is not so papular, the face is but little affected, the spleen is swollen, and there is no nasal or conjunctival catarrh. The early stage of a *small-pox* eruption is sometimes simulated by that of measles; the absence of catarrh and the history of headache, back pain and sickness, are in favour of variola. Roseolous eruptions, apart from specific fevers, may resemble measles, but will be distinguished by the absence of the characteristic fever and catarrh. Koplik's spots are of value in diagnosis, as they rarely occur in other eruptive diseases.

Prognosis. This is usually favourable. For the most part the mortality is from 1 to 2 per cent., though occasionally epidemics of much greater severity have occurred; and the prevalence of pulmonary and laryngeal complications increases considerably the percentage of deaths. Apart from these, the malignant cases are recognised by intense fever, dark or livid eruptions, and early collapse or prostration.

Prevention. The only successful specific method of prevention is to inject serum taken from a convalescent patient seven to eleven days after the tempera-

[1] The bracketed figures in *italics* are percentages from 747 cases in the Metropolitan Asylums Board's hospitals in 1914. No later data have been published.

ture has become normal (**48**). The serum which is also tested by the Wassermann reaction can be stored in the cold for many months; 6 c.c. are used for children under three months and 6 to 10 c.c. for older children, and the injection should be made during the first five or six days of incubation to prevent an attack; if later, *i.e.* up to the ninth day, the attack will be less severe.

Treatment. The general treatment of pyrexia should be consulted. Confinement to bed is scarcely necessary till the eruption appears. The catarrh which is present from the first should be treated as described under Bronchitis. The treatment of the fauces and of otitis is the same as in scarlet fever; of the nose and larynx as in diphtheria. Broncho-pneumonia with cyanosis has been treated successfully with the oxygen tent.

RUBELLA

(*Roseola, Rötheln, German Measles*)

This is an exanthem, resembling in many points both measles and scarlatina, but undoubtedly distinct from both. No specific micro-organism has yet been discovered in connection with it.

Ætiology. It is not so infectious as measles, being spread in much the same way, especially by close association with some one suffering from the disease. Restricted outbreaks are a common result, older children and young adults being readily infected.

Symptoms. The period of *incubation* is nine to nineteen days. A prodromal stage is either entirely absent, or at most lasts half a day before the appearance of the eruption; and this stage may be represented by a slight catarrh of the mucous membranes of the air passages or of the conjunctiva. But in some cases the *eruption* is the first indication of anything wrong with the patient. It consists of a number of pink spots, round or oval, very slightly raised above the surface, uniformly scattered, and generally discrete, though sometimes very closely set. The spots vary in size; when small and closely set there may be much resemblance to a scarlatinal rash; when larger there is more likeness to measles, but they are not commonly confluent, and do not take any crescentic form. Slight itching of the skin may be experienced. The eruption occupies the face, trunk, arms, and legs, appearing mostly on the face first and rapidly occurring on the other parts; it is generally of shorter duration than measles, often lasting only two days, sometimes three or four. As in measles, it may leave a little discoloration of the skin for some days afterwards; desquamation is commonly absent, and it is never in large flakes, as in scarlatina. The palate and fauces usually show some injection or spots and streaks of redness, and the tonsils may be a little swollen. The conjunctivæ are reddened, and coughing and sneezing are generally present to a slight extent. The *lymphatic glands* at the back of the neck in the occipital mastoid and posterior cervical regions are frequently swollen and tender, and sometimes those in other parts of the body. The swelling may persist two or three weeks, but suppuration has never been observed. Fever is, in the majority of cases, entirely absent; if it occurs, the temperature is only 1·5° or 2° above the normal, and it lasts one, two, or at most three days, showing the greatest variability in different cases, but often falling to normal before the eruption is completely developed. Many patients do not feel ill at all, and retain their appetite throughout. Any further complications than those indicated already are quite uncommon, and the prognosis is exceedingly favourable.

Treatment. This must be conducted on the lines laid down for measles.

Differential Diagnosis of Scarlatina, Measles and Rubella. *Initial stage.* In scarlatina the onset is sudden, and the first stage lasts twenty-four hours. There are nausea and vomiting, but not much catarrh. In measles there

are definite catarrh and conjunctival suffusion for over three days before the rash. In rubella there is slight catarrh, which may last only a few hours.

Adenitis. In scarlatina the glands below the angles of the jaw are definitely affected and are sometimes palpable in other regions. In measles there may be slight swelling below the angles of the jaw; very occasionally the posterior glands are affected, as in rubella. In rubella there is characteristic enlargement of the glands at the back of the neck.

Nature of Rash. In scarlatina there are minute papules and a general erythema, often brick-red in colour. It may be patchy on the extremities. There may be some apparent swelling of the skin. In measles the spots are large and red and may form definite patches with curved outlines. In rubella the spots are smaller, rounder and pinker than in measles, and more discrete. Coalescence into patches may sometimes occur.

Distribution of Rash. In scarlatina the palms, soles, and face are reddened but not affected by the rash. There is marked circum-oral pallor. The scalp also escapes. In measles and rubella all parts may be affected, and the circum-oral region is very constantly invaded.

Fever. In scarlatina the pyrexia is marked and the pulse rapid; sore throat is prominent, and there is intense injection of the palate, and, except in the septic form, there is usually no bronchial catarrh. Defervescence is rather gradual. In measles the pyrexia is definite, and there is much constitutional disturbance, without a sore throat. Koplik spots are present in over 90 per cent. of cases on the buccal mucous membrane. Bronchial catarrh is a usual feature, often leading on to broncho-pneumonia. In rubella the pyrexia is slight and sometimes absent, and the patient feels well. Sore throat, if present, is very slight, and there is usually no bronchial catarrh.

Tongue. In scarlatina the tongue passes quickly through three stages:—furred with red edges, patchy, strawberry. In measles it may be well coated, and is occasionally patchy, but not typically strawberry. In rubella there may be slight furring.

Skin after Rash fades. In scarlatina the skin looks rather opaque, like parchment, and more or less sallow from pigment. Desquamation is of the pinhole-and-flake type; the pinholes are usually best seen at the outset on the neck. Desquamation is often very copious. In measles there is dirty brown mottling. Desquamation is fine, branny and not very copious. In rubella there may be faint yellowish-brown staining for a few days, but this is unusual. The desquamation is as a rule almost inappreciable.

SMALL-POX

(*Variola*)

Small-pox is a specific contagious disease, with a characteristic pustular eruption, due to a virus which is probably ultra-microscopic.

Ætiology. This disease arises solely by contagion, chiefly, no doubt, by inhalation of the atmosphere surrounding infected persons. When cases are aggregated in hospital infection by aerial convection is believed to occur for at least a quarter of a mile. It is also conveyed by clothes, bedding, and other things, which have been in contact with patients; and it can be inoculated by means of the contents of the pustules. But patients are infectious before the eruption, and the virus is given off even from the bodies of those who have died. The susceptibility to the disease is common to all ages and both sexes; even the fœtus *in utero* may catch it from the mother; but the susceptibility then and in the first year of life is stated to be less than afterwards. The disease commonly occurs only once in the same individual; but second and third attacks

occasionally occur, and the second attack may even be more severe than the first, though it is generally milder.

The liability to the disease, and consequently the number and severity of its epidemics, have been reduced considerably since the introduction of vaccination at the end of the eighteenth century. For instance, in this country there were annually several thousand deaths from small-pox in the middle of the last century (**2**). In 1871, owing to infection introduced with refugees from Europe at the time of the Franco-Prussian War, the number of deaths amounted to 23,000; but since that time there has been a steady diminution, and since 1905 the number of deaths has always been under thirty. This favourable result cannot be due chiefly to vaccination, because the proportion of infants vaccinated to the number of births has decreased since the beginning of this century. It is due rather to increased facilities of diagnosis since the disease became notifiable, and also probably to the mild form of the disease in England at present.

Epidemics of small-pox vary in severity. The milder form is now called Variola Minor; it occurred originally as "alastrim" in Africa and America. The severer form of Asia and Europe is now called Variola Major. Both forms, on the whole, breed true to type, but they are the same disease, as is proved by immunity reactions.

Morbid Anatomy. In hæmorrhagic cases blood may be found effused into the solid viscera. Examination of the pustules shows that the process begins with hyperæmia of the papillary layer of the cutis; then the superficial layer of the cuticle is raised from the deeper layers to form a vesicle. The umbilication is sometimes determined by a hair, or the duct of a sweat gland preventing distension at this spot, or merely by cells of the rete Malpighi stretched into a fibre; bands and fibres formed in the same way constitute the septa dividing the vesicle into *loculi*. The pustule becomes hemispherical, in the later stages of suppuration, by the central band or *retinaculum* giving way. Whether the resulting scars are superficial or deep depends upon the extent to which the suppurative process involves the papillary layer of the skin. Micrococci due to secondary infections have been found in the pus and in various organs. The liver cells show fatty degeneration early in the disease.

Variola Major. The period of *incubation* is ten to fourteen days. The disease mostly begins suddenly with a distinct rigor or chills, with severe backache (lumbosacral pains), severe headache, vomiting and prostration. The temperature rises rapidly to 102°, 103°, or 104°, and the next day it may be still higher (Fig. 3). On the third day the typical eruption appears; but in the initial stage in a certain number of cases rashes occur, with which it is important for diagnostic purposes to be acquainted.

Early Eruptions. These are (1) *erythematous* and (2) *hæmorrhagic.*

(1) The erythematous rash tends to appear before the hæmorrhagic. In mild or modified small-pox it takes the form of irregularly shaped patches, which tend to be evanescent and migratory, and are not appreciably raised above the surface. It is often supposed to resemble measles, but rarely spreads any higher on to the face than the level of the lower jaw. In severe small-pox the erythema forms large areas, or plaques, of a brilliant colour, with well-defined margins on the external surfaces of the limbs and on the trunk. More rarely the whole body surface is covered with a continuous sheet of erythema, but this is not punctate like scarlet fever.

(2) The hæmorrhagic rashes indicate a more severe degree of infection. They have a special affinity for flexures and may begin as an erythema. One of the most characteristic is the "triangular rash," which occupies the lower half of the abdomen, from the umbilicus downwards, covers the groins, and extends on to the thighs. It has the form of an inverted isosceles triangle, with the base about the level of the umbilicus. It also frequently appears in the axillæ, and on the adjacent parts of the arms and trunk, and extends thence along the flanks

to the lower patches. It consists of small hæmorrhagic spots, or petechiæ, which on fading leave brown or yellowish-brown stains for a time. These initial rashes commonly appear on the second day, and last for about two days, co-existing with the early stage of the papular eruption, but disappearing before its full development.

Another form of hæmorrhagic rash is the *purpura variolosa*, which constitutes a very severe variety of the disease. On the second day, or even within twenty-four hours of the first symptom, a scarlatiniform rash appears, quickly followed by subcutaneous hæmorrhage, partly petechial, partly in larger patches. The face is red and puffy, the eyes suffused; there may be vomiting of bilious matters or of blood, with the passage of bloody stools, and the urine contains albumin or blood. The mind is generally clear till near the end; exceptionally delirium or coma is observed. The cases are nearly always fatal, often within three days of the commencement, and even earlier.

Specific or Focal Eruption. This commonly begins on the third day of the illness by the formation of small red papules on the face, forehead, and scalp, and the same appear subsequently on the chest, back, arms, and hands, finally on the lower part of the body, the legs and feet. These papules soon become

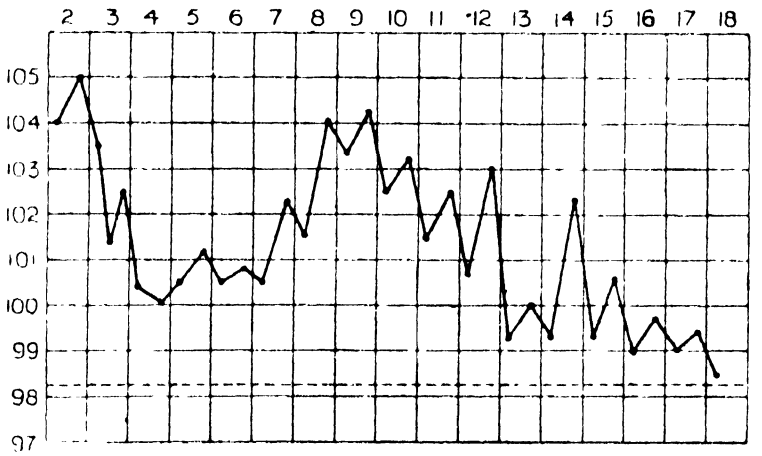


FIG. 3.—Temperature in Small-pox. (*After Strümpell.*)

prominent; they are firm, and give to the finger the impression of extending deeply, a condition sometimes described as "shotty." Towards the end of the second day of their appearance a small vesicle appears in the centre, which is at first clear and transparent. As it gets larger, during the next two days, a very characteristic change takes place: the centre becomes depressed, and the circumferential part forms a prominent ring round it. This process is known as the *umbilication* of the vesicle. If the vesicle be punctured, only a small quantity of the contained serum will escape, the retention of the remainder being due to septa which divide the vesicle into separate cavities or *loculi*. Almost coincidently with the umbilication of the vesicle, the contents become more opaque; and finally, about the sixth day (eighth of the disease), they are completely purulent. During this change in the vesicle the surrounding skin becomes pink, forming an inflammatory halo around it, and if there are many pustules—for instance, on the face—this leads to a great deal of swelling, which is often so considerable as to render recognition of the features quite impossible. The scalp becomes tense and tender, and the fingers also are often much swollen from the same cause. The stage of suppuration lasts two or three days, and then the pustules gradually dry up, beginning at the centre, and ultimately forming a brown or blackish-brown scab, which adheres for several days. Sometimes the desiccation is preceded by the escape of some pus from the vesicle, and with the drying up the swelling of the face and other parts subsides. Finally, the scab falls off, leaving a dark red spot,

which is at first slightly raised above the general surface, but in the course of some weeks forms a depressed white scar. The pustules form most abundantly on the face, and on the backs of the hands, and are less numerous on the trunk and covered parts of the limbs. Parts that have been the seat of initial erythematous or petechial rashes are by many said to be less liable to the specific eruption. All the stages of the eruption occur first on the face, and follow, a day or so later, on the trunk and extremities. On the other hand, parts which have been irritated, as, *e.g.*, by the application of plasters or blisters, are liable to an abundant formation of pustules. The pustules are not confined to the skin, but occur on the mucous membranes also; they are especially well seen in the mouth, on the hard and soft palate, but present different appearances from those on the skin on account of the constant moisture to which they are subject. They scarcely develop into well-formed pustules, but are only grey or pearly elevations, which are liable to become abraded and form superficial erosions or ulcers. The tongue is generally coated and more or less covered with pustules; rarely its substance is inflamed. Ulceration of the larynx or even perichondritis may occur; and the process may extend to the nasal mucous membrane, so that the breathing is obstructed by the swelling and the formation of scabs.

In mild cases the *primary fever* subsides with the appearance of the specific eruption (Fig. 3), and the temperature may become quite normal, so that patients who have remained at home during the first three days will go to their doctor or the hospital with an abundant crop of papules all over the body, but feeling comparatively well, free not only of the fever, but of the headache, lumbar pains, vomiting, and general malaise.

But when the pocks become purulent there is a fresh accession of fever, a *secondary* or *septic fever*, which may be ushered in by chills, or a rigor, and which lasts from three to six or eight days (Fig. 3). The temperature rises to 103° or 104°, is mostly remittent in its course, and is accompanied with sleeplessness, headache, and delirium, and a pulse of 100 to 120. All this again subsides as the scabs dry and the swelling of the skin decreases. With the fall of the scabs some patients lose their hair, and even their nails.

Confluent small-pox is a form in which the eruption is very abundant, and the general illness is correspondingly severe. The initial fever is high, and the temperature does not fall to normal with the appearance of the rash, as it does in mild cases. The rash appears early, even by the second day, and is very abundant, so that on the face, which is most affected, the pustules are closely set, the skin is enormously swollen, and in the stage of suppuration several pustules coalesce and form irregular and more or less extensive purulent blebs. The implication of the mucous membranes of the nose, throat and larynx is much more constant and severe. The secondary fever is also high, and is accompanied by prostration, rapid pulse, and delirium or coma. Complications are more frequent and serious, and the mortality is great, death taking place from exhaustion, or hyperpyrexia, or pyæmia.

Malignant small-pox, or purpura variolosa, in which hæmorrhages appear in the skin within the first forty-eight hours, has been mentioned; in another form the hæmorrhagic tendency shows itself later. The specific eruption appears, and then hæmorrhage takes place into the papules, or later still into the pustules, or into the skin between the pustules. The petechiæ often occur first on the lower extremities. The mucous membranes are also affected with hæmorrhages, or membranous patches, and bleeding occurs from the nose, lungs, rectum, kidneys, or uterus. The cases are mostly fatal.

Variola Minor. The following are the characteristics of the very mild form of the disease in England at the present time among the unvaccinated. The mortality is 0·4 per cent. The onset of the disease is sudden or insidious with headache, shivering, malaise, pyrexia, pain in the limbs and, exceptionally, backache—like influenza. There are no prodromal rashes or hæmorrhages, and no

prostration. The focal eruption does not appear constantly at the end of the third day, but sometimes as late as the seventh or eighth days. It appears first on the face, a few hours later on forearms and trunk, twelve hours later on the lower extremities. The pocks are smaller, more superficially situated, and their evolution is more rapid than in virulent small-pox. They fail to pustulate completely, but dry up into amber-like beads. The vesicles are unilocular. The distribution is the same as in ordinary small-pox. All constitutional symptoms disappear with the rash and there is no further pyrexia (**13**) (**52**).

The **Complications and Sequelæ** are chiefly as follows: abscesses and erysipelas, conjunctivitis, and sometimes destruction of the eye from suppurative keratitis; chronic otitis and caries of the bones of the ear; in the respiratory system, bronchitis, broncho-pneumonia, and pleurisy and the changes in the arynx above described. On the side of the nervous, system the following may occur: hemiplegia, probably from arterial thrombosis or encephalo-myelitis similar to that following vaccination.

Diagnosis. This is best considered according to the stage of the disease: (1) In the pre-eruptive stage, the occurrence of shivering, with severe pain in the head and back and vomiting, characteristic of small-pox, might also suggest influenza, acute rheumatism, lumbago, or other acute diseases. (2) Early eruptive stage: The petechial eruptions on the lower parts of the abdomen and in the groins are very characteristic, but when the hæmorrhages are more generalised (*purpura variolosa*), purpura, septicæmia and other causes of petechiæ, *e.g.* scarlet fever and food-poisoning, must be differentiated. The erythematous eruptions may closely simulate scarlatina or measles. The scarlatiniform eruption of variola is not punctate and is unaccompanied by inflammation of the throat. The morbilliform eruption is not raised like that of measles and is rare on the face. Syphilis also sometimes presents an eruption like it. (3) The specific eruption in the papular stage, appearing first on the face and often grouped in twos and threes, may resemble papular erythema, *e.g.* a papular measles rash. (4) In the vesicular stage, small-pox must be differentiated from chicken-pox (considered later on, p. 35) and pemphigus. (5) In the pustular stage, it may resemble pustular eczema. (6) In the crusting stage it may resemble chronic eczema or exfoliative dermatitis. (7) Finally, it is necessary to consider the possibility of an individual being recently scarred with small-pox, and this may give the clue to the nature of an obscure acute affection in other members of the family. Careful account must also be taken of the recent history of the patient.

The **Prognosis** of variola major depends on vaccination. Nearly all persons attacked in the first few years after vaccination recover. In later years any protective action may be difficult to trace. The typical hæmorrhagic form is always fatal. About one-third of ordinary confluent cases die, and 5 to 10 per cent. of discrete cases. The profuseness of the suppuration is the surest measure of the fatality.

Treatment. The general lines of treatment are the same as for the infectious diseases already described. The patient must be isolated.

When small-pox is fatal death occurs most commonly in the stage of secondary fever from suppuration of the pocks. The method introduced by Dreyer of Cairo in 1910 is the best treatment for severe small-pox. The skin of the whole body is painted over with a 3 or 5 per cent. permanganate solution once daily. A 1·5 per cent. solution may be used if the skin is sensitive. In confluent cases it is best to place the patient in a permanganate bath at body temperature for a quarter of an hour twice daily. This treatment, if begun early, lessens the suppurative process, prevents the formation of bedsores and general sepsis, increases the comfort of the patient, and lessens the risk of infection of the attendants. Opium may be given to procure sleep. In the severer cases stimulants may have to be given freely.

If an unvaccinated person has incurred the risk of small-pox he should be vaccinated at once, as it is certain that the disease may be favourably modified by this procedure.

VACCINATION

The virus of vaccinia or cow-pox are ultra-microscopic elementary bodies known as Paschen bodies; they are agglutinated by anti-vaccinal sera.

Prevention of Small-pox. *Inoculation and Vaccination.* The observation that small-pox, when conveyed by inoculation of the contents of the vesicle under the skin, produced a milder attack than that commonly conveyed by contagion, led to the use of inoculation as a means of protecting the individual from the more dangerous forms of the disease. Lady Mary Wortley Montagu introduced the custom into England in the early part of the eighteenth century, and her example was widely followed. But a serious disadvantage attached to this proceeding: the small-pox induced by inoculation, though mild, was contagious, and the spread of the disease was thus decidedly favoured. Inoculation consequently fell into disrepute, and finally yielded to vaccination—*i.e.* the inoculation of *cow-pox*, or *vaccinia*—first practised by Jenner in 1796. He was led to make the experiment from the facts, long observed in dairy farms, that cows were liable to a pustular disease of the udders and teats, which was often accidentally communicated to men and women milking them, and that these persons were subsequently insusceptible to small-pox, either by contagion or by the inoculation then in vogue. Conversely it was observed that those who had had small-pox did not catch the disease from the cows. Jenner inoculated patients with cow-pox, which produced its characteristic effects, and he subsequently found that certain of these patients were insusceptible to a small-pox virus, which set up typical variola in other unvaccinated persons.

The cow-pox may be conveyed from man to man by means of the lymph contained in the vesicles a great many times without any very obvious diminution of its power to reproduce the disease and to protect from variola. This arm-to-arm vaccination was in common use in the early days, and occasionally caused syphilis and other diseases to be transmitted, so that it has now been superseded by the use of lymph obtained direct from the calf previously inoculated with the virus. The introduction of this lymph was much facilitated by Copeman's demonstration that by thoroughly incorporating six parts by weight of a 50 per cent. solution in water of chemically pure glycerin with one part of the calf lymph or vesicle pulp, and afterwards storing the mixture for some weeks prior to use in sealed capillary tubes protected from light, any streptococci or staphylococci existing in the lymph, and even tubercle bacilli if introduced, are completely destroyed. The use of *glycerinated calf lymph* was recognised in the Vaccination Act of 1898.

The Method of Vaccination. The part selected for the operation is generally the outer side of the left arm, near the insertion of the deltoid muscle. The skin is first thoroughly washed and rendered aseptic, and put on the stretch by the use of the left hand. The vaccine may be introduced intradermally by needle and syringe; but usually a drop of lymph is placed on the skin and one line or scratch ¼ in. long is made just through the epidermis in the long axis of the limb and through the lymph. The lymph may be rubbed gently into the scratch with the side of the knife or needle used. If a prompt successful vaccination is required, up to four inoculations may be made on different parts of the arm. After the lymph has dried the spots may be painted over with flexible collodion, but later on when a vesicle occurs a pad of boric lint should be applied.

The English law requires that all children should be vaccinated before the age of six months, unless the parent makes a statutory declaration of his conscientious belief that the proceeding will prejudice the child's health. But vaccination should only be carried out if the child is healthy, *e.g.*, not suffering from

diarrhœa or eczema; unless absolutely necessary owing to presence of small-pox, vaccination should not be performed if the child has been exposed to infectious disease or if erysipelas is present in the house. It should be pointed out that there are at present two views as to how vaccination is to be used to prevent small-pox. One view insists on the importance of infant vaccination, with periodic re-vaccination as far as possible, and that individuals who have been in contact with a small-pox case shall also be vaccinated. The other looks on infant vaccination as unimportant, so long as vaccination of contacts is carried out. Vaccinal encephalitis, described later, is a very rare complication of vaccination, affecting chiefly children between five and fifteen who are vaccinated for the first time between these ages. The Minister of Health is of opinion that so long as variola minor alone is prevalent in this country it is not expedient to press for primary vaccination of such children. It has been recommended that infant vaccination should be carried out with lymph diluted 1 in 10, which incidentally gives much more satisfactory "takes" (8).

Vaccination in Man. When lymph from a vesicle of cow-pox is inoculated under the human skin, nothing occurs till the end of the second or the third day, when a papule appears at the seat of inoculation. This increases in size, and on the fourth or fifth day a vesicle forms, which enlarges and forms a circular bleb, flat or slightly depressed in the centre, and pale grey in colour. On the eighth or ninth day the contents begin to be purulent, and a pink zone of inflammation forms around it. The vesicle becomes more opaque; the redness increases in extent, and is accompanied by induration. The neighbouring lymphatic glands become swollen and tender, and a slight degree of fever and malaise is present at this time. About the tenth or eleventh day the pustule begins to dry, and a brown scab forms during the next few days. The surrounding inflammation subsides, and about the end of the third week the crust falls off, leaving a depressed, pitted, and permanent scar.

Vaccination is, in the vast majority of cases, a perfectly harmless procedure, but occasional accidents are observed. Erysipelas may attack the wound of vaccination, as it may any other wound by accidental infection; and gangrene has very rarely occurred. A rare complication is post-vaccinal encephalomyelitis, described later.

Cases of *aberrant vaccinia* are sometimes observed. Milkmen may become inoculated on the hands while milking, and in a case seen by the writer inoculation on the cornea led to blindness in one eye. Secondary vaccinia on the lips, tongue, tonsil, eyelids, etc., have been reported in individual cases, following ordinary vaccination on the arms.

Revaccination. The extent to which the first vaccination is efficient is generally estimated from the number and depth of the scars, and amongst fatal cases in epidemic times an inverse proportion has been shown between the number of the scars and the percentage of fatal cases, the mortality being least in those with four or more scars, greater in those with only one scar, and most of all in those stated to have been vaccinated, but without any visible scar at all. But in any case the protective influence of vaccination has only a limited duration, probably from twelve to fifteen years. It thus becomes desirable that every one should be again vaccinated in childhood or early puberty, and subsequently at any age, if small-pox should become epidemic. According to the extent to which the influence has faded, revaccination will have different results. It may fail entirely, or only produce a little local irritation; or it may produce a typical vesicle.

CHICKEN-POX

(*Varicella*)

Chicken-pox is a specific infectious disease characterised by an eruption of vesicles. The nature of the virus is unknown. It commonly occurs in children,

but may attack both infants and adults. Contagion is conveyed by the air or by clothes, and possibly by the pus from vesicles or scabs, as it has been successfully inoculated. An attack confers immunity, as a second attack in the same person is quite uncommon. Although it has often been confounded with small-pox, it is certainly a different disease: vaccination does not protect from varicella, nor varicella from small-pox. The association of varicella and herpes zoster is close; are both due to the same virus? (*see* Herpes Zoster).

Symptoms. The period of *incubation* is eleven to nineteen days. The eruption consists at first of pink spots or papules, on which, in twelve or twenty-four hours, vesicles form. These are generally tense, hemispherical, and from $\frac{1}{8}$ to $\frac{1}{4}$ inch in diameter. At first the fluid is clear and colourless, but it soon becomes opalescent or milky, and then the vesicle shrivels, and a yellow or brown scab forms, which adheres for a few days, and then separates, leaving a pink stain. The perfectly formed vesicle is surrounded by an inflammatory zone, which subsides as the vesicle dries. They are more superficial and less loculated than in small-pox. Some of the pocks, but never a large number, result in depressed cicatrices.

The period of invasion is represented by febrile reaction, which is generally very slight; a diffuse or patchy erythema may come out before the proper rash, which, however, shows itself within twenty-four hours. It appears earliest, and is seen most commonly on the chest, but the face, trunk, and limbs are also affected. The spots are not very numerous, but fresh ones form for two or three days after the first appearance, and altogether they number, as a rule, from fifty to 200. A few vesicles form on the mucous membrane of the mouth, palate, and lips. Whatever fever preceded the vesicles continues for a few hours, or for two or three days; it is generally not above 102°, but may reach 104°. The lymphatic glands of the neck may be enlarged. Very occasionally encephalitis is a late symptom (see later).

In *varicella gangrenosa* some of the vesicles increase in size, become purulent, form reddish-brown or black scabs under which the skin sloughs, and ultimately leave circular ulcers with clean-cut edges. The child becomes very ill, and death may take place. In *V. bullosa* large bullæ are found in addition to the usual vesicles.

Cases have been recorded in which *hæmorrhage* has occurred into and around the pustules, as well as at other points in the skin; while there have been bleeding from the nose, mouth, vagina, and rectum, and petechiæ under the serous membranes. Most of these cases have ended fatally.

Treatment of Varicella. Children should be isolated, but confinement to bed is not often necessary. Light diet and attention to the bowels are often all that are required.

Differential Diagnosis of Small-pox and Chicken-pox. Varicella is sometimes difficult to distinguish from modified small-pox, and in epidemics of the latter it has been found desirable to make varicella "notifiable" (*see* p. 13), so that no case of small-pox may escape the attention of the sanitary authorities. Since the differential diagnosis of these two conditions is one of the most important issues in the diagnosis of fevers, it is treated at some length. *See also* Diagnosis of Small-pox (p. 32). In the first place the patient must be examined in a thoroughly good light, and as much of the skin as possible should be seen at one time by making the patient take off his clothes and use a blanket as a covering.

According to Wanklyn (**2**) the four most important groups of clinical phenomena are as follows:

(1) Prostration. This is usually a reliable sign of small-pox when considered in proportion to the density of the rash. A copious rash preceded by complete absence of prostration is strongly against small-pox.

(2) Distribution of the rash is the most important of all. Killick Millard (**2**) writes as follows: "(1) Ignore the head and neck. (2) Divide the rest of the

body into (*a*) trunk and (*b*) limbs. Then, if the lesions on a careful count be more numerous on the limbs, the case is almost certainly one of small-pox; whereas if they be more numerous on the trunk it is almost certainly chicken-pox. It is true that there are a few cases in which the lesions may be almost equally divided, and in order that any error may be on the safe side—that is, in the direction of suspecting small-pox even though the case be one of chicken-pox, rather than *vice versâ*, it is well to weight the test by counting the buttocks and shoulders as being part of the limbs; though in reality I believe that these regions should be counted with the trunk if the test is to give the greatest proportion of correct results."

(3) Localisation or depth in the skin. In varicella the papules are superficial, in small-pox deep. It is specially useful to regard those lesions which occur on the tenderer portions of the skin, such as over the axillæ, chest, or flanks; relative depth in the skin is more readily appreciated in such situations, and by rolling a loose fold between the finger and thumb.

(4) Maturation. This means that the rash of small-pox tends to progress at a definite rate. In *varicella* vesiculation of papules occurs within a few hours, and is complete within twenty-four or at most forty-eight hours, the contents being turbid and not often really purulent. The pocks dry up in two or three days from the onset of the rash. In *small-pox* vesiculation of the papules is usually noticed on careful examination after forty-eight hours. It takes another four days before it is complete. Nearly all the pocks pustulate in severe small-pox, but the change is not complete until the sixth day of the rash. In variola minor fewer pocks become pustular. The whole rash may abort in the vesicular or semi-pustular stage. If a rash is papular and remains so for three or four days it cannot be small-pox. A hæmorrhagic case is often diagnosed by the supervention of the papular rash; that is only to say again that the rash of small-pox develops and matures.

MUMPS

(*Specific Parotitis*)

Mumps is a specific contagious disease, of which the essential lesion is an inflammation of the parotid gland.

It occurs mostly in children and young adults; young infants, as well as elderly people, are more rarely affected. Males are more susceptible than females. No micro-organism has been identified; but it appears that the virus is filterable, like that of poliomyelitis; and serum from the diseased parotid, injected into monkey's parotids, has produced symptoms comparable with those of mumps.

Symptoms. The period of *incubation* is fourteen to twenty-eight days. The commencement may be shown by slight malaise for a day or two, but the first symptom is often a feeling of pain and stiffness in the jaw and cheek of one side. Swelling then takes place just beneath the lobule of the ear, so that this is pushed out, and the depression between the jaw and the mastoid process is filled up. The swelling then spreads lower, beneath the ramus of the jaw, and may involve the sublingual and submaxillary glands. After a day or two the glands of the other side become involved, and thus there is a collar of swelling round the whole jaw from side to side. The swelling is pale, shiny, doughy in consistence, and tender when touched; but suppuration rarely takes place. Internally the tonsils and fauces are somewhat swollen. As a result the teeth can be separated with great difficulty, and not for more than half an inch or so; and mastication and deglutition are very painful, the pain on movement of the jaw being darting, and lasting for some time. The secretion of saliva may be normal, or increased, or diminished. There is a moderate degree of fever, the temperature rising often to 102°. There is a relative and absolute increase of the lymphocytes in the blood, and this condition lasts for fourteen days. The swelling lasts from seven to ten

days, and slowly subsides; and the patient is usually quite well within three weeks. Occasionally the skin over the gland desquamates. Cases of mumps have been described, in which the submaxillary glands have been alone affected.

Complications. As a result of mumps it happens occasionally that *orchitis*, or inflammation of the testicles, occurs just as the parotitis is subsiding, *i.e.* about the seventh or eighth day; but it may be earlier or later than this, and may, indeed, precede the parotitis. It occurs in from 20 to 30 per cent. of male cases, and is more common in adults than boys. The process begins in the epididymis; the testicle swells, and there may be effusion into the tunica vaginalis and œdema of the scrotum; it is accompanied by pain and tenderness, a rise in temperature, which may reach 104°, and in rare cases by acute delirium. The inflammation subsides in a few days, but it may be followed by a permanent atrophy. More rarely there is double orchitis. In females the mammæ may inflame (*mastitis*) or the external genitals swell, and rarely the ovaries are tender. Mastitis has also been seen in boys. *Pancreatitis* has also been recorded, occurring generally at the end of the first week, and lasting from two to seven days; but it has been known to precede the parotitis. It is shown by pain in the epigastrium and left hypochondrium, tenderness and swelling in the same region, pyrexia, nausea, vomiting, and occasionally by diarrhœa or the passage of fat in the stools. Diabetes has also been described. Meningitis, optic neuritis, otitis, peripheral neuritis, bulbar paralysis, endocarditis and nephritis are rare sequelæ.

The **Anatomical Change** in mumps is an inflammatory infiltration, serous and cellular, of the interalveolar fibrous tissue of the salivary glands.

The **Diagnosis** presents no difficulties, and the **Prognosis** is favourable.

Treatment. The patient should remain in one room; and confinement to bed is believed to lessen the liability to complications, especially in males, in relation to orchitis. Locally fomentations generally give relief.

INFLUENZA

This term, often wrongly applied to any severe nasal catarrh, is the name given to an acute febrile disease which in past times has frequently swept as an epidemic over Europe, but which was practically unknown among us after the violent outbreak of 1847–48 until the winter of 1889–90, when it again appeared. On this occasion it was first observed in Bokhara in the preceding May; it appeared at St. Petersburg in October, and soon invaded Austria, Germany, France, England, and other European countries, as well as the United States of America. A few months later it was conveyed to India, Australia, New Zealand, the African coast, and South America. The disease has again frequently broken out in the British Isles, and of late years has rarely been entirely absent. The last great epidemic, which appeared first of all in Spain, broke out in England in the form of three waves: the first and slightest in point of mortality in June and July, the second and most severe in November, 1918, and the third in February and March, 1919. It is a characteristic of influenza that, while children and elderly people usually escape death, the disease is particularly fatal between twenty and forty years of age.

Lesser epidemics, milder in form, characteristically precede and follow the major epidemic, the next visitation of which is prophesied between 1945 and 1955. Further, it would seem that before and after a major influenzal epidemic there are seen in epidemic form various diseases of the nervous system, of which the most consistent seem to be poliomyelitis, cerebro-spinal meningitis, and encephalomyelitis (lethargic or spasmodic) (**19**).

Ætiology. The true epidemic invasions of influenza have always been characterised by the extraordinary rapidity with which the population has been attacked, especially in crowded towns. Hundreds have been struck down at

the same time. This feature was especially marked in 1889–90. Infection takes place by inhalation of droplets of sputum or saliva projected into the air during coughing and speaking.

In 1892 Pfeiffer discovered a minute bacillus, which is commonly present in the sputum of influenza patients and less commonly in the blood. It is called the *Hæmophilus influenzæ*, and until recently has generally been regarded as the cause of influenza. The bacillus has been cultivated post mortem in 98 per cent. of cases of pneumonic influenza. But it is also present in various parts of the respiratory tract in a smaller proportion of people who have died of quite other diseases (**18**).

However, evidence has been forthcoming (**20**) that the cause of the disease is a virus or minute filter-passing organism. It is obtained from the nasal secretions of patients early in the disease, when the *H. influenzæ* is often absent, and influenza has been produced by cultivation of this organism, which has been named the *Bacterium pneumosintes*. Bacteria-free washings from the nasal mucous membrane of influenza patients, but not from a subject with a common cold, have been found to infect ferrets, and the disease can be passed on from ferret to ferret, while serum from influenza convalescents neutralises the virus of the ferret disease. The *H. influenzæ* probably plays an important but secondary *rôle* in the disease by producing the various respiratory complications; this has been proved to be the case with swine influenza, the virus by itself producing a very mild form of attack, while the fully developed disease results from a symbiosis of the virus and the influenza bacillus. An attack of influenza protects the subject for some months at least, but the acquired immunity is not indefinite. In the last epidemic about 20 per cent. of patients had had previous attacks.

Morbid Anatomy. Tracheitis, bronchitis and bronchiolitis are always present. There may be extreme congestion of the lungs, hæmorrhagic œdema or diffuse hæmorrhage without consolidation, or on the other hand solid hæmorrhagic areas involving a whole lobe, or occurring in patches like infarcts. There may be broncho-pneumonia or multiple abscesses, usually small and aggregated, or actual gangrene. There may be multiple small areas of collapse or massive collapse. Peribronchitis and interstitial emphysema may occur, and also pleurisy with or without effusion. The bronchial glands are inflamed. In most cases the sphenoidal sinuses and other accessory air sinuses are infected. The primary focus of the infection in the body is probably situated in the nasopharynx. The kidneys contain excess of blood, but otherwise look normal (*see* Acute Nephritis).

Symptoms. The incubation period is from just under forty-eight hours to five days. There is the greatest possible variety in the manifestations of influenza. In a large number of cases the symptoms are those of an acute febrile illness, without special determination to any one organ or system of the body. This may be described as the *simple* type, or *simple febrile* type.

The disease begins suddenly with severe frontal headache, pains at the back of the eyes and muscular aching and pains in the muscles of the loins, thighs, calves, and other parts of the body. Rigors are often absent, but the temperature rises within a few hours to 102°, 103°, or 104°. The other accompaniments of fever are present, such as quick pulse, thirst, and scanty, high-coloured urine. The systolic blood pressure falls by 10 or 20 mm. (**54**). The tongue is flabby, tremulous, indented, and covered with a thick white fur. The fauces and tonsils are red, and the breath is offensive; epistaxis is fairly common. The skin is generally dry, but there are sometimes profuse perspirations. The spleen is sometimes slightly enlarged. The patient is exceedingly ill, restless, sleepless, prostrate and depressed. No other symptoms may appear, and the temperature falls in twenty-four, thirty-six, or forty-eight hours as rapidly as it rose; but the general pains in the limbs continue for some time after the temperature has fallen,

and the sense of prostration, which is present from the first, persists for some days after the fever. However, it must be admitted that there is much variety in the course and duration of cases in this group ; and that while in some the fever is high, of short duration, and falls rapidly, in others the course is longer, and the fall of temperature more gradual, so that a confusion with other febrile illnesses, such as typhoid fever, is rendered possible. In either case there may be a relapse.

In the *pneumonic* type of the disease, which occurred in about 20 per cent. of cases ill enough to be admitted to hospital at Aldershot during the 1918–19 epidemic, the commencement presents the same features, namely, fever, headache, pains in the limbs, and prostration ; but it is soon seen that the respiratory tract is largely involved. There are rapid breathing, pain in the chest and troublesome cough. The signs in the chest are extremely variable : there may be no signs except a few scattered rhonchi in front and some crepitations behind ; again, the signs may resemble those of a lobar pneumonia ; again, râles may be heard everywhere with no signs at all of consolidation ; again, consolidation may appear in one part of the lung to be replaced on the next day by vesicular murmur, but to appear in another part of the lung ; again, signs of fluid may be present. The prognosis cannot be gauged at all by the extent of consolidation of the lung. The sputum may be either purulent and abundant or blood-stained, tenacious, frothy, and rather scanty. In the most serious cases there is a uniform heliotrope cyanosis over the face, associated with marked deficiency of oxygen in the arterial blood. Nephritis occurs in the majority of pneumonic patients. There is no œdema usually, but the urine contains albumin and casts. Nasal catarrh with suffusion of the conjunctivæ is occasionally a condition of influenza, but both the simple and respiratory forms commonly occur without them.

The *abdominal* type is less frequent, but varies with different epidemics. The patient has abdominal pain, diarrhœa, vomiting, and occasionally jaundice. The temperature is often less high than in the preceding forms.

Both the respiratory and the gastro-intestinal symptoms may appear to be rather complications and sequelæ than parts of the original disease ; that is, the fever and pains may be present for a few days before either of these systems is manifestly involved. Other systems are also involved more often secondarily or rather late in the history. Sometimes the pulse is irregular or intermittent, due to auriculo-ventricular or sino-auricular heart block ; there may be syncopal attacks. Tachycardia also occurs, and the heart may show evidences of dilatation. Hæmorrhages from the different mucous surfaces are sometimes observed.

The nervous system is frequently involved. Drowsiness occurs in early stages, with delirium in severe cases. Later there may be sleeplessness, a persistent neuralgia, or muscular pains. In a large proportion of cases, and without any special localisation of symptoms in the nervous system, there is prolonged weakness of the limbs, inability for physical and mental exertion, and great mental depression lasting for months after the beginning of the attack. The skin is occasionally the subject of eruptions in the height of the attack, or a little later. These are mostly in the form of rose-coloured spots, or erythematous rashes like those of measles, scarlatina, or urticaria ; alopecia may occur. In addition there is scarcely any local inflammation that may not in some case or other appear as a sequel of influenza ; for instance, otitis, which is rather common, orchitis, peripheral neuritis, myositis, phlebitis, parotitis, pericarditis, meningitis, encephalitis, myelitis, conjunctivitis, keratitis, arthritis, and lymphadenitis. Amongst the sequelæ are loss of taste and smell and almost any type of mental disorder.

Early in the disease the blood shows a polymorphonuclear leucocytosis. This is followed by a leucopenia with a deficiency of polymorphonuclear cells and a relative lymphocytosis (**21**). If pneumonia supervenes there is a leucocytosis

with a great increase in polymorphonuclear cells. The hæmorrhagic nature of the pneumonia may be associated with the diminution of blood-platelets (*see* p. 446), which has been observed.

Diagnosis. The great variety that influenza presents will lead to its being diagnosed in the early days of an illness, when further acquaintance with the case may show it to be some other febrile complaint, such as pneumonia, and especially enteric fever (*see* p. 78). The very sudden onset, the local pains, low systolic pressure, and the short fever are the chief distinguishing points of influenza; but there are slight cases which can only be diagnosed by way of exclusion, by the amount of depression succeeding it, or by its complications and sequelæ.

Prognosis. Death only occurs in a small proportion of cases attacked. Cyanosis in a pneumonic case is always a bad sign, and if the temperature suddenly falls in such a case, it is almost hopeless.

Prevention. There is statistical evidence that prophylactic inoculation with a stock vaccine containing 400 million *H. influenzæ*, 80 million streptococci and 200 million pneumococci prevents the onset of influenza or rather prevents the onset of the complications, which are the main part of the disease. It is important for all persons in attendance on influenza patients to wear masks consisting of several layers of butter muslin. In the last epidemic such masks were worn with effect by people in crowded places. The evidence in favour of taking quinine as a prophylactic is not good. The instillation into the nose of Glegg's paraffin and vaseline mixture, so effective against coryza (*see* p. 196), is well worth a trial during an influenza epidemic.

Treatment. The patient should save his strength by at once taking to his bed and the general treatment of pyrexia instituted. In the early stages the severe pains call for treatment, and may be met by sodium salicylate (10 to 15 grains every four or six hours), by aspirin (7 to 10 grains), or by phenacetin (5 to 6 grains). The great tendency to prostration after the illness makes it necessary to give these drugs with caution. Bronchitis or pneumonia may require treatment.

ACUTE POLIOMYELITIS

(*Acute Anterior Poliomyelitis, Acute Polioencephalitis, Heine-Medin's Disease*)

For years it has been known that children were liable to suffer from paralysis and atrophy of one or more limbs, or part of a limb; and that this paralysis was due to an acute inflammation of the anterior grey cornua of the spinal cord. Such cases were called *infantile paralysis*, and later *acute anterior poliomyelitis* (πολιός, grey). These cases occur sporadically, but two or more members of one family may be affected, and there are sometimes epidemics. Although the disease attacks the spinal cord most frequently, it may also attack any other part of the central nervous system. The term *polioencephalitis* has been used for certain of these cases; but it is best avoided, so as to prevent confusion with acute encephalitis, which is closely related, but is a different disease.

Ætiology. Whether sporadic or epidemic, the disease attacks infants or children with much greater frequency than adolescents or adults; for instance, in a large epidemic two-thirds of the cases were under six years of age, and five-sixths under ten years. It is most frequent in the summer and autumn months. The micro-organisms causing the disease are minute globoid bodies arranged in pairs, measuring 0·15μ to 0·3μ in diameter; these are so small that they readily pass through a porcelain filter; they can be cultivated anaerobically on a special medium, and cultures reproduce the disease by inoculation into monkeys, from which animals the organism can be again recovered in pure culture (Flexner and Noguchi, 1913). Washings from the nose, mouth, pharynx, upper air passages, and small intestines of patients when filtered produced the disease in monkeys,

and there is evidence that healthy people may act as *carriers*. The disease may also be spread by patients who have the *abortive* form of the disease. There is considerable doubt as to whether the virus is conveyed by flies, dust, or external objects. Milk was a vehicle in one small epidemic (**33**). It is believed to pass to the central nervous system along the axons of the peripheral nerves, and the axis cylinders of the olfactory nerves, which lie exposed in the nasal mucous membrane, may be the sole means of approach. The virus passes through the brain by axonal channels and has a special affinity for the grey matter of the cervical and lumbar enlargement. Paralyses may occur in domestic animals, particularly during epidemics; but they are probably not due to the same disease.

Morbid Anatomy. The essential lesion is in the nerve cell. The nerve cells, especially those of the anterior cornua, present various degrees of degeneration up to complete disappearance; and they may be seen infiltrated with polymorphonuclear and mononuclear cells (*neuronophagia*). The lesion of the anterior cornua is followed by secondary degeneration of the nerve fibres of the motor roots, and atrophy of the muscles supplied by them. Some secondary changes take place in the white matter, and the meninges. The pia mater is œdematous and infiltrated with mononuclear cells; there is œdema of the affected part of the cord, proliferation of cells in the sheaths of the blood vessels both in grey and white matter and in the meninges, and cell infiltration of the substance of the grey matter. The same acute processes may occur in patches in the medulla, pons cerebrum, cerebellum, and meninges.

In some fatal cases, in addition to the lesions of the nervous structures, the lymphoid tissues of the small intestine, the thymus and the spleen have been enlarged, and there has been some degeneration of the gland cells of the liver.

In cases dying after years of permanent atrophy of one or more limbs, the cord presents changes obvious to the naked eye. The motor nerve roots, coming from the part presumably affected, are diminished in size and number. On a transverse section the cord is smaller on the affected side, and the anterior cornu is shrunken. Under the microscope there is an almost entire absence of motor nerve cells and axis cylinders; the few nerve cells that remain are smaller than normal, shrunken, fusiform, and wanting in processes, and lie in a dense felt-like overgrowth of neuroglia. The motor nerve roots, both in and beyond the cord, show the destruction of axis cylinders, and are obviously degenerated.

The muscles in physiological connection with the damaged parts undergo fibrous or fatty degeneration, which may be partial or complete. They are pale pink, watery in appearance, and present under the microscope changes due to lesions of motor nerves.

Symptoms. For the sake of convenience, a number of clinical forms of the disease have been described depending on the part of the central nervous system attacked. It must be remembered that individual cases are often a mixture of two or more forms. Certain *general symptoms* common to all forms may first be described. The period of *incubation* is from four to twelve days. The onset is rapid: there are feverishness with headache, and drowsiness, and severe pains in one or more limbs, suggesting acute rheumatism. The pain is increased on movement. Convulsions, vomiting and diarrhœa sometimes occur. While drowsy the patient may pass urine and fæces involuntarily. There may be a diffuse erythema, or a vesicular rash, and occasionally herpes zoster. Tingling or formication may accompany the pain in the early stages, but there is never any considerable loss of sensation, and the above symptoms pass away in a few days. Catarrhal symptoms —nasal discharge, cough, sore throat—are uncommon.

The cerebro-spinal fluid in about 80 per cent. of the cases shows an increased cell count in the first week of the disease; in the earliest stages this may consist largely of polymorphs, but after the first two days lymphocytes predominate, and at the end of the first week polymorphs are seldom found. By the end of

the second week the cell count is usually normal. The protein almost always shows a slight increase; this occurs in the second week of the illness, and often persists after the cell count has returned to normal. The sugar and chlorides are not diminished.

1. *Spinal* Form. This accounts for about three-quarters of the cases. It usually shows itself as a paralysis of the limb muscles; but the muscles of the trunk, abdomen, and neck are also sometimes involved.

In the course of twenty-four or forty-eight hours it is found that there is weakness or definite paralysis of certain muscles, or a child may go to bed well and be found to be paralysed in the morning. It frequently happens that three or four limbs are paralysed at first, and recovery quickly takes place in two or three, leaving the others permanently affected; in other cases, certain limbs are affected from the first and remain so. The paralysis, however, need not involve the whole of a limb, but, it may be, only a part of it, or even one muscle group. If paralysis affects both legs, or the arm and leg on one side, it is not distributed uniformly, as in some other forms of paralysis. The affected muscles rapidly undergo atrophy, lose bulk, and become flaccid; when tested electrically some days after the onset they show the reaction of degeneration or in severe cases do not respond at all to either current. All the deep reflexes are lost in the most affected parts, and generally the superficial reflexes as well.

Although the disease in most cases attacks principally the grey matter of the spinal cord, a complete transverse lesion is occasionally seen; in the cervical region such a case shows loss of power and wasting of the muscles of the hands and arms and spastic paralysis of the legs. Mention must also be made of certain "jump" cases. The disease may, for instance, involve the legs and remain stationary for some days, when a more widespread paralysis affecting the muscles of the trunk or upper limbs suddenly takes place, or this extension may take place gradually. It may pass downwards along the cord as well as upwards. Some of these cases closely resemble Landry's paralysis. In addition, *relapses* may take place after some weeks' interval.

At the end of the febrile period the muscles which remain paralysed after the first partial recovery will themselves improve only very slowly after weeks and months. The amount of impairment in the use of the limbs will depend on the number of muscles atrophied; but after a time, in many cases, lost movements are restored by fresh combinations among the muscles which have been spared. Atrophy is, in almost all cases, a prominent feature, hollowing out the rounded part of the forearm, or reducing the upper arm or the leg to a mere stick. Sometimes, however, the loss of muscle may be entirely concealed by the presence of fat; the flabby condition of the muscle even then can be generally recognised. Associated with the atrophic condition of the muscles is generally a change in the vascularity of the limb; it is cold, shrunken, and blue or livid from retarded circulation. The nutrition of the bones and other parts is also involved, so that a limb paralysed in infancy or early childhood does not grow with the same rapidity as its fellow, and may be shorter by ½ inch, 1 inch, or more. Lastly, deformities may occur besides those directly due to loss of muscular substance, owing to faulty treatment. Some are the simple result of failing muscular support; thus, from atrophy of the deltoid, the humerus falls from the glenoid cavity. Others consist of permanent changes in the position of the limbs, such as talipes equinus, which so often results from paralysis of the anterior tibial muscles.

2. *Bulbar, Pontine, and Mid-brain* Forms. Any of the cranial nerve nuclei may be attacked as well as the tracts passing through this part of the brain. The seventh nerve is the one most commonly affected. Some cases hitherto diagnosed as Bell's palsy are due to poliomyelitis.

3. *Cerebral* Form. Hemiplegia is the commonest manifestation of this form of the disease; but it is not a common cause of hemiplegia in children, accounting for at most 10 per cent. of the cases (*see* also encephalitis). Athetosis is rare.

4. *Cerebellar* Form is indicated by the occurrence of cerebellar ataxy, the characteristics of which are described later.

5. *Meningitic* Form. Symptoms of meningitis are not at all uncommon in acute poliomyelitis. After severe headache the patient may become comatose with rigidity of the muscles at the back of the neck, with convulsions, and with typical changes in the cerebro-spinal fluid.

6. *The Abortive* Form is only recognised where there are epidemics of acute poliomyelitis. There are fever, headache, pains in the limbs, and general weakness, but no paralysis.

Diagnosis. The symptoms of fever, headache, vomiting, convulsions and pain may be caused by many acute illnesses, such as meningitis or pneumonia. The muscular power, the loss of which is the distinctive feature, should be critically examined from the first, in view of the fact that young children will not volunteer the information. After some days the diagnosis is confirmed by the rapid atrophy, by the loss of reaction to the faradic current, and the changed reaction to galvanism. The pain which is sometimes present may suggest *rheumatism*, but it is situate rather in bone and muscle than in the joints; in infants *scurvy* must be thought of. The disease may also be confounded with *Landry's paralysis*, with *multiple neuritis*, due to some other organism, to alcohol or other poison, or with acute myelitis, due to some other infection. Pain and tenderness are not usual in Landry's paralysis, but some cases described as Landry's paralysis have certainly been actually poliomyelitis. In the early stage, and in abortive cases, the diagnosis may often be established by examination of the cerebro-spinal fluid. The normal chloride content in poliomyelitis is a useful point in the differential diagnosis from tuberculous meningitis. A method of *serum diagnosis* is also available. This depends on the fact that a 5 per cent. emulsion of spinal cord containing the virus will cause the disease in monkeys if injected intracerebrally; but if mixed with an equal volume of serum from a patient who has recovered, it will be inert. By such means it is possible to find out definitely whether certain suspected cases had really had the disease, which would be valuable from the public health point of view.

Prognosis. In recent epidemics of this disease the mortality has varied from 10 to 20 per cent., a much higher mortality than was recognised in sporadic cases, in which life was not generally regarded as endangered. On the other hand, complete recoveries appear to be more frequent in epidemics. Death is due generally to respiratory paralysis or to broncho-pneumonia if the respiratory muscles are interfered with; it rarely occurs if the fourteenth day is safely reached. Not more than about 15 per cent. of cases show complete recovery. In the remainder most of the muscles originally paralysed eventually recover, but one or two groups remain permanently damaged. Most improvement takes place during the first six months, and it continues slowly for two years. After this time very little further improvement is likely to occur. Second attacks are extremely rare.

Prevention. Patients and contacts should have their nasal and buccal cavities frequently washed out with a solution of potassium permanganate of 1 to 2,000, to destroy the virus. The period of quarantine for contacts is fourteen days. The patient should be isolated for at least three weeks, and as long as there is any nasal discharge he should still be considered infectious. He may, like a case of typhoid, be treated in a general hospital ward.

Treatment. The general treatment for pyrexia is instituted. Aspirin or sodium salicylate may be given to relieve pain, or even morphia in extreme cases, in doses appropriate to the age. Hexamine may be given in doses up to to 50 grains, as being an antiseptic which is secreted into the cerebro-spinal fluid, provided that the urine is kept alkaline; but estimates as to its value vary. More active measures have been advised, *e.g.* lumbar puncture, which relieves pressure, and with this the intraspinal injection of adrenalin chloride solution

(1 to 1,000) in doses of 1 or 2 c.c. every six hours, or the intraspinal injection of an immune serum, that is, serum obtained from the blood of persons who have suffered from the disease months or years previously, in doses of from 10 to 30 c.c. daily (Netter). The serum of normal adults has also been found to render monkeys free from the disease when injected with the virus. The cases suitable for this treatment are (1) those in which the diagnosis can be made in the pre-paralytic stage; (2) those with symptoms of meningitis; (3) those in which the paralysis is extending. The treatment is useless for muscles which already show paralysis. Unfortunately, this treatment has recently been found to be useless when tested on a large series of controlled cases in New York, and in any case it has been argued on theoretical grounds that the serum should be administered intravenously rather than intrathecally (**31**).

Where there is respiratory paralysis life may be saved by means of the Drinker's respirator—a metal box in which the patient lies with the head projecting; the pressure inside the box can be varied so that the respiratory movements are performed. The Bragg and Paul apparatus might also be used. The chest is surrounded with an air-tight rubber bag furnished with an inextensible outer covering. The pressure in the bag is alternately raised and lowered by a motor pump. In these apparatuses treatment over weeks may be required. For shorter periods Eve's rocking method may be employed. The patient is fastened prone on to a stretcher, which is pivoted on a support like a see-saw. Tilting up and down causes the diaphragm alternately to descend into the abdomen and ascend into the chest.

The *immediate* treatment of the affected muscles consists in *rest*, in the so-called *neutral* position, so as to keep the muscles intermediate in length between contraction and relaxation. This position may be maintained by quite simple apparatus such as sand-bags or wooden splints. The correct position of the upper limb is with the thumb adducted, the fingers slightly flexed, the wrist straight and half-way between supination and flexion, the elbow slightly flexed and the shoulder partially abducted from the side. The lower limb should be placed with the foot at right angles to the leg and the knee slightly bent and the hip straight. When one leg is affected the other one should also be kept in splints to prevent asymmetry of the pelvis. In three or four weeks' time it will become obvious what special muscle groups are paralysed, and then the position of the limbs and body should be altered, so as to allow complete relaxation of the paralysed muscles, with a consequent overstretching of the healthy antagonists. In most cases this will mean that the shoulder must be abducted at a right angle and the wrist dorsiflexed. Light celluloid splints may be used, the splint being moulded on an accurate cast of the limb. If both legs and trunk muscles are paralysed, some degree of lordosis should be brought about by supporting the back in the lumbar region, as in this position the patient could eventually walk with the aid of retentive apparatus.

Re-education of paralysed muscles should begin as soon as the temperature has subsided and the pain has gone. This consists in getting the patient to use the muscles at stated intervals each day; he should attempt to move them himself, and even if no movement results the attempt should still be persisted in; the effect of gravity should be diminished or abolished, and the amount of work the muscle is called upon to do should be minimal to begin with. For instance, with a weakened quadriceps the knee is at first flexed to a small extent with the patient lying on his back, and he is told to straighten it. The amount of flexion is gradually increased. It is valuable sometimes to carry out these movements in a bath, as the water gives some support. Between the exercises the splints must be kept on, and during the exercises the paralysed muscle should *never* be allowed even for a moment to become overstretched, at any rate for the first few months. Galvanism should be used for completely paralysed muscles and massage after the first few weeks helps the circulation. The re-education of

the trunk and abdominal muscles can be best carried out by the patient walking about in the erect position. This can be done when the patient's paralysed legs have been splinted, if he uses a walking machine.

It must be recognised that if nerve cells are completely destroyed the muscular fibres dependent upon them will be irretrievably atrophied, so that later, surgical measures may be required.

PSITTACOSIS

This is a condition due to a filterable virus (**27**), which occurs among parrots (ψιττακός, a parrot), and in which enteritis, sometimes hæmorrhagic, is a prominent symptom. The disease is communicable to other small animals and birds, and also to man, probably by the feathers soiled with fæcal matter. In man the disease somewhat resembles typhoid fever. The incubation period is from seven to twenty-five days; and then occur suddenly fever with rather slow pulse, intense headache, generally occipital, anorexia, restlessness, delirium, abdominal distension, vomiting, diarrhœa and albuminuria. Broncho-pneumonia, with frequent cough, is observed in many cases, and the mortality is about 30 per cent. An epidemic occurred in Paris at a time when it became the fashion for ladies to carry about parrots as pets, and this disease again appeared in 1929 in this and other countries.

FOOT-AND-MOUTH DISEASE

(*Aphtha epizootica*)

This disease of cattle and sheep is occasionally transmitted to man. The typical feature of the disease in cattle is the formation of vesicles and bullæ on the mucous membrane of the mouth, lips, and tongue. The affected parts become swollen, and the saliva dribbles away. The vesicles break, leaving a grey layer covering the base. Vesicles also appear on the feet round the borders of the hoofs, and they become pustular and produce crusts. In cows vesicles form also on the udders and teats. There is a moderate degree of pyrexia. The disease lasts about a fortnight, and generally ends in recovery, except in calves, of which from 50 to 75 per cent. die, some from enteritis.

The disease appears to be conveyed to man by direct inoculation, and by drinking milk from an infected cow; but it may also be carried from man to man in boots or clothing.

The virus will pass the finest filter. The *incubation* is from three to five days. Slight pyrexia and loss of appetite first occur; then vesicles are observed in the mouth, on the lips, tongue, fauces, and hard palate. They reach the size of peas, become opaque, break, and form shallow ulcers, with a dark red base. The lips become swollen, and saliva and mucous are more abundant than normal. Mastication, swallowing, and talking are somewhat painful. There may be some diarrhœa and abdominal pain.

Sometimes vesicles form on the fingers, especially about the nails; they become pustular, and run together; and similar vesicles occur on the toes, on the soles of the feet, and on the nipples of women. The duration is from ten days to a fortnight, and the disease is rarely fatal.

Treatment. Washes of borax, of potassium chlorate, or of potassium permanganate should be used to the mouth, and painful ulcers should be touched with solid silver nitrate. Zinc or lead ointments or lotions to relieve itching should be applied to the eruptions on the fingers and toes.

GLANDULAR FEVER

This complaint, described by Pfeiffer, Park West, Dawson Williams, and others, consists of an inflammatory swelling of the deep cervical and other

lymphatic glands associated with fever. It may occur in epidemics, is mildly infectious, and affects chiefly children and young adults. It has an incubation period of from five to seven days. The patient is taken suddenly with stiffness in the neck, difficulty of swallowing, and febrile reaction, with anorexia and perhaps vomiting. The fauces are often reddened, but otherwise little affected. On the second or third day of pain the cervical glands, and generally those under the sternomastoid muscle and along its anterior border, are found to be enlarged and tender. In another day or two those of the other side are swollen, and the posterior cervical, axillary, and inguinal glands may be also involved. The glands on the left side are usually larger than those on the right. The enlargement may be delayed for two weeks or more or may be so slight as to escape notice (**10**). There is generally abdominal pain and tenderness; and the liver, spleen, and mesenteric glands may be enlarged. The glands begin to get smaller after from two to five days, and do not suppurate. The temperature may reach 104° on the third day, and it will continue high as long as the glands remain enlarged. Constipation is often troublesome. The disease subsides usually without complications; but hæmorrhagic nephritis occurs in 6 per cent. of cases, and convalescence may be retarded by anæmia. Various rashes have been described—macular, urticarial, and papular, as in paratyphoid fever, appearing after the fourteenth day of the illness. The bacteriology of the disease is at present negative. The characteristic blood change is an increase in the mononuclear cells, hence the name infectious mononucleosis; these are now regarded as always being lymphocytes though they may resemble hyalines; but they can be differentiated by *intra vitam* staining and the peroxidase reaction.

Diagnosis. The glands enlarge rapidly and there is no anæmia. In spite of the high temperature the constitutional disturbance is usually slight. This latter feature helps to distinguish the disease from acute leukæmia. Cases are often diagnosed as tonsillitis, mumps, acute tuberculous adenitis, or acute Hodgkin's disease (**26**). Paratyphoid fever may also be imitated.

The **treatment** consists in rest, a simple diet, the relief of the constipation by small doses of mercury or salines, and the use of preparations of iron during convalescence.

The following disease is due to Rickettsia:

TRENCH FEVER

During the great European war there was observed, at first almost exclusively in men returning from the trenches, but later behind the front, a form of febrile disease which presented new features, and was essentially different from anything formerly recorded.

Ætiology. The virus of trench fever is conveyed by lice. It has been transmitted by allowing lice that have fed on patients to feed on healthy men, and also by rubbing the excreta of infected lice into abrasions of the skin. There is good evidence that the virus of trench fever is a Rickettsia body. Although these bodies are difficult to find in patients, they appear in the body of the louse just when it reaches its most infective stage, *i.e.*, five to eight days after feeding on an infected patient.

Symptoms. The incubation period is from five to thirty days. The onset is somewhat sudden, and the patient suffers from headache, giddiness, sometimes nystagmus, shivering, and pains in the back and legs. Occasionally he vomits. There are three characteristic types of temperature chart: (1) The single short bout of fever, making the case resemble one of influenza. This is called the *short* form of the disease. (2) The *relapsing* type. The patient has an attack like that just described. After an interval of three or four days he is attacked by the same symptoms, and the temperature again rises, though not quite so high as in the original fever (*see* Fig. 4). (3) The type with the *prolonged*

initial fever, making the case resemble one of typhoid fever; but the symptoms are the same as in the other types.

The disease may last for six or seven weeks, and it is not fatal. Tachycardia

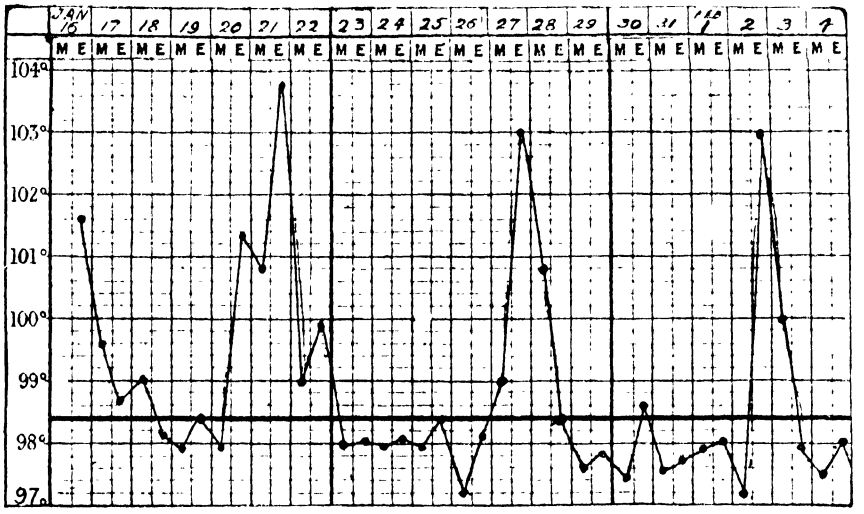


FIG. 4.—Chart of Temperature in Trench Fever.

frequently develops, the disease being a common cause of effort syndrome in soldiers. For further details the last edition of this book should be consulted.

Bacterial Diseases—I. Micrococcal

STREPTOCOCCAL INFECTIONS

A complete description of streptococcal infections would probably mean a description of the greater part of medicine as dealt with in this book, which is quite outside this article, and a brief summary must suffice. Streptococci may gain an entrance into the body through the skin or mucous membranes primarily by themselves, or secondarily in the wake of some other primary invader, *e.g.* the ultra-microscopic virus of influenza. After entering the body they may become localised in one particular area, producing (1) characteristic acute infections—in the skin erysipelas; in the throat tonsillitis which, when milk borne, may be epidemic, or in certain circumstances becomes scarlet fever; in the uterus puerperal fever; in the lungs broncho-pneumonia; in the urinary tract pyelitis; in the joints arthritis, and so forth—or (2) a subacute or low-grade infection—on the heart valves subacute bacterial endocarditis—possibly also acute rheumatism, in the periarticular tissues rheumatoid arthritis, in the tonsils chronic septic tonsillitis, etc.

By special bacteriological technique sixteen types of streptococci have been isolated, and evidence has been forthcoming that some of these strains may be converted into each other by modifying the culture media, etc. For clinical purposes streptococci are commonly divided into two groups: (1) the *S. hæmolyticus*, which on culture hæmolyses the blood cells, and which is usually isolated from acute infections and from some chronic infections too, and (2) the *S. viridans*, which forms a greenish pigment on blood media (probably due to partial hæmolysis), which appears exclusively in low-grade infections. But as in other infections, it is not only the virulence of the streptococcal invader, but the constitution of the host, that determines the exact nature of the infection. Hæmolytic streptococci have three properties apart from causing hæmolysis; they produce an erythrogenic toxin, which is dealt with in scarlet fever; they are pyogenic, and no anti-body has been prepared against this, and they invade

the tissues (**15**). In this connection Lancefield has found three different bodies among the antigens: (1) a nucleo-protein which is non-specific, as it is also formed from pneumococci; (2) a "type specific" protein corresponding to the particular type of streptococcus, and (3) a "species-specific" carbohydrate which is common to all hæmolytic streptococci and which, when linked to protein, acts as a specific antigen. Colonies of streptococci can be picked out when grown on media as a "matt" variety, which is virulent and contains the type-specific protein and an avirulent "glossy" variety which has lost the type-specific protein; but specific carbohydrate and the erythogenic toxin were always present. This will indicate the complexity of the subject from the immunity point of view. The relation of streptococci to acute rheumatism is dealt with later.

SCARLET FEVER

(*Scarlatina*)

Scarlet fever is a contagious disease, characterised by fever, sore throat, a bright red eruption on the skin, and a tendency to certain complications, of which the most important are acute nephritis and otitis media.

Ætiology. Scarlatina is a toxæmia due to the toxins of a hæmolytic strepto coccus (or group of streptococci) known as the *Streptococcus scarlatinæ* (**6**), of which four strains have been isolated. These streptococci can be isolated from the throat and tonsils of patients with the disease; they produce an "*erythrogenic*" *exotoxin* which has the property, when suitably diluted and injected into the skin, of producing an erythematous patch. This toxin is responsible for the rash and is also used for the *Dick test*, which is described later. If it is injected in large amounts into a susceptible individual a miniature attack of scarlet fever may be produced with vomiting, fever, furred tongue, generalised rash, cirum-oral pallor, sore throat, and eventually desquamation. The same toxin may be produced from other strains of streptococci, for instance erysipelas, though it is usually most actively produced by the streptococci of scarlet fever. In addition to the rash the streptococci invade the tissues and produce the various complications such as otitis media etc., acting like any pyogenic organism.

Scarlet fever has been produced artificially by swabbing cultures of the *Streptococcus scarlatinæ* on to the tonsils of susceptible people, and the contagiousness of the disease is due to the discharge of the organisms in droplets of spray from the throat while talking and coughing. But the disease may be spread by means of clothing, books, papers, and other articles to which the virus clings with great tenacity, and by milk used as food. It may be caught from a patient suffering from a streptococcal sore throat, without scarlet fever (**7**).

The vast majority of those attacked by scarlatina are young children; it is comparatively infrequent in adults, and infants up to six months, having received immunity through the placenta, are insusceptible. Protection is not always perfect, so that some people have a second attack. Patients with open wounds and women in the puerperal state appear to be particularly susceptible to scarlatina, probably because the wound or the uterus provides an easy entrance for the virus. The disease in the surgical cases is often mild and not infectious, since there is no discharge from the throat. The rash is partial and of short duration, so that the connection with scarlatina was for a long time misunderstood.

Morbid Anatomy. The organs after death from scarlatina present little that is peculiar. In malignant cases there are the changes (*see* p. 18) common to the pyrexial and septic disorders. The tonsils present the conditions of ulceration or suppuration that have been observed during life, and there may be streptococcal invasion with inflammation of other parts.

Symptoms and Course. The period of *incubation* is one to eight days. Generally the invasion is sudden: the patient has a rigor, or vomits, and complains of frontal headache, with languor, pains in the back and limbs, and loss of appetite. The temperature rises to 103° or 104°, the pulse becomes very rapid, and the respiration is quickened. Very soon there is some complaint of sore throat, and swallowing is painful.

On the second day—that is, generally between twelve and thirty-six hours from the first symptom—the *rash* appears. It is first seen on the upper part of the chest, in front and on the sides of the neck, but soon spreads to the abdomen and back, and then to the upper and lower limbs. It consists of minute red spots, bright in the centre, fading towards the edge, and set closely together, so that the paler edges almost coalesce. Sometimes the coalescence is complete, so that the skin has a uniform bright red colour; sometimes the eruption is more discrete, and areas of pale skin are visible between the spots. The face, forehead, and cheeks are, as a rule, deeply and uniformly flushed, without showing the punctiform arrangement of the rash which is seen elsewhere; but the skin round the mouth remains pale, forming a sharp contrast to the cheeks (circum-oral pallor). With an abundant rash the skin becomes slightly swollen. The eruption presents many varieties as to depth of colour and distribution. It may be only pale pink, or it is deep, livid purple; and in some severe cases papules may be raised above the surface, and may even vesicate or form minute points of pus; and occasionally petechiæ occur. In its distribution the rash may be very limited, occurring only on the chest, or in patches on the thighs, elbows, or ankles, and this occurs frequently in second attacks, and in the mild cases sometimes seen in patients with open wounds, to which reference has just been made. The rash reaches its height on the third or fourth day, and begins to fade on the fourth, fifth, or sixth day; altogether it may last from five to ten days. After the subsidence of the rash *desquamation* takes place—that is, the superficial layers of the cutis are shed. This occurs in the form of white, branny flakes on the sides of the neck, preceded (as pointed out by Caiger) by an appearance of pin-point depressions, due to the rupture of the epidermis at the top of each papule. This may be as early as the sixth or seventh day, while the eruption is still visible on the legs; but the amount of epithelium that is shed and the size of the particles are very variable—sometimes there is nothing more than a little roughness about the tips of the fingers or toes, or in the folds of the palms of the hands; while in other cases the epidermis peels off in large flakes, and in rare instances complete glove-like moulds of the hands and fingers are thrown off. Desquamation commonly takes from four to six weeks, but in these special cases a much longer time is required.

In the throat it is seen that the uvula, soft palate, and fauces are deep red, and often slightly œdematous; the tonsils are reddened, swollen, projecting towards the middle line, and presenting a number of yellow points, from the follicles being distended or covered irregularly with ashy or yellowish secretion. In later stages they may suppurate, or sloughs may form in them. The nasal mucous membrane also inflames, and secretes a quantity of mucus; and the submaxillary and cervical glands become enlarged and tender. The tongue is at first thickly covered with white fur, but in a few days this clears off from the tip to base, leaving a bright red, raw surface, on which the fungiform papillæ are unusually prominent, so as to give the appearance known as "strawberry tongue."

During the course of the disease a temperature of 106° may be reached. With this the skin is pungently hot and generally dry, but profuse sweating may occur. The pulse rises to 120, 140, or even 160. The disease may reach its height about the fourth, fifth, or sixth day, and then, with the fading of the rash, the temperature begins to fall, generally subsiding rather gradually, but sometimes more suddenly, till the normal is reached, and convalescence is gradually established.

Complications and Sequelæ. These are numerous and important.[1] Not only the tonsils, but also the soft palate and the uvula, may slough. More frequently the *glands* under the jaw and in the neck are much swollen, and the subcutaneous tissue about them is infiltrated, becoming brawny and indurated. The skin then assumes a dusky red colour, and sloughing takes place beneath it, separating it from the subjacent tissues over a large area. Such cases are often fatal. During convalescence also *adenitis*, both *simple* (*4·78*) and *suppurative* (*1·23*), is likely to occur. Extension of the inflammation from the throat up the Eustachian tube may cause *otitis* (*8·1*), or inflammation of the ear, resulting in abscess of the tympanum, rupture of the membrana tympani and otorrhœa. This occurs most commonly in the first five years of life. In the course of the scarlatina this may seem of little importance; but it lays the foundation for serious or fatal results months and even years afterwards, among which may be enumerated suppuration of the mastoid cells, meningitis, abscess of the brain, thrombosis of the lateral sinus or jugular vein, with pyæmia as a result, hæmorrhage from the lateral sinus, and facial paralysis. Deafness on the affected side may of course happen, and a double otitis in a young child may be

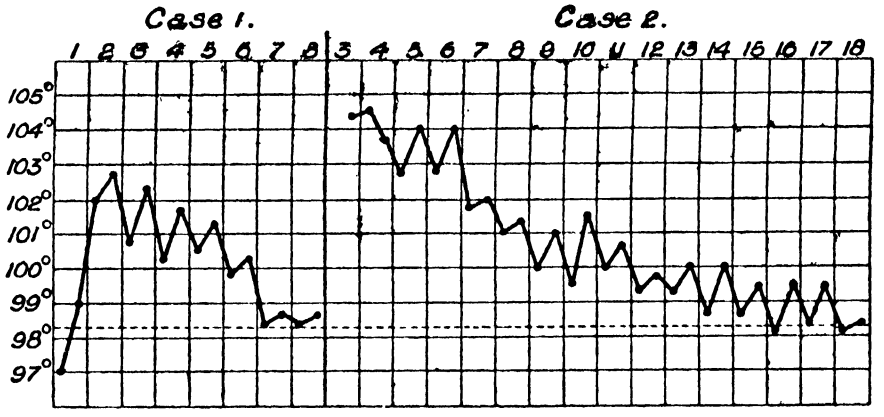


FIG. 5.—Temperature in Scarlatina.

the cause of permanent deaf-mutism. Other local lesions may occur as sequelæ, for instance, sloughing of the cornea, abscesses in the subcutaneous tissues, or cancrum oris.

The kidney is often involved in connection with scarlatina, and nephritis and albuminuria may occur in the following three ways: *Albuminuria* is often present in the stage of rash and fever, small in quantity, temporary in duration, and probably arising in the same way as it does in severe cases of other infections (*6·97*). Secondly, *nephritis* (*2·38*) may be first recognised as a sequela from two to three or four weeks after the beginning of the illness, when the patient is quite convalescent or suffering only from desquamation. It then begins with a chill and rise of temperature and the passage of turbid brown or blood-coloured albuminous urine, the whole subsiding again without the occurrence of dropsy. In other cases the first thing noticed is some swelling of the feet and face, and then the urine is found to be scanty, high-coloured, and albuminous, with blood pigment and granular, hyaline and epithelial casts. Recovery from slight cases is common; but the dropsy may become general, and death may result after six, twelve, or eighteen months, with the severe secondary complications which will be described elsewhere (*see* Nephritis).

Broncho-pneumonia, *bronchitis*, *pericarditis*, and *endocarditis* occur from 0·1 to 0·4 per cent. in each of the cases, and *pneumonia*, *laryngitis*, *meningitis*,

[1] The bracketed figures in italics represent the percentages obtained from 21,006 cases in the Metropolitan Asylums Board's hospitals, Annual Report, Medical Supplement, 1914. No later series of figures has been published.

pyæmia, chorea, jaundice, and *cervical cellulitis* still less often. Pneumonia and broncho-pneumonia are responsible for one-eighth of the deaths. Broncho-pneumonia may be caused by inhalation of septic materials from the throat. *Pleurisy* (*0·05*) may happen as a sequela; and if effusion take place, it often becomes purulent quite early. As in other severe fevers, dilatation of the *heart* sometimes occurs. An acute general *arthritis,* which is probably identical with rheumatic fever, often follows upon scarlet fever so closely that the joints may be swollen when the rash is still present. It is generally known as *scarlatinal rheumatism* and may be a streptococcal manifestation, causing valvular disease, etc. It is often valuable as clinching the diagnosis in a doubtful case of scarlatina. Exceptionally the joints suppurate. About one-fourth of the published cases of *purpura fulminans,* itself a rare condition, have occurred as a sequela of scarlet fever. Some relations of scarlatina to *diphtheria* are mentioned under the latter (*see* Diphtheria).

Varieties. Besides the ordinary forms of scarlatina of moderate severity, which end in recovery, one recognises cases that are called *scarlatina maligna.* This form—the *toxic* form—includes severe cases, some of which are fatal within five or six days from the intensity of the disease without complication other than sore throat; but the mental faculties are dulled; delirium is frequent, especially towards night; and drowsiness and coma supervene. Sometimes the patient is struck down with convulsions and collapse, and dies in twelve or twenty-four hours before the rash has had time to develop. In other cases there are severe rigor and vomiting, early intense or livid rash, high fever and delirium; and the patients die in two or three days.

Cases with severe throat symptoms have been called *scarlatina anginosa.* To this nearly corresponds the *scarlatina ulcerosa* or *septic form* of Caiger, in which the faucial ulcers form a septic focus, from which the system may be poisoned.

The term *latent scarlatina* includes cases in which the rash and sore throat have been so slight as to escape detection, and the illness has only been discovered by the occurrence of desquamation or anasarca.

Diagnosis. Scarlatina is recognised, especially when the disease is known to be prevalent at the time, by the occurrence of feverishness with sore throat, followed in a day by the characteristic punctate erythematous rash. The other characteristic features that may help in the diagnosis are—the sudden onset often with vomiting, circum-oral pallor contrasting with the red cheeks, the state of the tongue, at first furred with a red edge, later patchy, and finally "strawberry," pinhole-and-flake desquamation (*see also* p. 27).

In the early stage, when the presence of sore throat is the most prominent feature, scarlet fever is to be distinguished from diphtheria, tonsillitis, the anginous form of influenza, and secondary syphilis. When the rash has developed scarlet fever must be distinguished from measles, rubella (*see* p. 27), syphilitic roseola, typhus, and the "septic" rashes which may occur in puerperal fever and other septic conditions. Even quite insignificant septic foci, such as impetigo, may give rise to a scarlatiniform rash. Various drugs may also give rise to a rash resembling scarlet fever, and there are the rashes associated with intestinal disturbances from food or following the injection of horse serum. In these cases the skin may peel later.

The Schultz-Charlton blanching phenomenon provides a specific method of diagnosis: 0·2 c.c. of concentrated scarlatina antitoxin (1 in 10) is injected intradermally into an erythematous area; a blanching of the skin round the injection takes place in the course of ten to eighteen hours.

The **Prognosis** must be in all cases very uncertain. Even in the mildest cases, renal complications may be serious or fatal. The mortality, however, is variable, some epidemics being exceedingly mild, while in others the mortality may be 30 or 40 per cent. In the Metropolitan Asylums Board's hospitals in

1914 the mortality was 1·4 per cent., and in 1915 2·03 per cent. In individual cases the prognosis may have to be determined by the condition of the patient from day to day; complications increase the danger. Very severe angina and an intense or livid rash coming out late are unfavourable, and cases with sloughing of the cervical glands are generally fatal.

Preventive Measures. The period of quarantine is eight days. Isolation must be carried out at the earliest possible moment (*see* p. 11).

The frequency with which convalescent patients returning from fever hospitals to their own homes have conveyed the disease to their brothers or sisters, not till then infected, has given rise to the name *return cases* for the new sufferers. Since contagion is transmitted by secretions from the throat, nose, or ear, rather than by the desquamating skin, particular attention should be therefore directed to the former. Hence, while no patient should be allowed to mix with the unprotected till at least four weeks have elapsed, this period must be prolonged if there is still any sore throat or any discharge from the nose or ears. The final disinfection consists in the patient taking a warm bath and having his hair well washed. If in hospital he should be kept separate from other acute cases for some time before going home.

Susceptibility of individuals to scarlet fever is determined by means of the "Dick" test. 0·1 to 0·2 c.c. of a dilute solution of the toxic filtrate of the specific hæmolytic streptococcus is injected intradermally, the heated toxin being injected as a control into the other arm. A local area of redness, 20 to 30 mm. in diameter, beginning to appear in four to six hours, and reaching a maximum in twenty-four hours, indicates a positive reaction. Negative, pseudo and combined reactions are obtained as in the Schick test (*q.v.*). If scarlet fever breaks out in a children's ward, it is not necessary now to close the ward. The scarlet fever patient is removed to a fever hospital. All the patients are "Dick-tested," and on the following day all "Dick-positive" children are given a dose (5 c.c.) of scarlatinal antitoxic serum intramuscularly, then re-Dick-tested on the third day and a further dose of serum given if required (**14**). Unfortunately, the Dick test is not so certain as the Schick test in diphtheria.

Treatment. The administration of specific antitoxic serum during the first four days of the disease brings about a rapid recovery and prevents septic complications: 10 to 60 c.c. of concentrated scarlet fever antitoxin-globulins are injected; it has been injected intravenously, but a death was recorded (**11**).

The general treatment must be carried out in the same way as that of other fevers (*see* Pyrexia).

Local remedies to the throat are applied partly as palliatives, partly as antiseptics. The patient may be given ice to suck if the throat is painful. One of the most useful ways of applying remedies is by syringing. The patient lies on his side. The syringe is introduced nearly as far as the tonsil that is resting uppermost, the fluid being collected in a dish. Boric acid (half-saturated solution), or eusol may be employed. Where syringing is difficult swabbing may also be carried out, lotions of permanganate of potassium (2 grains to ℥j), formalin (1 in 200), chinosol (1 in 600), the tincture of ferric chloride (℥ss to ℥j), carbolic acid (2 grains to ℥j), boroglyceride, being applied every four hours with a brush or pledget of lint. In somewhat stronger solution they may be used as a spray. A useful solution for the spray consists of carbolic acid, 120 grains; iodine liniment, 2 drachms; rectified spirit, 1 drachm; water to 12 ounces. For pain or swelling in the neck and about the angles of the jaws hot fomentations or boric lint wrung out of hot water should be used.

Complications will require special treatment. Abscesses should be opened early. In otitis, relief of pain may be best obtained by applying small ice-bags to the mastoid regions, as the writer saw them used in Berne; hot fomentations and the gentle introduction of warm water into the meatus are less effective. If

suppuration of the middle ear is recognised, the membrana tympani may require puncture ; and the meatus may be gently syringed with warm water, or diluted Condy's fluid, or solution of boric acid (1 in 20). For synovitis salicylate of sodium should be given in 10- or 15-grain doses, and chloroform or belladonna liniment may be used locally. The prevention and treatment of scarlatinal nephritis will be considered hereafter (*see* Nephritis). In the severe typhoid forms, with quick, feeble pulse, stimulants must be given.

STREPTOCOCCAL SEPTICÆMIA

Ætiology. An acute septicæmia may arise at any time in the course of any localised streptococcal infection, or it may follow directly after the entrance of the streptococcus into the body. Thus doctors and medical students may become infected through accidental wounds sustained at operations and autopsies. Again a streptococcal septicæmia is a common form of puerperal fever, where the streptococcus gains entrance to the body from the uterus after childbirth.

Morbid Anatomy. The post-mortem findings in acute streptococcal septicæmia, apart from possible metastases, are not striking. The spleen will be large and soft ; there will be ecchymoses beneath the serous membranes ; the interior of the aorta and endocardium may be stained pink from hæmolysis, and there will be pin-point vegetations on the aortic cusps. Other changes described under Pyrexia may be present.

Symptoms. In *acute streptococcal septicæmia* the temperature may be hardly raised at all in extremely virulent and fatal cases. In other cases it may be continuous, remittent or intermittent, as shown in Fig. 1 (p. 18), with spikes sometimes reaching to 105° or even 106° F. Rigors are common and the pulse rapid. There are certain characteristic features. Diarrhœa is often frequent and troublesome ; the urine contains albumin, red cells and casts, while it may be definitely smoky—all signs that indicate that there is a streptococcal nephritis ; there is a rapidly progressive anæmia and emaciation and sometimes jaundice ; the tongue is raw or desquamated, and looks smooth and red (**53**). Then there may be some splenic enlargement, purpura and erythema, with evidence of the involvement of the lungs or mucous membranes. The peritoneum was involved in one case of the writer's. There may be a leucocytosis up to 30,000. The mental condition may be alert right up to the end, and is characteristically mildly euphoric in the subacute type. Polyarthritis, more commonly non-suppurative, is frequent (12 out of 31 cases) and pus may collect anywhere in the body ; the occurrence of these so-called " fixation " abscesses is a favourable feature, since the streptococci tend to become localised there. Fixation abscesses are not so common as in staphylococcal septicæmia.

The *subacute streptococcal septicæmias* are identical clinically with the various varieties of infective endocarditis ; in fact a case of streptococcal septicæmia running a prolonged course, but without the typical vegetations of infective endocarditis on the valves or walls of the heart, must be rare.

Diagnosis. The absolute diagnosis consists in isolating the streptococcus from the blood stream or from some localised lesion. The presence of a leucocytosis and a negative Widal will exclude typhoid. In most cases of pneumococcal septicæmia there will be some lung involvement and the respiration rate will be high.

Prognosis. This is a very serious disease, but recovery may occur even if the blood culture is positive. A high leucocytosis is a favourable feature.

Treatment. Intravenous injection of 30 to 60 c.c. polyvalent antistreptococcal serum may be used, or the same quantity of the concentrated scarlatinal antitoxin globulins. Surgical measures must be carried out as required.

ERYSIPELAS

(St. Anthony's Fire, The Rose)

Erysipelas is a specific contagious disease, characterised by a peculiar form of inflammation of the skin, and due to the invasion of a hæmolytic streptococcus.

Ætiology. The most common determining cause of erysipelas is the presence of a wound; and infection takes place through this breach of surface, and spreads to the surrounding skin. It affects infants and people over forty years of age more frequently than others; men and women are about equally prone to it. Some conditions of the individual increase the liability: chronic disease of the liver and kidneys, chronic alcoholism, and malnutrition from insufficient food. Cold and damp weather, overcrowding, bad ventilation, dirt, and bad food and water may act in the same way. There may be also an individual tendency, for it often recurs in the same person; at any rate, the immunity conferred by it seems to be short-lived.

Pathology. Microscopic examination of the skin of the affected part shows that the cutis and subcutaneous tissues are swollen, œdematous, and filled with large granular leucocytes, which in the upper layers of the cutis closely surround, as well as fill, the lymphatic vessels. The disease is spread through the superficial lymph spaces. It is often checked or stopped at lines where the skin is closely adherent to subjacent parts, as, for instance, along Poupart's ligament and the crest of the ilium.

Streptococci are found in the lymphatic vessels and lymph spaces at the advancing margin of the disease, as well as in the deeper layers of the skin of the central parts; and rabbits and human beings have been successfully inoculated from cultures.

Symptoms. Apart from injury and operation, erysipelas most commonly attacks the face, and the present description applies especially to that region. The *incubation* of the disease is probably only a few days—from three to six, or in some instances much longer. The *invasion* is generally by a chill or rigors and such malaise as commonly accompanies the onset of the specific fevers—headache, anorexia, furred tongue, and general pains. Within a few hours a red, tender spot shows itself on some part of the face: the side of the nose, the inner canthus of the eye, or the external ear. It may be determined by a lesion of the skin if this exists, and not infrequently it begins at the point of junction of the skin with the mucous membrane of one of the orifices—the nose, mouth, or external ear. The spot enlarges, and the skin becomes bright red, swollen, and very tender, and pits slightly on pressure. The inflammation may confine itself to one side of the face, but more often affects both, and may extend to the scalp. It spreads with varying rapidity, the advancing edge is sharply defined, thick, and raised above the surface, and small tongue-like projections can be felt under the skin in front, which is not yet reddened. The whole face may be thus covered in three, four, or five days. At the height of the disease the face presents a remarkable appearance: the features are enormously swollen, of bright or dusky red colour; the eyelids are distended so as to look like bladders; generally some muco-pus is oozing from between them; the ears are thickened and much enlarged, and the patient is absolutely unrecognisable; the scalp is also swollen and puffy. Often blebs form upon the cheeks or eyelids, which contain yellow sero-purulent or purulent fluid, and these may burst and leave yellow scabs, which further disfigure the patient. The lymphatic glands in the neighbourhood are enlarged and tender, and may be thus affected even before the beginning of obvious inflammation of the skin.

The disease is generally accompanied by high fever. The temperature generally rises early to 102° or 103°, and reaches a maximum of 104° or 105° on the third or fourth day. About the sixth day it tends to fall rather suddenly, but may remain high if the cutaneous inflammation persists, or may rise again with

any fresh outbreak of the local disorder. Indeed, it is closely dependent upon the inflammation of the skin ; in some cases, perhaps more often when the erysipelas is not extensive, the temperature may not rise above 102°. The pulse is quick and full, numbering 100 to 120, or more. The tongue is covered with a thick white fur. The urine is scanty, and in many cases contains some albumin, which may be present for some days. The inflammatory condition invades also the mucous membrane ; the palate, fauces, tonsils, and occasionally the laryngeal mucous membrane, may be reddened and swollen, and cause difficulties in respiration and deglutition. The blood shows a polymorphonuclear leucocytosis. Delirium is common in severe cases, and is generally of a low, muttering kind ; and coma may follow. While the inflammation is still advancing on one side, it may begin to subside at the points first affected. This receding edge is then less well defined, graduating both in colour and elevation into healthy skin, as contrasted with the advancing margin. The swelling, tenderness, and pitting on pressure subside in turn over the whole of the affected area ; the colour fades somewhat, but mostly changes to a brown tint ; and large, thick flakes of dead epidermis now begin to desquamate. This process may take some days. After erysipelas of the scalp the hair often falls out at the same time as the skin is shed, or somewhat later.

Death takes place from exhaustion, with delirium and coma, especially in older patients, habitual drinkers, and those with chronic visceral disease. It may also occur from complications.

Complications and Sequelæ. Abscesses may form under the skin, which may be due to secondary staphylococcal invasion, or the tense skin may slough, and induration, or rarely suppuration, of the lymphatic glands may ensue. The laryngeal œdema may cause asphyxia ; pneumonia and pleurisy are occasional complications, and peritonitis and endocarditis have been recorded. Pyæmia and meningitis have been frequently mentioned in connection with erysipelas, but both are rare as direct results of the erysipelas itself. The former may arise from the wound which preceded the specific inflammation ; the latter may occur if the original lesion has been a fracture of the skull, or if infection spreads inwards from the orbit. In erysipelas of the scalp, the delirium may be violent or maniacal, and accompanied by delusions, but of itself this is not sufficient to justify a diagnosis of meningitis. Mental disturbance may also be a sequela.

Diagnosis. Facial erysipelas may be confounded with erythema, acute eczema, herpes zoster, alveolar abscess, and even mumps. Erythema occurs in red patches, generally two or more in number, much less raised, and without pronounced fever. The vesications of an acute eczema and of herpes are distinctive, and herpes is unilateral and confined to one of the areas of distribution of the fifth nerve. Characteristic features of erysipelas are the spreading of the redness so that the maximum is always remote from the point of origin, the implication of the ear in the inflammation, and the great tenderness of skin in the advancing zone.

Prognosis. Though in most cases favourable, it is dangerous in proportion to the extent of surface involved ; and it is often fatal in old patients, and in the subjects of chronic visceral disease, alcoholism, or malnutrition.

Treatment. Since the infection spreads through the superficial lymph spaces of the skin, it may be arrested by contracting the spaces. This is carried out by painting non-flexible collodion in a ring outside the spreading edge. The application must be repeated several times a day as the collodion flakes off. Good results have sometimes followed the use of an antistreptococcal serum, injected subcutaneously in doses of 15 or 20 c.c. once or twice daily. Tepid or cold sponging may be resorted to where the fever is unusually prolonged or high. The diet should be light, easily digestible and nutritious, as in other febrile cases.

STAPHYLOCOCCAL INFECTIONS

Staphylococcal infections, though common enough, are by no means so common as streptococcal infections. They have a much greater tendency to localisation, so that while a staphylococcal septicæmia is uncommon, a staphylococcal pyæmia with metastatic abscesses is the rule, and when the disease is once established these pyæmic abscesses may keep on appearing in different parts for weeks or months, especially in the muscles, skin, or prostate. Like the streptococcus, the staphylococcus may invade any tissue of the body, and by far the commonest pathogenic variety is the *S. aureus*, though the writer does remember the case of a young man who had pyelitis with a highly ammoniacal urine, and *S. albus* was obtained consistently on cultivation. *S. aureus* readily gains admission to the body through the skin by means of gnat bites, scratches, etc., and local boils and whitlows, commonly result. Internally *S. aureus* is commonly responsible for cellulitis and osteomyelitis in young people where the infection begins on the diaphysial side of the epiphysial line, and otitis media. In adults abscess (carbuncle) of the kidney with perinephritis or perinephric abscess is more common. A staphylococcus arthritis is uncommon. The *S. aureus* tends to spread locally, so that a septic spot on the face may spread inwards, causing a local meningitis and a cavernous sinus thrombosis (**16**).

Staphylococcal Septicæmia. This is an even more serious condition than streptococcal septicæmia. When resulting from osteomyelitis it causes abscesses in the lungs and heart and a pericarditis. In another acute form there may be a meningitis so that organisms can be grown not only from the blood but from the C.S. fluid. For *treatment* injection of anti-staphylococcal serum may be tried (**17**), or in long-standing cases a vaccine. Abscesses may be opened, or they may be aspirated and filled up with flavine 1 in 1000.

PNEUMOCOCCAL INFECTIONS

The micro-organism first found by Sternberg in the saliva, and subsequently recognised by Fraenkel as the causative agent of acute lobar pneumonia, was called by him the *Diplococcus pneumoniæ;* and it is otherwise known as the *Diplococcus lanceolatus*, and more generally as the *Pneumococcus*. It consists of oval Gram-positive cocci, of about 1μ in diameter, often united in pairs or in short chains of five or six. Each is surrounded by a distinct halo or capsule of colourless homogeneous material.

This organism is responsible for acute and severe inflammations in many organs and parts of the body, and is chiefly known in connection with acute lobar pneumonia, of which it is the cause in from 80 to 90 per cent. of the cases. However, it also attacks other organs. Thus there occur pneumococcal pleurisy, empyema, peritonitis, meningitis, arthritis, enteritis, endocarditis, pericarditis, nephritis, endometritis, and subcutaneous, intramuscular, and intravisceral abscesses. It is rather characteristic of pneumococcal infections that pus formation takes place relatively late, after a copious exudation of serous fluid. The pus, too, when formed often sinks to the bottom, leaving a fairly clear layer of serous fluid on top.

Four types of pneumococci have been isolated, which resemble one another morphologically and culturally, but have different biological characteristics. Types I. and II. account for two-thirds of pneumonia cases in this country and America, and anti-sera have been prepared which have been used successfully in treatment. Type III. occurs in the most severe cases, and the corresponding anti-serum is useless. Type IV. resembles the pneumococci found normally in the mouth, and is a mixed group containing those strains that do not conform to the other three types. It is of low virulence, and the resulting pneumonia is very mild.

Method of Typing. This can be carried out in a few minutes by mixing on a microscope slide the three standard diagnostic serums, Types I., II., and III., with a fleck of the sputum to be tested. The specimen is then examined with the dry lens ($\frac{1}{6}$ inch objective) and 4 ocular with substage condenser removed. The pneumococci, which are normally only just visible with this magnification, appear greatly enlarged in a positive reaction, the characteristic lanceolate pairs equalling in long diameter the size of a red blood cell. This apparent enlargement is the result of association of the pneumococcal capsular substance with the specific anti-body contained in the homologous serum, producing a change in the refractive index of the material surrounding the pneumococci which become conspicuous (**24**).

GONOCOCCAL INFECTIONS

The acute inflammation of the generative organs, male and female, known as *gonorrhœa*, is an infective disease, of which the micro-organism is the *Micrococcus gonorrhœæ* or *gonococcus*. The gonococci are found in the pus discharged from the urethra, and are largely contained within the leucocytes. They are decolorised by Gram's method.

The course of the disease, which is very variable, may be classified under five heads :

(1) *The Primary Focus.* Infection is, as a rule, by direct contact, and involves usually the urethra in the male, and the urethra, cervical canal, and, to a less extent, the vagina in the female. Gonorrhœa of the female genital organs is a fertile source of gonococcal conjunctivitis and other ocular lesions in the newborn infant.

(2) *Area of Local Spread.* The infection may spread along the lymphatics to the passages and organs in the neighbourhood of the primary focus, and may cause inguinal bubo, vesiculitis, epididymitis, orchitis, cystitis, prostatitis, pyelitis, endometritis, salpingitis and pelvic cellulitis and peritonitis.

(3) *Gonococcal Septicæmia, i.e.* a general blood infection without focal lesions. This is a rare condition, and in this sense the gonococcus resembles the staphylococcus, which rarely produces a pure septicæmia.

(4) *Metastatic Gonococcal Infection,* or focal sepsis. The spread of the infection from the primary focus to other parts of the body takes place by the blood stream. In severe cases there is also a general blood infection (septicæmia), as may be found in the more severe cases of gonococcal arthritis, or gonococcal endocarditis, which is one form of malignant endocarditis. However, in most cases the metastatic infection is not accompanied by a septicæmia.

The commonest infection of this type is the so-called *gonorrhœal rheumatism*, which includes arthritis, fibrositis, teno-synovitis, bursitis, myositis and perineuritis. Periostitis and osteo-myelitis are rare. The eye is not uncommonly affected by metastatic infection, the principal lesions being iritis and conjunctivitis. It is probable that some cases of " simple " mitral disease are secondary to gonorrhœa. There is a gonococcal pleurisy.

Gonorrhœal rheumatism, from its resemblance to acute rheumatism, requires separate notice. It begins at an interval of fourteen days or three or four weeks from the commencement of the urethral discharge, sometimes while the discharge is still purulent, more often during the subsequent stage of gleet.

Morbid Anatomy. There are serous effusion into the joint, infiltration and œdema of the tissues around it, and in severe cases suppuration, erosion of the cartilages, disorganisation of the joint, and ankylosis. The synovial membrane is primarily affected in the acute cases, and the surrounding fibrous tissues are chiefly and first involved in the subacute forms.

Pathology. The gonococcus has frequently been found in the fluid of the

inflamed joints and of the sheaths of the tendons when they are affected. If suppuration takes place, pyogenic organisms may also be present. In more chronic cases the gonococcus is not found. It may be tucked away in the recesses of the joint. Another suggestion is that the inflammation is due to the gonococcus toxin.

Symptoms. In *acute* forms of gonorrhœal rheumatism several joints are at first affected with pain and swelling, but the disease often, after a time, localises itself in one only, which may be the elbow, knee, ankle, wrist, or foot. There is very extensive redness, with swelling, pain and tenderness. The redness often spreads up the limb far beyond the joint, and the tissues are infiltrated to a corresponding extent. This infiltration may be actually mistaken for abscess, and it may also have a closer resemblance to gout than to rheumatic fever. The pain is very severe on the slightest movement; the fever is not high. The inflammation only slowly subsides, and leaves a good deal of stiffness behind; but the joint does not often suppurate. Cardiac complications are only occasionally observed. The late N. C. Davies-Colley stated that this form of gonococcal arthritis was as common in women as in men.

In other less acute or *subacute* cases the resemblance to a mild rheumatic fever is in some respects closer; the joints are swollen, not so red, and less generally infiltrated. All the joints in the body may be affected; but the knees, ankles, and wrists are most often involved. Not infrequently there is much pain in the fasciæ, especially in the plantar fascia, and the sheaths of tendons may be involved. Spondylitis occurs in a certain proportion of the cases. As in the acuter forms, the inflammation tends to be persistent and does not readily subside and come again, as it does in ordinary rheumatic fever. It lasts two, three, or more weeks, and leaves a great deal of stiffness or even fibrous ankylosis.

Diagnosis. The disease is most likely to be mistaken for *rheumatic fever* until it is discovered that the patient has a discharge, or until the persistence of the arthritis in a few joints makes one suspect the nature of the case. The resemblance may be increased by a history of previous attacks, for, though gonococcal synovitis does not itself recur after long intervals like rheumatic fever, other attacks are often induced by fresh infection. The acuter forms of the disease may closely resemble *erysipelas*, *abscess*, or *acute gout*. The age of the patient and the position of the inflammation will generally exclude the latter. *Pyæmia* may be a cause of multiple synovitis after gonorrhœa; but in this case the illness is generally more severe, with rigors and such serious complications as pericarditis, endocarditis, pneumonia, or pleurisy.

An investigation of the common vulvo-vaginitis of children up to 15 years has shown that 36 per cent. are gonorrhœal, and 64 per cent. are non-specific and due to staphylococcus (**51**).

Treatment. It is, no doubt, desirable to cure the urethral discharge as soon as possible. For the arthritis alkalies and iodide of potassium have been largely employed, the latter in full doses; but it is probably better to give plenty of good food, with cod-liver oil and iron or cinchona. Vaccine treatment is also employed. Autogenous vaccines are obtained by cultivating the gonococcus from the patient's discharges, and may be injected repeatedly. But the cure often takes five or six weeks. Stock vaccines are prepared from a number of different strains, and not from the patient's own organisms. Recently sensitised and detoxicated vaccines have been used. The former is a mixture of a vaccine with antigonococcal serum. The latter is a vaccine with the virus much attenuated, either by treating the organisms with *caustic soda* or by prolonged cultivation on *artificial media* outside the body. Locally the joints may be painted with iodine. In acute cases the limb should be kept completely at rest by means of a plaster of Paris splint; and anodyne applications, especially the compound mercury ointment, with extract of belladonna, may be used. As soon as the inflammation has subsided the tendency to fixation must be met by friction, massage, and passive movements.

CEREBRO-SPINAL FEVER

(*Cerebro-spinal Meningitis, Spotted Fever*)

This disease was first recognised at Geneva in 1805. Since 1860 it has been prevalent in the United States and in Germany. In 1846 it appeared in Ireland, and again in a severe form in 1866–68; and in 1906–8 some hundreds of cases occurred in Glasgow and in other towns in Scotland, and a few in London. The disease is endemic, sporadic cases occurring, especially in infants. In the latter the disease used to be described as *posterior basal meningitis*. Every now and then the disease assumes epidemic form. This occurred in this country in 1915 and 1916.

Ætiology. The specific organism is a diplococcus (*D. meningitidis intracellularis* of Weichselbaum or *meningococcus*), which is seen in the polymorphonuclear leucocytes of the meningeal exudations, but also lying free between the cells; it is also sometimes found in the blood, in pus from the joints, in pneumonic foci in the lungs, and in the mucus of the naso-pharynx. Meningococci when tested by their agglutination reactions fall into two main groups; they are sometimes called meningococci and parameningococci. Each group is again divisible, also by agglutination, into a number of different strains. As far as their cultural characteristics are concerned, the different groups cannot be separated from one another, and there is not much evidence that they produce different symptoms. Meningococci may be found in the naso-pharynx of perfectly healthy people, who are known as *carriers*. It is possible that the meningococci latent there assume a virulent form from time to time so that an epidemic breaks out. It is noteworthy that carriers do not very often themselves contract the disease; but they disseminate the organisms by projection of their saliva in talking and coughing, so that susceptible people become infected by inhalation and get the disease. Normally about 5 per cent. of the population are carriers; when the number reaches 20 per cent. an epidemic may break out. An epidemic does not sweep through the community like influenza; it is only people here and there who contract the disease. Previously the young have most often been sufferers, 80 per cent. of cases being under sixteen, and the most susceptible age of all being from birth to five years. This tendency was not shown in the 1915–16 epidemic. As a rule the sexes are attacked nearly equally. The disease is usually more prevalent in the winter months; it is probable that overcrowding, such as occurred among the troops at the beginning of the War, and the presence of catarrhal throat affections, owing to sneezing and coughing, tend to its dissemination.

Pathology. Much discussion has taken place as to how the meningococcus obtains access to the meninges. The older view that it spread direct to the brain from the naso-pharynx *viâ* the sinuses or the cribriform plate has received some support from the finding of pus in the sinuses at post-mortem. However, in many cases suppuration of this kind has not been found although carefully looked for. On the other hand, the meningococcus was isolated from the blood and from skin lesions before the onset of meningitis in cases during the last epidemic, so that, as in other septicæmias, the meninges were probably infected *viâ* the blood stream, the naso-pharynx being the primary focus.

A third view has been recently expressed (**28**), viz., that infection passes from the blood to the choroid plexuses and then to the intraventricular fluid. The normal passage of the fluid carries it through the roof of the fourth ventricle out to the subarachnoid space, while there is a special tendency for the inflammatory products to accumulate at the periphery where the fluid is normally absorbed, *i.e.* at the superior longitudinal sinus, and in the spinal canal. The evidence for this is: (1) That in fulminating cases meningococci are found in the ventricles alone, while there is no perceptible inflammation of the meninges, but

there is acute inflammation of the choroid flexuses; (2) In less acute cases the fluid from ventricular puncture, though it has the same composition as fluid from lumbar puncture, always contains fewer pus cells, suggesting that these have accumulated at the periphery. In favour of this view, it has been shown in dogs that Indian ink, when injected into the ventricles, travels from the fourth ventricle upwards in the subarachnoid space along the sulci, resembling the distribution of pus in meningitis.

Morbid Anatomy. There is an acute lepto-meningitis of the brain and spinal cord. The pus and lymph are abundant at the base of the brain, in the quadrilateral space and on the convexity, along the larger blood vessels and in the fissures. In the spinal cord the posterior surface is more affected than the anterior, and the lumbar region more than the other parts. The ventricles of the brain contain turbid serum or pus. In the early stages they are reduced in size, owing to œdema of the brain substance. Punctiform hæmorrhages, accumulations of leucocytes, or actual abscesses are found in the cortex of the brain. Other changes found are congestion of the lungs, liver, spleen, and kidneys, fatty degeneration of the renal epithelium, and granular degeneration of the voluntary muscular fibres, sometimes ecchymosis of the pericardium and pleura and suppuration of the joints. In fulminant cases there is often hæmorrhage into the adrenals. In cases of long duration pronounced hydrocephalus is present, and the pia-arachnoid has an opaque appearance, as if flour had been dusted on its surface. This is due to increased connective tissue formation, the result of the previous inflammation. The hydrocephalus is due to the sealing up of the outlets of the cerebro-spinal fluid round the base of the brain (foramina of Majendie and Luschka), because during the acute stage pressure is exerted at this spot by the swollen brain being forced down into the rigid foramen magnum. In infants suppurative meningitis is sometimes found on the vertex of the brain as well as at the base, while at other times the vertex is free and the base and spinal cord alone affected. It is this latter condition that has caused the disease to be known as "posterior basic meningitis."

Symptoms and Course. The incubation period may be as short as one or two days, but it may also be much longer. The disease itself is extremely variable, so that many different clinical forms have been described. There are, however, two chief phases: (1) the general blood infection; (2) the localisation in the meninges, which usually follow one another in this order. The following is Rolleston's classification:—

1. The *fulminating* type; this is usually fatal within forty-eight hours. It may begin with maniacal symptoms, or the patient may suddenly become unconscious. Again, from the outset there may be collapse, vomiting, and severe headache, and sometimes diarrhœa and a purpuric eruption with large hæmorrhagic areas. There may be no meningitic symptoms at all, the patient remaining fully conscious to the end. In other cases coma rapidly comes on.

2. The *acute* form begins suddenly like an attack of influenza with headache, fever, vomiting, and, especially in children, with convulsions. Meningitic symptoms appear within a few hours; there is stiffness of the muscles of the back of the neck, which may be shown by attempting to bend the head forwards, and often the head is drawn back by the contraction of the deep muscles; the dorsal and lumbar muscles may be similarly affected, so that the back is kept straight (*orthotonus*), or even arched with the concavity backwards (*opisthotonus*); and sometimes the legs and arms are flexed in tonic spasm. Pains frequently extend down into the muscles of the lower extremities, and cutaneous hyperæsthesia may be also present. The knee jerks are often active, but may be absent; Kernig's sign is practically constant. There may be, in different cases, ptosis (*3·6*)[1] or strabismus (*25*); usually dilatation, or inequality of the pupils;

[1] The bracketed numbers in italics indicate roughly the percentage of cases in which the particular symptom occurs. These percentages vary greatly in different epidemics.

or contraction of the facial muscles; but trismus is rare. Optic neuritis (*10*), and conjunctivitis (*5·6*), and panophthalmitis (*1·4*) occur. Pain in the ear, tinnitus and defective hearing are not uncommon, and suppuration of the labyrinth or of the tympanum may occur. Deficiency of the sense of smell has been noted. Drowsiness, delirium, and coma, sometimes with Cheyne-Stokes breathing, or convulsions, supervene in due course; and death takes place with varying rapidity in different cases. Fever is present from the first, but it runs no regular course; it is remittent or intermittent, perhaps normal for a day or two, and then rising to 102° or 103°, seldom exceeding 104°. Occasionally the fatal termination is preceded by a temperature of 108° or 109°. With recovery the temperature falls slowly and irregularly. The pulse is variable. An important feature of epidemic meningitis is the occurrence of cutaneous eruptions; the earliest to appear are rose spots, papules, or petechiæ, which are due to emboli in the septicæmic form of the disease; herpes facialis, which is usually regarded as the commonest rash (*50*), occurs about the fourth day; herpes zoster is much rarer. The rashes may be present together. Sometimes the joints are inflamed, hot, red, painful, and swollen, due to synovitis (*10*)—a condition which generally subsides, but may go on to suppuration. The abdomen is often retracted; the spleen is not often enlarged. The urine may contain a little albumin, or a trace of sugar. Epididymitis and orchitis, bronchitis, pneumonia, pleurisy, endocarditis, and latent pericarditis sometimes occur. A leucocytosis of from 15,000 to 60,000 is constant, and is nearly always polymorphonuclear; only occasionally in infants and young children is there a lymphocytosis. If a lumbar puncture be performed the fluid withdrawn may be clear in the early stages, but is usually turbid and may be purulent; it comes out under an increased pressure of from 150 mm. to 500 or 600 mm., and its quantity may reach 20 or 30 c.c. It contains increased quantities of albumin and globulin, and shows in acute stages polymorphonuclear leucocytes, which contain the *meningococcus*. The organisms may also be free in the cerebro-spinal fluid. In chronic cases lymphocytes may sometimes be present in excess.

3. The *abortive* forms are of two kinds: (A) those cases which do not progress further than the septicæmic stage and then get better within twenty-four or forty-eight hours before the meningeal invasion; (B) mild cases with both kinds of symptoms. Relapses or recrudescences are apt to occur in abortive cases.

4. The *chronic* forms: (1) Purely septicæmic, and not often recognised, may last for weeks with periodic rises of temperature resembling malaria, joint pains, orchitis and various skin rashes; sometimes it follows a definite meningitic attack. (2) *Encysted and loculated meningitis*, due to the shutting off by adhesions of some of the space containing cerebro-spinal fluid. This type occurs, particularly in infants, as a sporadic disease, and was known previously as *posterior basic meningitis*. It is distinguished from most adult forms by—(*a*) the chronicity of the disease; (*b*) the rarity of skin eruptions; (*c*) loss of vision quite early in the disease without visible retinal changes or optic neuritis; (*d*) the rarity of deafness: there is often hyperacuity, the child screaming at the slightest noise; (*e*) the prominence of opisthotonus owing to the flexibility of the spine; (*f*) the bulging of the fontanelle from increased intracranial pressure; (*g*) Kernig's sign is rather inconstant at first, but it usually occurs late in the disease. The course is most variable; the child may lie semi-conscious for weeks, at first well nourished, but later it begins to waste. Complete recovery may take place, or hydrocephalus, cerebral diplegia, mental deficiency, or deaf-mutism may result.

Diagnosis. This is not difficult in the course of an epidemic. The characteristic features are the sudden onset, the headache, vomiting, pain in the back and limbs, stiff neck, and the herpes labialis. The purpuric eruption also seems to distinguish it from tuberculous and other forms of suppurative meningitis,

e.g. pneumococcal, influenzal, streptococcal, etc., which must always be carefully considered. Obscure toxic conditions, such as those arising from some kinds of food poisoning, have been mistaken for the disease. It is desirable in all cases to perform lumbar puncture, and prove the nature of the disease by microscopic examination, or by culture, of the meningococcus. In the later stages of the posterior basal form, the organisms may not be seen in the fluid, and lymphocytes may replace the polymorphonuclear leucocytes. The organism may also be cultivated from the blood in the early stages. Intra-ventricular puncture has also recently been used in diagnosis (**28**). In infants fluid may be obtained through the anterior fontanelle. In adults Goetze's channel borer is used for piercing the cranium on the vertex either 1 cm. or 4–6 cm. from the middle line.

Many diseases have been at different times confounded with cerebro-spinal fever, especially in early stages, such as pneumonia, influenza, and measles. Acute poliomyelitis, in its so-called meningitic form, may closely resemble it; and the diagnosis may be only possible after a lumbar puncture.

Prognosis. The mortality has varied from 20 to 90 per cent. in different epidemics, but is rarely below 50 per cent. in untreated cases. The disease is most fatal during epidemics among infants, and in the fulminating cases. With efficient serum treatment the mortality has been diminished to 18 per cent. The impression was gained from the last epidemic that, apart from deafness, the patient, if he survived, was not likely to suffer from permanent disability.

Prevention. After the disease has appeared in the military and naval forces and institutions where there is crowding, it is now considered useless to segregate contacts, since the carrier rate is equally high among the contacts and the remainder of the men. The best plan is to space out the beds, improve ventilation, prevent indoor crowding in canteens, and possibly treat carriers with a fine spray containing 1·5 to 2 per cent. zinc sulphate. An oily spray might be used (**29**). A case has been made out for protective inoculation with a stock vaccine during an epidemic.

Treatment. Apart from general treatment applicable to any pyrexia, the treatment consists in withdrawing cerebro-spinal fluid to relieve pressure and in injecting antimeningococcal serum. It is essential to give the serum corresponding to the particular strain of organism, and when this is not known, as, for instance, at the beginning of the attack, a multivalent serum may be given. The sooner the serum is administered, the better is the prognosis. At the very beginning of the attack in the septicæmic stage doses of 20 to 40 c.c. are injected intravenously until 200 to 600 c.c. have been given in all. In the meningitic stage the serum is given both intravenously and intrathecally (**30**). Since the present multivalent serum is weak it has been suggested that an initial dose of 100 to 200 c.c. should be given intravenously, and this is repeated in forty-eight hours if there is no clinical improvement. Lumbar punctures are repeated at twenty-four or forty-eight hours' interval; the cerebro-spinal fluid which is under pressure is allowed to run out through the lumbar puncture needle, and the serum should be allowed to run in slowly in less amount than the amount of fluid removed. Twenty to thirty cubic centimetres are given twice daily for three or four days, and the foot of the bed is raised to allow it to run down towards the brain. After the serum treatment is finished, a raised cerebro-spinal pressure should still be relieved by lumbar puncture at intervals of one to several days. If the fluid does not run freely *cisternal puncture* should be carried out. In a recent case of the writer's—a girl aged six—eleven lumbar punctures and fourteen cisternal punctures were required over a period of forty days and recovery was then complete. Irrigation of the theca with normal saline or 3·8 per cent. sodium citrate has been of value in preventing adhesions. Where adhesions have formed and the intracranial contents are shut off, the lateral ventricles may be tapped and serum injected. In young children this can be carried out through the anterior fontanelle.

Bacterial Diseases—II. Bacillary

DIPHTHERIA

Diphtheria (from διφθέρα, a prepared hide, piece of leather) is an acute infectious disease, of which the essential clinical feature is a peculiar inflammation of surface tissues resulting in the formation of a so-called "membrane." This commonly affects the mucous membrane of the mouth, pharynx, nose, or larynx, more rarely some other mucous membrane (conjunctiva, vagina), or the abraded skin, or the surface of a wound.

The specific micro-organism of diphtheria is the bacillus described by Klebs and Loeffler. It is a non-motile rod, varying in length in different circumstances, from 2·5μ to 6μ. It is slightly curved, and often clubbed at one end. It is Gram-positive and shows "beading" with Loeffler's methylene blue. The *B. diphtheriæ* is found for the most part in the deep layers of the diphtherial membrane, but may be present in small numbers in the lymph glands, and in the liver, spleen, and kidneys.

Ætiology. Diphtheria is contagious, being conveyed directly, as in kissing, or by means of droplets of saliva, projected into the air as the result of coughing or talking, as well as by clothes and other objects. The bacillus survives drying, and has been found in the dust of the sick-room, and there is evidence to show that it may be sometimes transmitted over considerable distances of country by the wind. Milk is a well-known channel of infection; but this is due to human contamination, and not to any disease of the cow. Water sewage and sewer gas are not known to be vehicles of infection.

The *diphtheria-carrier* is also a source of contagion. In one-eighth of convalescent cases the bacillus is found in the throat for one or two months after the first symptom, and in a few cases for three or four months (*convalescent carriers*). From 8 to 30 per cent. of those in contact with a case of diphtheria become *contact* carriers; but in the later periods of the infection the bacilli have often lost their virulence, and in any case a carrier is not necessarily an active source of contagion. Diphtheria bacilli have been found in 10 per cent. of Baltimore school children. These were classified as *healthy* carriers, as only a very small proportion had ever been in contact with a case of diphtheria. In the majority of these healthy carriers, the bacilli disappeared in a few weeks without treatment. They were non-virulent, and remained so when inoculated into the throats of five healthy persons. Virulence can be tested by inoculating a guinea-pig, and from these experiments it would seem advisable to make this test before deciding to isolate and treat diphtheria carriers.

Diphtheria sometimes complicates measles and scarlatina (about 2 per cent. of each at the M.A.B. hospitals); it is more frequent in rural than in urban districts, especially in the more exposed parts of the former; and it affects both sexes and all ages, but it is especially frequent in children up to ten or twelve years of age. Its maximum incidence is in October and November.

Pathology. The inflammatory change which is characteristic of diphtheria is the formation of a "false membrane." It is the combined result of necrosis of the superficial tissues and the exudation of fibrin and leucocytes. A membrane which does not extend beyond the base of the epithelial layer is called a "croupous" membrane, and can easily be pulled off without bleeding. This is the case in the trachea in diphtheria, where it consists chiefly of fibrin and leucocytes, and is loosely attached to the surface. In the fauces, on the other hand, the stratified epithelium is infiltrated with fibrin as well as the subepithelial connective tissue, and necrosis takes place, causing the formation of a greyish white or white layer firmly adherent to the deeper tissues. This is called a "diphtheritic" membrane. It is difficult to remove and leaves a bleeding surface. In the smaller bronchi the exudation is purulent; the lungs often present lobular pneumonia, with occasional hæmorrhages.

Diphtheria toxin has a profound effect: (1) On the *circulation*, causing a fall in blood pressure and concentration of the blood, the percentage of hæmoglobin being greatly increased. The plasma passes out into the tissue spaces. In fatal cases the cells of the suprarenals show chromatolysis (Harding). (2) On *nerve fibres*, causing disintegration of the myelin sheaths and rupture of the axis cylinders. Degeneration of anterior horn cells has also been described. The toxin primarily attacks the nerves locally, and this explains the fact that paralysis of the palate is such a common accompaniment of faucial diphtheria. Similarly in wound diphtheria the paralysis affects the muscles in the neighbourhood of the wound (Walshe). It is possible that it passes up the nerves to the central nervous system, like tetanus toxin and the virus of hydrophobia.

It is remarkable that in *laryngeal diphtheria* this toxic action is not very noticeable. Possibly this is due to the membrane being "croupous" in character, so that toxins are not readily absorbed.

The changes in the various organs are attributable to the influences of the toxins circulating through the body. The heart may be pale, soft and friable; the muscular fibres show a cloudy swelling and fatty changes, and blood is extravasated. The convoluted tubules of the kidney show fatty degeneration, and the epithelium is in many places separated from the basement membrane.

Streptococci and staphylococci are often present in the superficial layers of the diphtherial membrane, and sometimes lead to secondary suppurative lesions.

Symptoms and Course. The *incubation* is two to ten days.

Faucial Diphtheria. The disease, though febrile, begins insidiously; there are generally malaise, loss of appetite, and headache, and there may be nausea, vomiting, or shivering. Sore throat is soon complained of, and it is seen to be inflamed. Within a short time one or more patches of a creamy white deposit form on the inflamed surface. There are *five* areas where such patches occur in diphtheria, between the pillars of the fauces on both sides, *i.e.* over the tonsils (2); the uvula (1); the soft palate on both sides (2). It is characteristic that there is never more than one patch in a particular area, but any number of the areas may be affected at the same time. The patch is raised above the surface of the mucous membrane, and the edges are sharply defined; the colour may be glistening white, bluish, yellow, or grey. Coincidently with the inflammation of the throat the lymphatic glands at the angle of the jaw enlarge, and they can always be felt on one or both sides, according to the lesions within. Sometimes the typical membrane is preceded by a grey mucous secretion. Gangrene occurs occasionally in the severe cases.

The temperature of diphtheria is very variable, and runs no definite course; it may rise to 103°, 104°, or 105°, but is often throughout the whole illness much lower. The appetite is lost, and feeding becomes difficult and painful from the condition of the throat. In a large proportion of cases, variously estimated at 25 to 60 per cent., the urine is albuminous, and this occurs, not after the illness, as in scarlatina, but during the height of the throat symptoms. In some cases the specific inflammation spreads to adjacent mucous membranes—those of the nose and the conjunctiva, the Eustachian tube (causing otitis media), and the larynx and respiratory passages. Severe cases may be hæmorrhagic in type with epistaxis, bleeding from the throat and subcutaneous ecchymoses. Apart from these complications, there may be cardiac failure with death at the beginning of the disease; but the characteristic feature is a gradual fall of blood pressure which begins at the end of the first week, reaching a maximum between the eighth and twelfth days and disappearing in twelve to twenty-two days. This hypopiesia is responsible for 50 per cent. of the deaths in the first three weeks; it is accompanied by vomiting without pain, continuous air hunger, sighing, extreme restlessness when the systolic blood pressure is below 60 mm., and is proportional in amount to the severity of the disease in the early stages. The pulse rate, size of heart, apex beat, first beat sound, are normal and the pulse is regular (22).

Nasal diphtheria may occur alone, or as the result of a direct spread from the fauces. There is more or less obstruction to nasal respiration, the mucous membrane is swollen, and a muco-purulent or thin pale brown mucoid secretion runs from the nostrils, reddening or excoriating the alæ and adjacent upper lip. It may be streaked with blood, or decided epistaxis may occur.

Laryngeal diphtheria presents the symptoms of laryngitis, and the obstruction, due to the swollen mucous membrane, is increased by the presence of the diphtherial false membrane. It is rare in adults.

The *first stage* is indicated by the presence of a loud, brassy cough and a rough, hoarse voice, and it lasts for at most two days.

In the *second stage* there is respiratory distress with cough and aphonia. Stridor develops owing to narrowing of the glottis, being most marked during inspiration. As obstruction increases the supra-clavicular, supra-sternal, and intercostal spaces are sucked in with each inspiration; and in infants and young children with soft yielding bones the lower end of the sternum, or the three or four lower ribs, are drawn in, showing the extent to which the air is hindered from access to the lungs through the glottis. Slight degrees of obstruction may persist some days without much change, but more often the case gets progressively or rapidly worse. The face, at first flushed, with bright eyes, gets cyanosed. The child is restless, putting its hand to its mouth or throat, as if to remove the impediment. The cough becomes husky, and from time to time there may be spasmodic closure of the glottis, in which violent inspiratory efforts are made, and the cyanosis becomes extreme.

In the *third asphyxial stage*, which only lasts a few hours, the pulse becomes weaker, and the respiratory effort is lessened. The skin is livid, the extremities are cold, the mental faculties are blunted, and stupor supervenes. Sometimes there are convulsions before the end.

As a rule, in laryngeal diphtheria the process is not confined to the larynx; it spreads to the trachea and the bronchi, forming a continuous membrane in the former, which, in the middle-sized and smaller bronchi, is gradually changed into a purulent secretion. These morbid products naturally increase the difficulty of breathing, though it is not always easy to recognise their presence by physical signs; in fact, death not uncommonly occurs from blocking by a plug of desiccated mucus or loose membrane at or below the bifurcation of the bronchi after a successful tracheotomy (Biernacki). Generally a loud and stridulous noise is heard in the chest, caused by the obstruction at the glottis. It may be mixed here and there with mucous râles, and there may be patches of tubular breathing, due to the broncho-pneumonia which is so frequent a result of the spread of diphtheria into the lungs.

Laryngeal diphtheria is often primary, though there is usually some catarrh of the throat, but it may be associated with faucial and nasal diphtheria.

Complications and Sequelæ. Complications are chiefly the extension of the disease to different parts, which have been described.[1] *Pleurisy* may accompany the *pneumonia* (*0·3*), or *broncho-pneumonia* (*1·0*). *Albuminuria* (*23·3*) is rarely more than a symptom, but occasionally a definite nephritis (*0·7*) may persist or occur as a sequela. The lymphatic glands may inflame and suppurate or slough with about one-third the frequency of occurrence in scarlet fever; thus *suppuration* in the acute stage (*0·2*), in convalescence *simple adenitis* (*2·1*), and *suppurative adenitis* (*0·6*).

The most important sequel of diphtheria is the affection of the peripheral nerves, which results in *diphtherial paralysis* (*8·8*). This shows itself first in the soft palate. Some days, or a week, or several weeks, after apparent recovery, the child is noticed to speak with a nasal, twanging voice, and when it swallows liquids a small quantity is regurgitated through the nose. These defects are due

[1] The bracketed percentages in italics are from 6,184 cases in M.A.B. hospitals in 1914.

to paralysis of the soft palate, which fails to shut off the mouth from the nose, as it should during speaking and swallowing. Shortly after this the child is noticed to be weak in the legs, and unable to walk any distance, or the knees give way on standing for a short time. The knee jerk is lost quite early. In older children and in adults failure of accommodation of the eye for near objects is often noticed, due to paralysis of the ciliary muscle; and the extrinsic muscles of the eye may be also affected, producing strabismus or squint. In many cases the paralysis does not proceed beyond this stage, and in a few weeks the muscles recover their power completely. In others the muscular system throughout the body may be affected. The patient lies motionless in bed, respiration is rendered difficult from paralysis of the intercostal muscles or diaphragm, and food given by the mouth is rejected, from inability to swallow it. The paralysis of the diaphragm is often followed by collapse of the lower lobes of the lungs (*see* Lesions of the Phrenic Nerve). The laryngeal muscles are also sometimes affected—one, or many, or all of them. Thus there may be paralysis of one cord, or paralysis of the abductors, or paralysis of all the muscles, with cadaveric position of the cords. The voice in the last case will be lost completely, and variously modified in other cases (*see* Paralysis of the Larynx).

Sensory symptoms may occur, but in children they are frequently not detected. They consist in a feeling of numbness, or formication, or distinct anæsthesia, especially in the extremities. Ataxy has been observed with very little actual paralysis, and rarely transient muscular spasms. Sometimes the muscles or the nerve trunks are tender on pressure. In severe cases electrical reactions are diminished, and some muscular atrophy ensues. Recovery generally takes place within three or four months, and the paralysis rarely, if ever, becomes chronic. Death, however, results sometimes from paralysis of the diaphragm, with gradually increasing accumulation of secretion in the bronchial tubes, and sometimes from cardiac paralysis, shown by a feeble, irregular or intermittent, generally quick, but sometimes slow, pulse, with vomiting and cyanosis.

Diagnosis. *Faucial Diphtheria.* The cardinal features are—insidious onset; characteristic membrane already described; relatively slight pyrexia; lowered blood pressure and weak pulse; albuminuria; onset of paralysis. The diagnosis can only be positively established by the bacteriological cultivation of the Klebs-Loeffler bacillus from the secretions of the affected part. This is generally done by means of a swab of cotton wool on the end of a piece of wire: the swab is smeared over the fauces or tonsil, inserted in a sterilised glass or metal tube, and sent to the bacteriological laboratory for cultivation. It is important to remember that bacilli are sometimes cultivated from the throat, both together with the Klebs-Loeffler bacillus and apart from it, which resemble it closely, but, unlike the *B. diphtheriæ*, are not virulent to guinea-pigs. The most important of these is *Hofmann's bacillus*, which is often found. It is about 2μ in length, and generally arranged in pairs.

In *follicular tonsillitis* small yellow, sometimes white, plugs are seen; they can be easily removed. There are often several plugs in the same area, as contrasted with one patch in diphtheria. The temperature is usually high. The tonsillitis and pharyngitis of *scarlatina* must also be considered, and also influenzal sore throat, herpes, and secondary syphilis. *Vincent's angina*, which is described under Diseases of the Throat, resembles diphtheria in its membrane.

Laryngeal Diphtheria. The diagnosis will be easier if there is simultaneous faucial or nasal diphtheria. It must be distinguished from catarrhal laryngitis, which may be simple, or may herald the onset of measles. Clinically it is often impossible to distinguish the two, so that a swab must be taken at the earliest opportunity. It is safest to assume the case is one of diphtheria until the contrary has been proved. Laryngeal diphtheria must also be distinguished from (*a*) obstruction below the larynx, such as broncho-pneumonia where there may be recession of the ribs, but not aphonia; and pressure from enlarged glands;

(*b*) obstruction above the larynx, such as retro-pharyngeal abscess; (*c*) œdema of the glottis, due to sepsis, nephritis, urticaria, and various other conditions.

Prognosis. The mortality from diphtheria has been considerably reduced since the introduction of the treatment by antitoxic serum in 1893. In the hospitals of the Metropolitan Asylums Board during 1891, 1892, 1893, the annual mortality was 30 per cent.; in 1913 to 1915 it averaged 7·17 per cent. The chance of recovery is diminished by every day, or half-day, that the treatment is delayed. Extensive formation of membrane, spread of the disease to the nose, rapid failure of strength, feeble pulse and hæmorrhages, are of unfavourable prognosis. Laryngeal diphtheria is more fatal, because, though laryngeal obstruction may be obviated by tracheotomy, death may occur from purulent bronchitis or broncho-pneumonia, caused by extension to the lungs. In these cases also the mortality has been much diminished by antitoxin. Diphtherial neuritis generally recovers, but is occasionally fatal through paralysis of the diaphragm.

Prevention. It must be remembered that the bacilli may remain in the throat long after the patient is himself quite well, and hence the risk of contagion remains. It is usual to keep a diphtheria patient from contact with others until bacilli can be no longer cultivated from the throat or nasal secretions. Sometimes a period of several weeks elapses before the patient is free; but 50 per cent. lose them at the same time as the membrane, not more than 7 per cent. retain them for one month, and not more than 1 or 2 per cent. for three months (Ledingham and Arkwright). These carriers may be treated as described under Cerebro-spinal Fever. Favourable results have also been obtained with vaccines, but tonsillectomy may be required in the last resort.

Other measures of prevention are—taking care of the milk supply; removal of susceptible children; periodical swabbing of throats in institutions; prophylactic injection of serum (1,000 units).

Undoubtedly the most important method of prevention is the Schick test (**25**). This test is used for determining whether individuals are susceptible to diphtheria infection or not. A small dose of diphtheria toxin—one-fiftieth of the minimum lethal dose for a 250-gramme guinea-pig in 0·2 c.c. of normal saline—is injected into the flexor surface of the forearm intradermally, not under the skin. The needle, which is of fine calibre, is passed nearly parallel to the skin within its substance. The injected fluid should appear and feel like a small button in the skin. A control injection of the toxin heated to 75° C. for ten minutes is made into the opposite arm. A " positive " reaction, which means that the individual is susceptible, is shown by a circumscribed area of redness accompanied by slight infiltration of the skin, measuring from 1 to 2 cm. in diameter. This appears in about twenty-four hours, and reaches a maximum in four or five days. There is no change on the control arm. In the " negative " reaction, which indicates immunity from diphtheria, there is no change in either arm. In a " pseudo " reaction, which indicates susceptibility to the foreign proteins of the injection and immunity to diphtheria, there is an equal area of redness in both arms, which is not so well defined, and reaches its maximum in twenty-four hours and rapidly fades. In the " combined " (positive) reaction both arms give a reaction; but that of the inoculated arm is larger and usually presents a distinctly defined central red area. The " pseudo " element disappears early, leaving a persistent positive reaction.

By this test infants up to six months are found to be immune, and the percentage of persons susceptible to diphtheria is greatest between the ages of two and five years. This coincides with the age-period when the incidence of clinical diphtheria is greatest. Active immunisation with toxin-antitoxin has been carried out with success in susceptible people, and this may be of value in the case of doctors and nurses or of children when diphtheria is prevalent in the locality; the tendency of public health authorities is to immunise all children up to six

or even ten years without preliminary Schick testing, because it has been found that most of them are positive (**23**).

Treatment. Immediately upon the diagnosis of diphtheria being known, and even before, if there is a high probability of the suspicion being confirmed by the bacteriological test, *diphtheria antitoxic serum* should be injected.

The initial dose required is from 10,000 to 40,000 units, according to the severity of the disease (*see* Immunity). If the case is urgent the serum (preferably the concentrated antitoxin-globulins) is injected intravenously or intramuscularly; otherwise it is made under the skin of the flank, or into the vastus externus, with antiseptic precautions. An effect is very often observed in a few hours either in the fall of the temperature or at least in the arrest of the progress of the symptoms. The dose may be repeated at intervals of twelve or twenty-four hours during the next two days, and the amount must be estimated by the intensity of the disease, and not by the age of the patient. Serum disease often follows these injections.

The general treatment described under Pyrexia should be employed. The fever is not often so high as to require special attention; but if the heart dilates, and the pulse becomes feeble, tincture of digitalis and other stimulants may be given. Recent experiments on animals suggest that blood transfusion may be of value in the circulatory failure associated with severe toxæmia (Harding).

The treatment of the throat in Faucial Diphtheria is the same as that described under Scarlatina.

For the removal of the offensive and irritating secretions when the nasal mucous membrane is involved the nostrils should be syringed with dilute disinfectant solutions, such as potassium permanganate and carbolic acid, or these may be administered by the nasal douche.

In laryngeal diphtheria the patient should be subjected to an atmosphere saturated with moisture. In a small room it will be sufficient to use a bronchitis kettle, the steam from which may fill the room. Much relief is also sometimes given by a hot bath. If improvement is not apparent in a few hours, intubation or tracheotomy should be performed, and this must be done at once if there is sucking in of the chest, if the patient is drowsy or becoming cyanosed, or if the forehead is cold and clammy. The probability of success is greater the earlier a tube is introduced into the larynx or trachea; and if it is suspected that the obstruction will increase, the operation should be done while the child is strong and of good colour. Generally in diphtheria tracheotomy is to be preferred to intubation. The latter is bloodless, and if it fails can be succeeded by tracheotomy; but it requires special skill in its performance, and the risk is run of pushing membrane down into the trachea. Nearly always some improvement follows an operation; the child breathes freely and deeply and sleeps tranquilly; but the danger of broncho-pneumonia still remains, and, as already mentioned, obstruction may take place from a plug of desiccated mucus lower down. To avoid this steam should be used, and oxygen, if given, should be passed through water. If obstruction occurs, spraying through the tracheotomy tube with sodium bicarbonate (10 grains to 1 ounce water) during inspiration may loosen the plug so that it is coughed up. In the last resort forceps should be passed down and the attempt made to get hold of the plug (Biernacki). Internally expectorants, such as ammonia or ipecacuanha in small doses, may be tried. The tracheotomy tube may often be removed in from one to four days. (See also Oxygen tent.)

If there are any signs of diphtheritic paralysis, the patient must be kept lying down. In the more severe cases, where swallowing becomes difficult, feeding by the nasal tube will be necessary. There will also be special danger in these cases of failure of the circulation. If the paralytic signs persist into convalescence, the patient should only be allowed to get up gradually, when all danger from the heart has disappeared. Strychnine in small doses is often prescribed for paralysis. Later on massage and electricity may be used for the muscles. They practically

always recover their function completely. In diaphragmatic paralysis the Drinker machine is used.

WHOOPING-COUGH

(*Pertussis*)

Whooping-cough is a disease characterised by a peculiar convulsive cough, followed by a long-drawn inspiration through the nearly closed glottis, by which a crowing noise, or " whoop," is produced.

It is spread by droplet infections, commonly from patients in the pre-catarrhal stage; but healthy " carriers " of this disease have been known. Children are very susceptible, and most people have the disease in early life, while it quite rarely attacks adults. A second attack in the same patient is even more rare than in the case of the exanthems. It is most common between the ages of one and eight years, and girls are more liable to it than boys. It occurs in epidemics, but there is not much evidence that such epidemics are determined by climate or weather. It has often been observed that an epidemic of whooping-cough has immediately followed an epidemic of measles.

Pathology. Whooping-cough is caused by the bacillus of Bordet and Gengou (1907), which is now called the *Hæmophilus pertussis*. The blood serum of convalescent cases agglutinates this bacillus, and gives the deviation of complement reaction with it. Vaccines prepared from it have appeared to influence favourably the course of the disease (Freeman). While the cough must be due to the secretion set up by the organisms, the whoop is not so readily explained. It is generally thought to be caused by a spasmodic closure of the glottis, but a passive approximation of the cords, or a failure to open freely when the sudden inspiration takes place, would probably account for it.

The **Morbid Anatomy** of pertussis is that of its complications, usually broncho-pneumonia.

Symptoms. The period of *incubation* is seven to nineteen days. The limits are four to fourteen days. The first stage is catarrhal. There are cough, expectoration in children old enough, a few rhonchi in the chest, and slight pyrexia; but sometimes with the cough there is an unusual repetition of the expiratory effort, which may lead to suspicion of whooping-cough. This preliminary bronchitis lasts from seven to ten days, and then there is a more or less rapid transition into the second or convulsive or whooping stage. First, perhaps, a long-drawn inspiration follows the cough, and then an unmistakable " whoop." But the cough itself is as characteristic as the whoop. The child may be playing with its toys, apparently well, when it suddenly stops, seems distressed for a moment, and then perhaps runs to its mother or nurse. A short cough occurs; this is quickly followed by another and another without any intervening inspiration, each successive cough getting less loud and more stifled until they have mounted up to fifteen or twenty expulsive efforts in the course of seven or ten seconds. Then follows a long-drawn inspiration with loud laryngeal sound, the " whoop "; another burst of short coughs succeeds, with another " whoop "; and this sequence may occur once or twice more, with less violence and less noise, until finally a little tough mucus is expectorated, or vomiting takes place. During the coughing efforts the face becomes congested or cyanosed, the features swollen, the eyes starting from the head, the tongue hanging from the mouth, blood-stained saliva is coughed in all directions, and little relief takes place even from the inspiration, until the final expectoration of mucus or the cessation of the paroxysm. During this time the child is quite given up to the absolutely uncontrollable reflex process; a child in bed, when it feels the attack coming on, will seize the porringer and place it under its mouth, and in another few seconds it will be entirely at the mercy of the cough, and regardless of what is going on around. As a result of the obstruction to respiration during the coughing efforts,

hæmorrhages may take place, bleeding from the nose, mouth, or gums, subconjunctival ecchymosis, petechiæ under the skin, and in very rare cases cerebral hæmorrhage. Sub-lingual ulcer is characteristic. After a time the face often acquires a puffy and bloated appearance from the frequent obstructions to the return of blood to the chest. The attacks often appear to be spontaneous, but they constantly occur if the child cries or gets in a passion, or even if the child is disturbed, as when the nurse begins taking off the clothes for an examination of the chest. The number of paroxysms, which may, as above shown, include three or four actual "whoops," ranges from one to sixty in the twenty-four hours, but it is very rare to have more than forty attacks, and many cases never reach thirty in the twenty-four hours. In the intervals the child may be perfectly well, and is free from fever, unless there is some complication. The second stage of whooping-cough lasts a variable time, often from three to six weeks, but sometimes up to three months or more. The attacks gradually get less frequent, until they cease altogether, or as they diminish they may be accompanied by attacks of simple cough, not followed by a whoop, and this may last a few weeks longer. Death rarely occurs directly from the paroxysms ; it may occasionally do so from prolonged closure of the glottis, or from cerebral hæmorrhage.

Other **Complications and Sequelæ,** however, occur which may make whooping-cough a serious and even dangerous complaint. Amongst the former may be classed *bronchitis*, which may continue throughout, and *broncho-pneumonia* (*11·5* per cent. of 889 cases at the M.A.B. Hospitals in 1914). Often, but not always, the whoop is absent during broncho-pneumonia, as it is if any other febrile complication ensues. *Otitis* (*6·5*) is less frequent than in scarlatina and measles. General convulsions (*2·7*) sometimes occur, either as a direct result of the paroxysm or less commonly as the indication of cerebral hæmorrhage or thrombosis, or, it may be, of the onset of pneumonia. As sequelæ continued bronchitis, emphysema, and bronchiectasis with clubbing of the fingers occasionally occur. There does not seem to be any relation between whooping-cough and tuberculosis.

Diagnosis. This mainly depends upon the whoop, on the convulsive character of the cough, and on the regularity of the course from the catarrhal to the convulsive stage. Enlarged bronchial glands may cause a cough something like that of pertussis, but there will be no history of infection and no whoops ; while other symptoms of independent lung diseases may be present. In whooping-cough the leucocytes are increased to 15,000 or 30,000 per cubic millimetre ; and a differential count gives 60 per cent. of lymphocytes to 40 per cent. of polymorphonuclears, with a few eosinophils. These changes occur quite early, and are of use in diagnosis (H. T. Ashby). A certain diagnosis can be made from a culture of the *H. pertussis* by collecting the cough-droplets on suitable media in Petri dishes (9). It has been obtained from 75 per cent. of cases in the catarrhal stage, from 54 per cent. in the paroxysmal stage, and from only 9 or 10 per cent. after five weeks.

The **Prognosis** is to be made from the severity of the complications.

Treatment. The child should be kept in a warm but well-ventilated room, but confinement to bed is not necessary in an uncomplicated case. A variety of drugs has been used to check the paroxysms of pertussis. Belladonna is much used in the form of tincture, of which 2 or 3 minims may be given to a child two years old three times a day, and larger doses to older children. The dose may be cautiously increased up to 10 to 15 minims in a child of five or six. Dilute hydrocyanic acid (1 to 2 minims), chloral (2 to 5 grains), potassium bromide (2 to 5 grains), hydrobromic acid (3 to 10 minims), antipyrin (2 to 5 grains), and bromoform (2 to 5 drops mixed with almond oil and mucilage of tragacanth or acacia), have been given. Recently benzyl benzoate has been tried with great success. It is a powerful antispasmodic. A 20 per cent. alcoholic solution is used, and the dose is 5 to 40 minims in water three or four times a day, depend-

ing on the age and severity of the attack. Benzaldehyde may be added in amounts varying from 1 to 5 per cent., and this increases the effect. Treatment in the oxygen tent, with or without carbon dioxide, is very effective in stopping the paroxysms. Where the cough results from a tickling in the throat, relief may be obtained by painting the lingual tonsil with tincture of iodine. Broncho-pneumonia may also require treatment.

THE ENTERIC FEVERS

In the early part of the nineteenth century, the fevers, excluding the exanthemata, which were characterised by a definite cutaneous eruption, were divided into continuous and intermittent. The intermittent were those now known as malarial. When the continuous fevers were further differentiated they included typhus, typhoid, and relapsing fevers. Though the distinction between typhus and typhoid was convincingly demonstrated by Sir William Jenner in 1849 to 1851, the absence of characteristic features in individual cases led to difficulties, and until comparatively recently these two fevers were still in Germany included under the common name *typhus*, the former being called typhus exanthematicus, from the prominence of its eruption in typical cases, and the latter typhus abdominalis, from the presence of intestinal lesions with their corresponding symptoms. In English practice for many years the term *enteric fever* has also been in use both to represent this characteristic feature and to accentuate the difference from the pathologically distinct typhus. This distinction was confirmed when, in cases of typhoid or enteric, Eberth discovered a bacillus, now known as *B. typhosus*. In 1901, however, it was found that in some of these cases, which clinically could not be regarded as other than enteric, the causative bacillus differed in certain particulars from Eberth's organism. Two such organisms have been identified which have been called *B. paratyphosus A* and *B. paratyphosus B;* and it is found, as a rule, with certain exceptions to be mentioned hereafter, that the serum of patients suffering from typhoid fever will agglutinate only the *B. typhosus*, while the serum of a patient with paratyphoid fever, whether *A* or *B*, will agglutinate the paratyphoid bacillus, whether *A* or *B*, which is the cause of his illness.

At present, therefore, it is convenient to speak of all these forms as Enteric Fevers, or forms of enteric fever, and to distinguish them as

Typhoid Fever, due to the *B. typhosus;*
Paratyphoid Fever *A*, due to *B. paratyphosus A;*
Paratyphoid Fever *B*, due to *B. paratyphosus B.*

Typhoid fever will be first described, and subsequently the differences which are presented by the fevers caused by paratyphoid organisms.

TYPHOID FEVER

Typhoid fever is infectious chiefly through the excretions. It has a febrile period of about three weeks' duration, and occasionally one or more relapses of the same length. The distinctive pathological lesion is inflammation and ulceration of Peyer's patches in the small intestine.

The specific micro-organism discovered by Eberth is a bacillus, 2–3μ in length, with round ends, and provided with from eight to twelve fine flagella of about twice its length. It bears a close resemblance to the *B. coli communis*, but can be distinguished from it by bacteriological tests. Eberth's bacillus has been found during life in the stools, in the blood, in the urine, in the sputum, and in the pus of abscesses resulting from periostitis and other similar lesions months and even years after the attack. After death it has been found in Peyer's patches, in the mesenteric glands, spleen (abundantly), liver, gall-bladder, kidneys, meninges, bone marrow, and, rarely, in the lungs and testicles.

Ætiology. Enteric fever shows little preference for either sex; but age has a marked influence, and the disease is much more frequent amongst young people. The quinquennial period which presents the highest percentage of cases (viz. 27 per cent.) is that between fifteen and twenty years; nearly 50 per cent. of the cases occur between fifteen and twenty-five, and more than 84 per cent. between five years and thirty (Corfield). The disease does, nevertheless, occur (1 or 2 per cent.) in people over sixty-five years of age. It is more prevalent in the latter part of the year—that is, in the four months August to November inclusive—and cases are more numerous during hot and dry weather than under the opposite condition. It is not affected by overcrowding, poverty, and uncleanliness, in the same way as typhus and relapsing fever, which are transmitted by external parasites. As a rule, doctors, nurses, and students in hospitals do not take enteric fever directly from the patients. The agent of transmission is, in the vast majority of cases, the fæces; and in those not very common instances in which nurses have contracted the disease from their patients it was probably by direct contact with linen or bedclothes soiled with the fæcal discharges. But bacilli are found in the urine in some cases, and are constantly present in the pus from the bone lesions (*e.g.* periostitis) which sometimes follow typhoid fever; both these secretions may therefore be the means of transmitting the disease.

A frequent cause of the spread of typhoid fever in a town or a country district is the contamination of its water supply by the stools of a single case. The opportunity arises from the imperfect means so often employed for the disposal of sewage. In the country, wells used for drinking water may be poisoned in consequence of the soil being saturated with sewage which has leaked from a neighbouring privy or imperfectly constructed cesspool. In one case a well was contaminated by the slops from a laundress's house leaking into it; enteric fever broke out in the house supplied by the well shortly after the laundress had received some linen soiled by the discharges from a patient with this disease. Where the drinking water is conveyed by pipes, the disease may find an entrance if the pipes by any chance are defective, and if they lie in a porous soil sufficiently close to any collection of sewage, imperfectly confined, which has received any enteric stools; and a whole reservoir may be infected in the same way. Drinking water is, however, not the only source of danger. Epidemics of enteric fever have been traced to the milk supply, the probability being that the milk itself has been first infected by being stored in vessels washed with water exposed to contamination by typhoid sewage. Typhoid has also been traced to ice-creams sold in the street, and to oysters, cockles, mussels, and clams, supplied from breeding areas exposed to sewage contamination, and eaten uncooked. Watercress or celery may be an agent in a similar way.

Contamination of food by flies, which have had access to the excreta of enteric patients, may spread infection. This fact was proved by experience in the Spanish-American war in 1898 and in the South African war.

But the transmission of the disease by the bacillus is not confined to the period during which the patient is suffering from the fever. Months or years after recovery, when apparently in perfect health, he may still be harbouring the bacillus; and indeed the organisms may exist in those who are not known to have had typhoid fever at any time, and yet may be the cause of infection to persons coming into contact with them. These are all called *typhoid carriers*, and are divided into groups. *Convalescent* or *temporary carriers* are those who have had the disease within two or three months; *chronic carriers* are those in whom the bacillus persists for months or years; *healthy carriers* are those who are not known to have had the fever, and yet are infecting others; and *early carriers* are certain persons, also healthy at the time when bacilli are found in their fæces, who only subsequently develop typhoid fever. The test of a carrier is that the bacilli should be found in the fæces or in the urine; in a large proportion the blood gives the Widal reaction. That the bacillus of typhoid

fever is constantly found in the gall-bladder is well known, and in a large proportion of chronic carriers gall stones are formed and give rise to the usual difficulties. The carriers infect others by direct contact, or by unconsciously conveying the bacilli to water, milk, or things they handle.

Morbid Anatomy. The essential lesions of enteric fever occur in the *Peyer's patches* and *solitary follicles* of the small intestine. These become infiltrated with lymph corpuscles, and a Peyer's patch so affected swells, and projects upon the inner surface of the intestine; it is grey, fawn-coloured or pink, but the surrounding mucous membrane may have its natural colour. The lymph corpuscles at first multiply in the follicles, but subsequently infiltrate the mucous membrane above and the deeper structures below. As the patches become larger they acquire a creamy-white colour, and about the tenth day or a little later they begin to ulcerate or slough, presenting at first a superficial abrasion at one point of the surface, which becomes deeper and deeper until a great part of the gland is removed; or a whole patch may slough at once. When the slough is still adherent, it is often stained yellow by bile pigment. By these processes the muscular coat or the peritoneal covering may be exposed in the floor of the ulcer, and finally the peritoneum may slough, ulcerate, or tear, so that the contents of the bowel escape into the peritoneal cavity, and set up intense peritonitis. The stage of ulceration generally occupies part of the third week, and towards the end of that time, in favourable cases, the process of healing by cicatrisation begins. Ulceration does not necessarily occur: in mild cases the inflammatory swelling subsides without any destructive change. The number of Peyer's patches affected is very variable, and though the cases with severe diarrhœa generally have extensive inflammation of the bowel, there is no necessary correspondence between the extent of ulceration and the severity of the other symptoms. The patches near the ileo-cæcal valve are those first attacked, and the process spreads upwards. The change in the solitary follicles of the lower end of the ileum is of the same kind, and in some cases the lymphoid follicles of the large intestine (mostly the cæcum) are also enlarged and ulcerated. Coincidently with these lymphatic structures of the intestines the *mesenteric glands* are inflamed; they are enlarged, fleshy, pink, red, or purplish, and their histological changes resemble those of Peyer's patches. The other post-mortem appearances are similar to those that occur in any febrile condition (*see* p. 18).

Symptoms and Course. The period of *incubation* is three to twenty-three days, usually about a fortnight. The beginning of the disease is often very little marked. The patient feels ill, depressed, unfit for work; he has headache, pains in the limbs and back, loss of appetite, and perhaps nausea. These may come upon him so that he scarcely knows when they began, but he can frequently fix a day on which he says he first fell ill. Often the headache is severe, and forms the most prominent complaint. There may be diarrhœa in the first few days. Constipation, however, is also extremely common. Sometimes on the first feeling of illness a purgative is taken, and the bowels continue loose. The patient may go about, struggling to do his work, for five or six days, but generally towards the end of the week he is obliged to give up and take to his bed. The temperature has been stated, in the first four or five days of enteric fever, to rise two degrees each evening, and to fall one degree each morning, so that at the end of that period it will have reached 103° or 104°. So many cases escape accurate observation in the early days that it is not always easy to confirm this, but it is certain that in some cases the thermometer may rise on the first evening of illness to 103° or higher. The high level of 103° to 104° once reached, the temperature commonly remains at nearly the same level till the tenth to the fourteenth day, oscillating, however, between morning temperatures of 102° to 103° and evening temperatures of 103° to 104·5°. The pulse is quick, full, soft, and markedly dicrotic. Though in some cases very rapid, it is generally, in relation to the temperature, much slower than in typhus and many other

febrile conditions; it may never exceed 100, and a pulse of eighty may co-exist with a temperature of 102° or 103°. The respirations are increased in frequency, and there is very frequently slight bronchitis, indicated by sibilant rhonchi, and accompanied, it may be, by mucous expectoration. About the seventh to the tenth day the patient commonly begins to present the characteristic appearance of enteric fever. He is dull, listless, apathetic, but not so dull and stupid as in typhus; the eyes brighter, the pupils often dilated; the face pale, with flushed cheeks and dark lips; the tongue dry, with a band of dry white fur on each side, the sides, tip, and middle clean and red. As the disease progresses, or in severe cases, the tongue tends to become thickly furred and dry all over its surface. Occasionally profuse perspiration occurs, or bleeding from the nose. At the end of the first week, or later—that is, from the sixth to the twelfth day—appears the characteristic *rose rash* of enteric fever; it consists of rose-pink spots, circular, slightly raised above the surface, flat, convex, but not pointed, so that they are often described as *lenticular*, from 2 to 4 mm. in diameter, disappearing under firm pressure with the finger, and never petechial like the typhus rash. They are seen first on the abdomen and front of the chest, and may be confined to these parts; but they also occur on the sides, back, and the upper arms and thighs. In number they vary from half a dozen to twenty or thirty, but they may be much more numerous, and in a certain number of cases (10 to 20 per cent.) are entirely absent. Each spot has a limited duration, gradually fading in three or four days; but spots continue to come out day after day until the end of the third week, or in some cases even later. They are not visible after death. In the second week also the *intestinal symptoms* become prominent. The abdomen is generally full, even distended, and resonant on percussion; and there may be both tenderness and pain, but the former is more common than the latter. Pressure in the right iliac fossa, over the seat of the cæcum and lower end of the ileum, often elicits a little pain. *Diarrhœa* is a familiar symptom of enteric fever, but it is very variable in duration and in severity. Often there is a sharp attack of diarrhœa in the first week, and after this the bowels are confined; sometimes (up to 40 or 50 per cent. of the cases in some epidemics) there is *constipation* throughout. In other cases diarrhœa is constant, and the motions number three, four, or five or more daily. The stools, moreover, are distinctive in being liquid, of the colour of pea-soup, and of a peculiar offensive odour. They commonly contain particles of undigested food, intestinal epithelium, bile pigment, micrococci and bacilli, crystals of ammonium-magnesium phosphate, and after a time shreds of sloughs from the diseased Peyer's patches. They are alkaline and ammoniacal. The intestinal lesions further show themselves occasionally by the occurrence of *hæmorrhage*. This often happens in the stage of separation of the sloughs or of ulceration, and large quantities of bright red blood are discharged from the bowel, so as to cause severe collapse, with pallor and depression of temperature; but the bleeding may be quite slight, and this more often in the earlier stages of the illness. The *spleen* is generally enlarged; this may be manifest only from the results of percussion; but in most cases the organ can be felt on deep inspiration 1 or 2 inches below the costal margin. The *urine* is scanty, dark, and of high specific gravity; the urea and uric acid are increased, but the sodium chloride is much diminished. Late in the illness albumin is found in a small proportion of cases. But for the headache and some giddiness the cerebral functions may be very little disturbed in mild cases; the headache rarely lasts beyond the tenth day, and there may be then only a little drowsiness or tendency to wander at night. A temporary deafness is not uncommonly noticed. Such mild cases reach their acme at the end of the second week—the tenth to the fourteenth day. The temperature then takes a characteristic course; hitherto standing always at a high level, it now falls every morning quickly lower and lower, while the evening temperatures, though also falling, come down much less rapidly. Thus the morning temperature in four or five

days reaches 99° or 98°, while the evening temperature stands at 102° or 101°. This may be called the *remittent* stage. From this point to the end of the illness the fever has for three or four days an *intermittent* character; it is about normal in the morning, but rises to 101° or more in the evening. Then rather suddenly the evening fever ceases, the temperature remains normal or subnormal, and convalescence has commenced. During this falling temperature spots may continue to come out, the spleen is still perceptible, and there may be a little diarrhœa; but the mental condition of the patient generally improves, and he often acquires an appetite some days before the fever has entirely left him.

On the other hand, the graver cases are mostly accompanied by an increase in the intensity of the nervous symptoms, to which the symptoms of cardiac failure, or severe abdominal troubles, may be added; more or less continuous delirium may supervene, with drowsiness or even coma, extreme muscular prostration, subsultus tendinum, and plucking at the bedclothes. The face

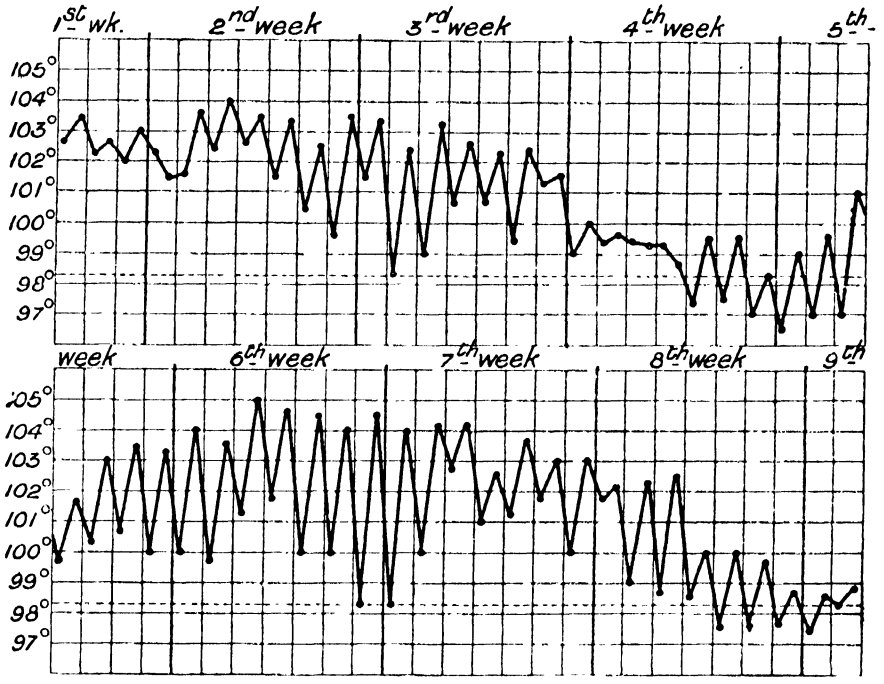


FIG. 6.—Temperature in a Case of Enteric Fever with Relapse.

becomes dusky, the tongue dry, sordes collect on the lips and teeth, the pulse is rapid and soft, the heart sounds are feeble, and the bases of the lungs are congested, as shown by râles and a very feeble respiratory murmur. The urine may be retained, or both fæces and urine are passed unconsciously. The condition resembles that described under Typhus Fever; the patient is in a truly *typhoid* state. The delirium is less often violent than in typhus, but occasionally patients get out of bed or refuse food. Sometimes there is evidence of cardiac dilatation, and the pulse may be irregular or intermittent. With the increase of the nervous symptoms the abdominal troubles are often prominent, the diarrhœa becomes profuse, and the abdomen is much distended, tense and tender; in this stage the ulcerated bowel may give way, and peritonitis may result from the escape of fæcal matter into the cavity of the abdomen. Death may occur almost at any time after the tenth or twelfth day; but recovery occurs after lengthened periods of coma and other severe symptoms, the temperature slowly returning to the normal, and convalescence being very protracted.

Relapses. A true relapse of enteric fever occurs in a certain proportion of cases, which have been found by different observers to be from 3 to 10 or 11 per

cent.[1] It consists of a repetition of all the phenomena of the illness: ulceration of Peyer's patches, fever, diarrhœa, and rose spots; and it occurs after an interval which may be as long as eleven days from the termination of the original fever, but is often much less. Sometimes, indeed, there is no interval of actual apyrexia, and the relapse seems to be continuous with the primary fever. Its duration is often quite as long as that of the first attack (Fig. 6), and, as a rule, it is somewhat milder. Death may, indeed, take place in the relapse, but this is more often from complications, such as perforation of the intestine and peritonitis, or hæmorrhage, than from the severity of the pyrexia or toxæmia alone. Occasionally a second relapse occurs after another interval of apyrexia; and even third and fourth relapses have been observed, though very rarely.

Complications. The complications are numerous and varied, but a large proportion of patients escape them. As might be expected, the most important are those connected with the intestinal lesions.[2] *Hæmorrhage* (*6·0*) has been already mentioned (*see* p. 74). *Peritonitis* is a frequent cause of death. It arises most commonly from perforation of the floor of one of the ulcerated Peyer's patches, through which the contents of the bowel are extravasated into the peritoneal cavity; it occasionally happens from extension of inflammation through the peritoneal coat without any perforation being discovered; and it has also been caused in rare cases by the softening of inflamed mesenteric glands and infarctions in the spleen, and by rupture of the gall-bladder. *Perforation* of the bowel takes place in more than 30 per cent. of fatal cases of typhoid fever. In more than two-thirds of the cases it occurs in the second, third, or fourth week, but it is rare before the ninth day. The perforation usually occurs in the last 2 feet of the ileum, and not infrequently there may be two or more perforations. Its onset is often accompanied by acute pain, collapse, and perhaps vomiting or rigors; the abdomen is tender, sometimes flat and rigid, at others distended, but in both cases moving scarcely at all on respiration; the pulse is small and rapid, and the temperature sometimes falls. But its advent may only be marked by collapse and increased distension; and in very severe cases, with much distension of the bowel as well as coma and delirium, there may be no certain signs to indicate peritonitis, so that perforation and peritonitis are occasionally found post mortem when not suspected during life. A progressive increase in the total leucocyte count from hour to hour is a valuable diagnostic point in doubtful cases. So long as the ulcer remains unhealed there is a possibility of a rupture taking place; and such a rupture may be induced by any disturbance of the bowel, as by vomiting, defæcation, the exertion of sitting up, or the administration internally of indigestible food or of aperients; and thus even cases which are running a mild course may be fatal from this cause. *Ulcerations of the pharynx* have been observed. They are mostly superficial, situate upon the pillars of the fauces, and sometimes accompanied by swelling of the lymphatic glands; they may occur early in the illness, and have been wrongly attributed to syphilis or diphtheria.

A slight amount of *bronchitis* is frequent in enteric fever, but occasionally it is so severe as to constitute the main feature. The face may be quite livid, and a more or less venous tinge may be given to the whole surface; the chest is filled with râles and rhonchi, and there is expectoration of mucus or muco-pus. *Ulceration of the larynx* occurs sometimes in severe cases. The ulcer is situate commonly over the arytenoid cartilage, and this may be even exposed and in a state of necrosis. Sometimes an abscess forms around the cartilage in consequence of *perichondritis*. As results of these laryngeal com-

[1] At the Metropolitan Asylums Board's hospitals in twelve years from 1900 to 1911 the percentage was 10·3. In 1914 in 316 cases the percentage of relapses was 6·96.

[2] The bracketed figures in italics represent the percentage occurrence of each complication among 316 cases in the Metropolitan Asylums Board's hospitals in 1914; no later data have been published.

plications there may be hoarseness or complete aphonia; subcutaneous emphysema, from air being forced during expiratory efforts from the larynx into the connective tissues; and cicatricial stricture of the glottis in cases that recover. A temporary aphonia may occur without any evidence of ulceration. *Pneumonia* sometimes becoming gangrenous, *broncho-pneumonia* (*5·4*) and *pleurisy* (*0·9*), both serous and purulent, occasionally occur, and much more rarely *pneumothorax*. *Jaundice* is of rather rare occurrence; it may be due to hepatitis or to the well-established affinity of the bacillus for the gall bladder. The stools are not necessarily deprived of bile pigment, and recovery may take place without any further indications. There may be *cholecystitis*. *Acute nephritis* (1·3), sometimes with abundant albuminuria or hæmaturia, may occur. In about one-fourth of the cases of enteric fever the bacilli are found in the urine, especially in the third week; sometimes they are so abundant as to cause a visible deposit (*bacilluria*), and sometimes they give rise to *pyelitis* or *cystitis*. They may persist there for years, as has been stated in connection with typhoid-carriers. *Otitis* (*3·2*) and *otorrhœa* may occur during or after the fever, and may lead to deafness, or to the more serious conditions of *septicæmia* and *meningitis*. Meningitis from the typhoid bacillus has been recorded as occurring without intestinal lesions. Double *optic neuritis* is sometimes seen, but it is rare. Other local inflammations occasionally occur either during the fever or during convalescence, and may considerably delay recovery, such as *parotitis* (*0·3*), which may be followed by suppuration, or extensive infiltration of the neck; *orchitis; myositis; cancrum oris;* abscesses (*2·2*), boils (*0·6*) and facial *erysipelas*. *Periostitis* (*1·3*) occurs especially on the tibiæ, but also in other bones, such as the ulna or metacarpals; and *perichondritis* of the costal cartilages may occur. Pain in the lumbo-sacral region aggravated by walking, and persisting for a long time, has been called *typhoid spine;* in some cases the Röntgen rays have shown ostitis, periostitis and perichondritis about the lumbar or lower dorsal vertebræ. Another condition is described as *tender toes;* in this the toes and soles of the feet are painful on pressure during attempts at walking. In severe cases *bed-sores* may form, in spite of careful nursing. *Thrombosis* (*2.2*) of the femoral vein, generally on the left side, may occur during early convalescence, leading to œdema of the foot and leg, and tenderness in the course of the vein. It mostly subsides without much trouble, but the thrombosis may extend into the large abdominal veins, or portions of clot may be detached, and lead to pulmonary embolism and death. *Rigors* are of rare occurrence. Among the nervous sequelæ, besides meningitis, are *encephalitis* (rarely); *mental disturbances*, especially a Korsakow's syndrome, and in a few cases a permanent memory defect; *peripheral neuritis* and, rarely, localised muscular atrophy.

Varieties of Typhoid Fever. There are few diseases more variable than typhoid fever. Though its duration is characteristically three weeks, it may be as short as ten days or as long as five or six weeks; and though short attacks may sometimes be fairly represented as abortive attacks, they may be followed by a relapse of precisely the same nature and duration. Sometimes the temperature begins to fall in the manner described (*see* p. 73), and then, before reaching the normal, persists in its remittent type, oscillating between 100° (morning) and 102° (evening) for eight or ten days, so that the fever is prolonged into the fifth week, although the patient is feeling better every day, and has no obvious complications. In other cases the prolongation of the fever corresponds with a continuance of the high temperature characteristic of the second week, and these are generally severe cases. In some cases the illness is so slight that patients go about their ordinary occupations until, perhaps, an indiscretion in diet or the use of aperients, given in ignorance, leads to a fatal perforation. Cases so mild as this in their general symptoms, and yet so dangerous from their possible termination, have been called *ambulatory typhoid*. Ataxic and adynamic forms have been described, but these terms simply indicate the predominance of

symptoms in one or other system of the body. Very rarely a *hæmorrhagic* form occurs, in which there are purpuric eruptions on the skin, bleeding from the mucous membranes, epistaxis, hæmoptysis, hæmatemesis, and hæmorrhage into the muscles and internal organs. (Compare Measles and Small-pox.) Typhoid fever is very often mild in children, often of short duration, and associated with less extensive disease of Peyer's patches than in the average of adult cases The remissions of temperature, which are well marked in the latter half of the illness in adults, are often still more marked in children, and the "infantile remittent fever" of older writers was undoubtedly enteric fever. In elderly persons also the rose spots and enlarged spleen are often absent.

Diagnosis. In every case of pyrexia which is in any way suggestive of enteric fever, an attempt should be made at the earliest possible moment to isolate the organism by blood culture. Blood is withdrawn from a vein under strictly aseptic precautions; enough sterile sodium citrate is added to make a 0·5 per cent. solution. This is to prevent clotting. The blood is then mixed with 5 to 10 times its volume of sterile broth and incubated at 37° C. At least 5 c.c. of blood should be withdrawn and several culture tubes prepared. Blood culture gives a high proportion of positive results if performed within the first seven days of the disease. It may, however, be positive very much longer, and, at whatever stage of the disease the patient is seen, it should always be attempted. In cases of over seven days' duration a specimen of blood should also be taken in order to test the agglutinating power of the serum against the enteric group of micro-organisms (Widal's reaction). It is advisable as a routine measure to send specimens of fæces and urine for cultivation. Positive results, however, cannot be secured at all stages of the illness, and negative reactions must not be hastily regarded as excluding the disease. It is therefore necessary to give full consideration to all the clinical features of the illness, as well as to the several points in the ætiology and history of the case. The Widal reaction is not usually positive until about the fourteenth day of the disease, but may remain so for many months after convalescence. The value of the reaction in the diagnosis of the paratyphoid fevers and in persons who have been inoculated is discussed later.

A great number of diseases may be confounded with enteric fever, from the variety of forms which it assumes, and from the frequency with which its own typical symptoms are absent or badly marked; but it may be briefly stated that the characters which are the most constant and the most suggestive of the enteric fevers are *headache*, *persistent fever*, *rose spots*, and *enlarged spleen*.

In early stages it is distinguished from the exanthems by the absence of characteristic eruption. Severe joint pains may lead to a suspicion of rheumatic fever. A prolonged febrile complaint which has come on insidiously, and presents no obvious local lesions, should always make one think of enteric fever; but the great prevalence of *influenza* gives rise to frequent mistakes. For though influenza is often a much more sudden and quickly prostrating disease, it presents so much variety that almost any illness beginning with headache, backache, and fever is liable to be mistaken for it. If typhoid fever is present, the temperature remains high, or even rises, and the diagnosis may be soon confirmed by diarrhœa, enlargement of the spleen, or rose spots. Tenderness over the gall-bladder and muscular resistance in the right hypochondrium are said to be early signs of typhoid infection, but of course they may be due to local inflammatory lesions.

Later stages present a resemblance to different diseases according as the head, chest, or abdomen shows the most prominent disturbance. Thus the headache of typhoid, which rarely continues beyond the tenth day, and the subsequent delirium may suggest *tuberculous meningitis*, and the two diseases are frequently confounded together. Lumbar puncture and the examination of the cerebro-spinal fluid for cells and protein and tubercle bacilli will decide the diagnosis. When pulmonary symptoms are marked, *acute general tuberculosis* may be simu-

lated by the abundant bronchitic râles and crepitations accompanied by a remitting fever. The abdominal diseases which may be confounded with typhoid fever are especially *tuberculous peritonitis* and *appendicitis*. In both there may be high fever, abdominal distension and tenderness; and in tuberculous peritonitis the stools may be frequent and yellow from accompanying tuberculous ulceration. In appendicitis there is localised pain and tenderness. The *pyæmic* or *septicæmic* condition associated with abscess or suppuration in other parts of the abdomen, such as hepatic abscess and perinephritis, may also give rise to confusion; and the rare disease *suppurative pylephlebitis*, in which local evidence of the liver being involved may be little or none, must not be forgotten. In most of these conditions *leucocytosis* is present. *Infective* or *malignant endocarditis* is not infrequently mistaken for typhoid fever. Trichinosis, the disease caused by the multiplications of the *Trichina spiralis* within the body, has been mistaken for typhoid fever; it is distinguished by severe muscular pains, œdema of the eyelids, and sometimes of the whole body.

Undulant fever presents some resemblances to typhoid fever, and should be thought of when the illness has been contracted in places where the former disease is prevalent. Certain types of malarial infection, especially malignant tertian, may almost exactly simulate typhoid fever. They may be distinguished by the demonstration of parasites in the blood, the evidence of red cell destruction seen in a blood-film and the reaction of the pyrexia to quinine. It must not, however, be forgotten that malarial infection and typhoid fever not infrequently co-exist in the same patient.

An examination of the blood (*see* Diseases of the Blood) may give some help in diagnosis. In all but the earliest stages of typhoid fever there is a reduction of the neutrophil leucocytes, which reach their minimum in the period of declining pyrexia. The lymphocytes are also diminished at first, but increase again at the end of the stage of continuous pyrexia, and remain abundant throughout the fever, and for some weeks into convalescence. Eosinophils disappear at first, and reappear with the increase of the lymphocytes (Nägeli). Secondary infections, or other complications, may increase the leucocytes again, especially the polymorphonuclear cells.

Marris has found that in the enteric group of fevers the heart's action is not quickened by atropine to the same extent as it is in healthy persons. This difference is observed about the tenth day of the fever, though sometimes earlier; and the normal response to atropine may be resumed at any time after the fourteenth day, though it may persist much longer, and will vary with relapses. In persons over fifty years of age, and in those suffering from heart disease or from arterio-sclerosis, the failure to quicken may be due to pre-existing cardio-vascular changes, and not to the typhoid poison.

The pulse rate is taken and recorded minute by minute till it is steady. One thirty-third of a grain of atropine sulphate is then injected subcutaneously, best over the triceps. After twenty-five minutes the pulse is again recorded minute by minute till it is clear that its rate has reached its highest point, and is now falling. Marris concludes that an increase of the pulse rate by twenty or more beats in the minute after atropine may be accepted as an indication that the patient is probably not suffering from typhoid fever or one of the paratyphoid series. An increase of less than ten beats is suggestive of infection by one of these diseases. Readings between ten and twenty are uncertain.

Prognosis. The mortality of typhoid fever varies in different epidemics from 5 to 20 per cent. Complications contribute largely to the deaths, and their occurrence will modify the prognosis at any time. Apart from them, the intensity of the fever is an important guide. If the temperature is, although high at the end of the first week, subsequently never above 103°, the case is favourable; if the temperature is maintained at 104° or higher throughout the second week, it is much more dangerous. Some cases sink rapidly by the twelfth, eleventh, and

tenth days, or even before this. Perforation is almost certainly fatal unless it is promptly treated by surgical methods. Hæmorrhage is less dangerous, but may be responsible for about one-fifth of the deaths; and the mortality amongst cases with free hæmorrhage is much above the average. A severe hæmorrhage, even if not fatal, renders the patient very anæmic, and considerably prolongs convalescence. Much abdominal distension, profuse diarrhœa, incontinence of urine and fæces, severe general bronchitis, and a feeble and irregular heart, are all unfavourable.

Prevention. Since typhoid fever is spread mainly by the fæcal discharges and the urine, these should be disinfected as described in the introduction. Soiled bed-linen, clothes and towels must also be disinfected. Specially marked crockery should be put aside for the patient's meals and a bowl of 2 per cent. lysol is placed by the bedside, so that the hands of doctors and nurses can be sterilised after attending the patient.

Preventive Inoculation. But even if the risk of exposure to infection cannot be avoided it is possible to diminish the susceptibility of the individual by the inoculation of a vaccine consisting of dead cultures of typhoid bacilli. This has been done as a routine measure in the army for some years. A vaccine containing 500 millions of bacilli is first injected, and a second injection of 1,000 millions is made ten days later. A certain amount of local and general reaction takes place, but soon subsides. It is estimated that the liability to the disease was thereby reduced to one-eighth, and the mortality among those who had the disease to one-half; but still more striking figures have been published. Moreover, both larger and more frequent doses have been inoculated. An inoculation of 1,000 millions should be repeated at about yearly intervals.

The treatment of typhoid-carriers presents many difficulties. Intestinal antiseptics are valueless; and the gall-bladder has been drained, and even removed, in some cases with notable success. The use of vaccines has been tried in doses of several millions of sterilised typhoid bacilli at intervals of two or three weeks; but even if the organisms disappear for some time from the urine and fæces the permanence of the cure cannot be guaranteed. The only efficient means of meeting the difficulty of the typhoid-carrier is to keep him under observation and ensure disinfection of his excreta until he is shown to be permanently free. Particular care must be taken that his employment does not in any way necessitate his handling or preparing food for other persons. In purely urinary cases urotropine will reduce the number of bacilli as long as it is being taken.

Treatment. The general treatment of pyrexia applies to a case of typhoid fever, and the description already given should be consulted. The special dangers of perforation and hæmorrhage from the ulcerated bowel should never be lost sight of. In choosing a diet special care must be taken to avoid articles of food that leave a residue or may irritate the ulcers and cause perforation. Not so long ago milk alone was allowed, but at present a varied diet of 2,000 calories or more is prescribed which may include thin bread and butter without crust, mashed potatoes, vegetable juices and fruit juices (*see* Pyrexia).

As to medicinal treatment, in mild cases little or none is wanted. A small dose of dilute mineral acid, or of a saline diaphoretic like the acetate of ammonium, may be grateful to the patient; and the body may frequently be sponged with tepid water. Stimulants are often unnecessary. If required, they may be given on the principles laid down (*see* Pyrexia).

This purely expectant line of treatment suffices in many cases, especially those of milder type; the patient is cared for while the disease runs its course. The methods of treatment by which it has been sought to influence directly the progress and prevent the accidents of the fever are those by (1) hydrotherapy, which has done much to lower the mortality in typhoid (*see* Treatment of Pyrexia), (2) antiseptics, and (3) antitoxic serum or vaccine.

The *antiseptic* treatment consists in the use, internally or by enema, of such drugs as carbolic acid, sulphurous acid, naphthol, hydronaphthol, naphthalene, bismuth salicylate, salol, oil of cinnamon and chlorine. They are said to diminish diarrhœa and tympanites, and to make the stools less offensive; but they have little or no influence on the changes in the bowel, or on the duration of the pyrexia, nor do they prevent relapse. The doses employed for adults have been of β-naphthol 3 to 5 grains, suspended in mucilage, every four hours, of hydronaphthol 2 to 3 grains every two to four hours, of sulphurous acid 20 to 30 minims, of salol 5 to 7 grains, and of oil of cinnamon 3 to 5 minims every two hours.

The treatment of enteric fever by a *serum* is yet in its infancy. The recognition that the poison of the typhoid bacillus was mainly an endotoxin, and that little exotoxin was formed, suggested that the bacterial cell juices should be injected into the horse in order to produce an *anti-endotoxic* serum. Such a serum, employed in the treatment of typhoid fever, has awakened hopes that it may influence the course of the disease (Macfadyen, Hewlett).

Non-specific protein therapy in the form of T.A.B. vaccine, given in a dosage of 150 to 250 million organisms intravenously each day for four to six days has been very favourably reported on. Severe rigors follow the injection. Not infrequently the fever is terminated by crisis, and in other cases there is marked amelioration or complete abolition of the toxæmic features. Hyperpyrexia is best avoided by not giving the injection at a time when the temperature is actually rising. Rarely cardio-vascular shock and hæmorrhage have followed the injection.

Special symptoms of complications may have to be met, such as bronchitis, by small doses of expectorants (*see also* Bronchitis), or persistent headache by phenacetin, 5 to 10 grains, or aspirin, 5 to 10 grains. If the bowels are not opened more than four times in the twenty-four hours, no treatment is required; but it is generally desirable to check diarrhœa if it exceeds this limit, and this is best done by the use of a starch enema with 15 to 20 minims of tincture of opium; and bismuth carbonate or salicylate, or the vegetable astringents, may be given internally. Any linen that is soiled by fæces or urine should be at once removed, not only for the sake of keeping the patient clean and free from the risk of bed-sores, but also to prevent the possibility of the attendants being infected. If constipation occurs, the bowels may be left for two or three days without harm, and it is then safest to use a soap enema from time to time as required. In cases where meteorism is marked, this symptom may be relieved by injection of 1 c.c. of pituitary extract.

For hæmorrhage from the bowels opium internally or morphia by hypodermic injection is probably the best treatment. Acetate of lead, tannic acid, oil of turpentine (10 minims), ergot, and adrenalin chloride have at different times been used, and more recently chloride of calcium in 10-grain doses every three or four hours, or intramuscular injections of calcium chloride, gr. i. to 100 minims of distilled water. Tympanites may be relieved by the application of ice, in small lumps, between two pieces of flannel, and by use of turpentine enemas.

If perforation is recognised, laparotomy should be performed at once, the abdomen should be washed out, and the ulcer closed. Without operation the condition is practically invariably fatal. With operation the recovery rate is about 20 per cent. It has been shown that the prognosis is very much better if laparotomy is performed within twelve hours of perforation occurring.

Both for the treatment of bacilluria and cystitis when they occur, and for the prevention of infection in others, urotropine (10 grains three times a day) or helmitol should be used during the fever and for three weeks of convalescence.

During convalescence purgatives must be carefully avoided, or used only in the form of enema. Even in favourable cases without complications or sequelæ the bodily and mental vigour returns with remarkable slowness, and the patient

should not be too early allowed to exert himself. Rarely is he fit for work under three months from the commencement of the illness, and in the graver forms, or in case of relapse or of complications, this period may be prolonged to five or six months. Specimens of fæces should be examined bacteriologically on three separate occasions during convalescence in order that typhoid-carriers may be detected.

PARATYPHOID FEVERS

The organisms which cause paratyphoid fever are two in number, distinguished as *Bacillus paratyphosus A* and *B. paratyphosus B*. They differ from *B. typhosus* in cultural characters such as their fermenting action on different sugars, their action on milk, and their agglutinative reactions.

These two have had a somewhat different geographical distribution, the *B. paratyphosus A* having been found in many parts of the world, including Germany and India, but rarely in England, whereas the *B. paratyphosus B* was found more commonly in England, but also in Germany and America. But both forms have been present in the enteric fevers prevalent in the Dardanelles and in Egypt during the Great War, and there the cases of paratyphoid outnumbered those due to *B. typhosus*.

Ætiology. The ætiological factors in the spread of the paratyphoid fevers appear to be the same as those which favour typhoid itself. The diseases are spread chiefly through the fæces of those who are ill, and of the different groups of *carriers*, but also by clothing, bedclothes, etc. Drinking-water, milk, flies, dust, shellfish and other agents are concerned in different cases as in typhoid.

Symptoms and Course. The symptoms and pathology of the two forms are identical, and they can only be distinguished from one another by agglutination tests or by isolation of the bacillus from the blood or fæces. They are also not materially different from the symptoms and the pathology of typhoid itself, and the following are the chief conditions which have been observed to be more or less frequent than in typhoid. Thus it is stated that a sudden onset is more common in the paratyphoids; that the rose spots are redder and more profuse; that the spleen is more often or more considerably enlarged; that the pulse is unusually slow, as compared with the elevation of temperature, so slow even as fifty in the minute; that abdominal pain is not infrequent, and hence a risk of confusion with appendicitis, and if there is much diarrhœa with dysentery; but the great variations in the symptoms of typhoid fever must not be forgotten.

The duration of the pyrexia may be as little as ten days, but it may be as much as eighteen or twenty-one days, the longer period more often in paratyphoid A than in paratyphoid B. It oscillates often between 100° and 102°, and is rarely above 103°.

The spots are as variable in number as in typhoid, and in the shorter forms may not appear till near the end of the pyrexia.

In the paratyphoid fevers complications occur similar to those seen in typhoid fever; that is, there are inflammatory lesions of other organs besides the intestine, due either to the paratyphoid bacillus or to other infections. And sometimes these occur so early in the disorder as to distract attention from the main disease unless the specific tests are applied. By Dr. C. H. Miller several forms of paratyphoid fever are recognised, determined by the organs or systems most severely or earliest attacked in different cases. Thus he describes dysenteric, biliary, nephritic or urinary, pulmonary, rheumatic, influenzal and septicæmic varieties. Accordingly during paratyphoid epidemics the possibility of this infection must always be remembered in cases of jaundice, dysenteric diarrhœa, acute bronchitis, pneumonia, or nephritis.

The mortality among paratyphoid cases has generally been regarded as slight, namely, from 1 to 3 per cent.; but in cases occurring among soldiers it has sometimes been as high as 5 or 6 per cent. (Miller).

Post mortem in some cases no intestinal lesions have been found, in others ulceration of Peyer's patches, or of the solitary follicles in the ileum, cæcum and colon. Enlargement of the spleen and of the mesenteric glands is also found.

Diagnosis. The diagnosis between paratyphoids A and B and typhoid infection can only be made with any certainty by bacteriological examination and agglutination reactions. A positive finding from culture of the blood, urine, or fæces will decide the diagnosis at once. Failing this, the serum of the patient must be tested for agglutinating power against the various organisms. If the patient has never received any prophylactic inoculations against the enteric group of organisms, diagnostic results may be obtained by an agglutination test on one occasion only. If, however, he has at any time been inoculated with typhoid organisms or with a mixed vaccine of typhoid and the paratyphoids, the agglutination reactions are markedly affected. In such cases, to be of any diagnostic value, the tests must be performed by the quantitative macroscopic method introduced by Dreyer. He has shown that there is a gradual rise followed by a fall in the agglutinating power of the serum towards the organism that is causing the infection. In order to establish this agglutination curve at least three tests must be carried out at intervals of about four days. Thus, for example, in a case of paratyphoid A who has been inoculated with all three organisms it will be found that the serum agglutinates all three, but that there is a rise of agglutinating power for paratyphoid A, followed later by a fall as convalescence is established.

Prevention. The known ætiological factors, drinking-water, soiled clothes, flies, dust, etc., have all to be considered; and preventive inoculation by means of vaccines prepared from the two kinds of bacilli can be employed where, as in the case of a campaign, the risk of infection is almost certain to be incurred.

Treatment. This is the same as is required in typhoid fever.

TUBERCULOSIS

Tuberculosis is an infection by a specific micro-organism—the *Bacillus tuberculosis* of Koch, which is characterised by the formation in one or more organs of certain bodies called *tubercles*.

Ætiology. Tubercle bacilli are minute rods, straight, or very slightly curved, measuring 3μ in length and $0{\cdot}5\mu$ in breadth (*see* Diagnosis of Phthisis). Certain observations point to the possibility that tubercle bacilli are not, as formerly thought, fission fungi, but that they belong to the class of *Streptothrix*, one of the Hyphomycetæ. The bacilli are widely spread in nature. Human, bovine, avian, reptilian and piscine types exist, having different biological characters. It is claimed that by special methods of cultivation these differences can be abolished. Both human and bovine types are pathogenic to man.

Tuberculosis is practically an endemic disease: the human type of bacillus is probably widespread in all large communities; and there is good reason to believe that it infects and causes the growth of tubercle in a great number of persons, without its presence ever being detected. Post-mortem observations show that old healed foci of tuberculosis are present in most people. Living bacilli have also been found latent in the glands of about 10 per cent. of people where the autopsy has revealed no macroscopic or microscopic evidence of tuberculosis. The conditions determining its development are (1) the virulence of the organism, (2) the susceptibility or resistance of the recipient individual, and (3) the mode of introduction.

1. Under the first head there is little that can be said but that the *virulence* undoubtedly varies.

2. In regard to the *condition of the recipient* importance attaches to *hereditary* influence. The conclusion has been drawn from statistics that the children of tuberculous individuals have a special hereditary predisposition to the disease

(Pearson). At the same time it must be remembered that such children are brought up in surroundings where they may receive massive doses of bacilli, as dealt with later. On the other hand, the long narrow chest, showing deficient apical movement, may predispose to phthisis. This is often a congenital characteristic. Experiments with animals have shown that the semen from tuberculous vesiculæ seminales or testes may in some cases produce a tuberculous fœtus. Placental tuberculosis may also do the same, but these factors are of no importance as a cause of tuberculosis in later life.

Circumstances which favour the *acquirement* and rapid progress of the disease are those which expose the body to massive infections or seriously lower its vitality, whether these be a deficient supply of food and fresh air, or prolonged debilitating illnesses, or special toxic influences. The most frequent of these are —(*a*) overcrowding and deficient ventilation, working in close rooms in the fumes of gas, etc.; (*b*) deficient supply of food; (*c*) exhausting work; (*d*) exposure to damp and cold winds—Buchanan showed that amongst communities living on damp and imperfectly drained soils there was an undue proportion of deaths from phthisis and lung diseases; (*e*) excessive indulgence in alcoholic drink; (*f*) diabetes mellitus.

In the case of the lungs, (*a*) inflammatory lesions may prepare the soil for the growth of tubercle. This is particularly shown by the liability of tuberculosis of the lungs to follow pneumonia and the broncho-pneumonia of measles and whooping-cough. (*b*) Chronic irritation from the inhalation of dust particles (pneumoconiosis), which is described later. (*c*) Lack of blood supply, as in congenital heart disease, is also a factor predisposing to phthisis. On the other hand, it is noteworthy that in mitral stenosis, where the lung is chronically congested, phthisis is very rare.

The *age* of the individual is an important factor. The mortality is greatest during the first years of life, when the infection gains access through the lungs, and less often through the intestine. The mortality falls off rapidly during the second and subsequent years, and is at a minimum from the fifth to twelfth years. It then rises again, and there is a second maximum in early adult life. This second rise is due mainly to apical phthisis, the result of a re-infection after the original infection of childhood has died out (**56**).

3. Tubercle bacilli may enter the system by *breach of surface of the skin*, by the *genito-urinary tract*, by the *respiratory* passages, and by the *alimentary canal*.

The first two modes are rare and of no practical importance; but in the past persons performing post mortems have sometimes had their hands infected, contracting a post-mortem wart (*verruca necrogenica*), in which tubercle bacilli are found. Butchers occasionally contract similar lesions. They are very slowly progressive, and the tubercle very rarely spreads to other organs.

There has for a long time been a controversy as to the relative frequency of infection by the *respiratory* and *alimentary* tracts; the former is now held chiefly responsible. To answer this question we must first of all consider whether bovine or human tubercle is the commonest. (1) *Bovine* tubercle may be contained in milk from tuberculous cows and in tuberculous meat. The latter is not an important source of infection, because, apart from stringent regulations about its sale, meat is never eaten uncooked in this country. Infection by bovine tubercle will necessarily take place by the alimentary canal. (2) The researches of Cornet discovered the chief agent in the diffusion of *human* tubercle. It is not the air expired by the phthisical patient, but the sputum, which may be loaded with the specific micro-organisms. If this is repeatedly ejected on to the floor of a room and allowed to dry, or if quantities of it dry upon handkerchiefs, the air of the room may at length be sufficiently impregnated to become dangerous to healthy people breathing it. From the floor and walls of rooms formerly tenanted by phthisical people Cornet obtained bacilli by the inoculation of which he produced tuberculous disease in healthy animals. This helps to explain the

deadly influence of deficient ventilation in workshops, factories, barracks, and similar institutions. Human tubercle bacilli may thus be readily inhaled; but it does not necessarily follow that infection will take place by the lungs, because it has been argued that the bacilli and other dust particles are caught up in the mucus of the bronchi, are carried upwards by ciliary action or by coughing, and, reaching the mouth, are eventually swallowed, and so produce infection by the alimentary tract. However, experiment has shown that dust particles and bacteria can readily penetrate by inhalation to the inmost recesses of the lungs, and further that guinea-pigs and cattle can be more readily infected in inhalation experiments than when equal doses of bacilli are ingested. Again, in the industrial disease known as silicosis, which strongly predisposes to tubercle, the particles are obviously inhaled, because the lung and bronchial glands may be quite solid, while the mesenteric glands are hardly affected.

Several careful observations have been made on the frequency of bovine and human tubercle in different types of the disease and at different ages, the bovine variety being distinguished by its greater virulence on injection into rabbits. Bovine tubercle accounts for rather less than 1·5 per cent. of phthisis cases. On the other hand, in tuberculosis affecting the cervical and axillary glands 73 per cent. are due to bovine tubercle in children under ten, and about 30 per cent. in children over ten. Again, in tubercle of bones and joints, the percentage of bovine cases was found to be 28 per cent. under five years, 25 per cent. between five and ten, and only 9 per cent. between ten and sixteen (Griffith). Bovine infection is responsible for an average of 18 per cent. of genito-urinary tuberculosis in England (**34**). Fraser found a considerably higher percentage of bovine tubercle in surgical tuberculosis at Edinburgh, viz. 61·2 per cent. It is probable that variations occur in different localities. Tuberculous meningitis in children is most commonly secondary to caseous bronchial glands, and it has been found that over 90 per cent. of such cases are due to a primary tuberculous focus somewhere in the lungs (Ghon, Canti). This argues in favour of tuberculous meningitis being in most cases due to human tubercle, and this has been found to be so (Park and Krumwiede). In this connection mention must be made of some further work by Eastwood, F. Griffith and A. S. Griffith on thoracic tuberculosis in children. These authors found that out of sixty-six cases when the anatomical evidence was strongly in favour of infection by inhalation sixty-five were due to human and only one to bovine tubercle; however, in the north of England and Scotland, nearly 4 per cent. of cases of pulmonary tuberculosis are bovine, and 0·6 per cent. in the south of England (**35**). Out of twenty-three cases where the anatomical evidence was in favour of infection having taken place through the alimentary canal, eighteen were due to bovine and five to human tubercle. The conclusion from these figures is clear; it is that tuberculosis in adults is mainly of the human variety, but in young children a fairly large proportion may be due to bovine tubercle, and this will usually be the case if anatomical considerations point to infection by the alimentary tract. Further, from the relatively favourable course of cervical gland and abdominal tuberculosis in children we may draw the conclusion that bovine tubercle in man produces a milder disease than human tubercle.

The importance of infection from a human source has been shown in another way by Ward, working in rural and semi-rural districts in South Devon. In two series of all types of tuberculous cases at all ages 60 per cent. had been in contact with other tuberculous cases, whereas in a series of control non-tuberculous people only 12 per cent. had been in contact with tuberculous cases. The occurrence of conjugal tuberculosis pointed in the same direction: in 60 per cent. of cases where the husband or wife was tuberculous, the other partner also had tubercle. Similar results have been obtained from the study of children, who have lived with patients suffering from open tuberculosis, *i.e.* with patients constantly discharging bacilli from the lungs. It has been pointed out that the

danger to children does not lie so commonly in massive infection from parents, as the latter have been taught to collect and destroy the sputum, but in the unrecognised open tuberculosis of a grandparent, the nature of whose winter cough has never been recognised.

Morbid Anatomy. An elementary inflammatory focus caused by the *Bacillus tuberculosis*, which is too small to be seen by the naked eye, has the following structure: externally *lymphoid* cells, within these *epithelioid* cells, and in the centre a *giant cell*, with several nuclei formed by the enlarging of an epithelioid cell and divisions of nuclei inside the cell (**36**). These cells are connected together by a delicate protoplasmic network, and the characteristic *bacilli* are present in the body of the giant cell or lying between the epithelioid cells. Sometimes the giant cells are absent, sometimes also the epithelioid cells, so that the tubercle may consist only of lymphoid cells. As the tuberculous focus enlarges the cells undergo a process of coagulative necrosis from deficient vascular supply—for no vessel penetrates within the focus—and as a result of some chemical substance secreted by the bacilli.

A tubercle in its earliest stage, known as a *miliary* tubercle, is a translucent pearly grey nodule about the size of a millet seed, consisting of a central core of necrotic material surrounded by elementary foci. As it enlarges it becomes opaque yellow and cheesy in the centre, while at its periphery the tubercle may be invading more and more of the organ in which it is situated, the new tubercle becoming cheesy in its turn. In this condition it is known as a *caseous* tubercle. Under the microscope the caseous material shows shrunken cells, fat granules and *débris*. In the solid organs, large, spherical caseous masses are formed, as may be seen in the brain and spleen. If the disease invades a surface, vascular tuberculous granulation tissue is formed, similar to ordinary granulation tissue, but containing large mononuclear, epithelioid and giant cells, and sometimes well-formed tuberculous foci. Ulceration readily occurs. This may be seen typically in the intestine.

Some caseous masses ultimately undergo *calcification* (largely by formation of calcium phosphate), the tubercle bacilli are destroyed, and the lesion ceases to be infective. Another way in which tubercle terminates is by a *fibroid change*; chronic inflammation and induration of the surrounding tissue take place, and the tubercle itself shrinks into a fibrous nodule. This is more common on the surface of the pleura and peritoneum, but also takes place in the lungs.

Pathology. After the initial introduction into the body of tubercle bacilli the patient enters the primary tuberculous state, which is characterised by an epithelioid type of tissue reaction unaccompanied by allergy—*e.g.* hypersensitiveness to tuberculin. This period varies from two to ten weeks, usually averaging about six weeks. The patient may now recover completely, healing taking place by rapid calcification without the development of hypersensitiveness to tuberculin, or he may pass into the secondary state, which is characterised by the rapid development of a high degree of allergy (the intradermal tuberculin test showing a positive reaction to 0·1 c.cm. of 1/100 to 1/100,000 tuberculin). This early secondary allergic state may heal by resorption or may progress, breaking down the lymphatic gland defences to spread along the lymphatics or by the blood stream, and causing either metastases or generalised tuberculosis (miliary tuberculosis and caseous broncho-pneumonia). This generalised condition is described as the *late* secondary state. When recovery from the primary or secondary states occurs, there results a degree of immunity; if reinfection now takes place, the resulting condition, known as the "third state," differs essentially from the two previous states. The high tissue immunity allows a localisation of infection to take place in the lung tissue; if the glands become involved (which is less likely) the infection is chronic, and not acute as in the primary state; fibrosis is a further evidence of high tissue resistance. This third state is adult "phthisis."

TUBERCULOSIS IN CHILDHOOD

The pathology of the primary and secondary states of tuberculosis just described has a special reference to childhood, though it is also applicable to adults of native races, unaccustomed to tuberculosis, when they come among civilised peoples. Such was the case with North African troops when they were draughted over to Europe during the war.

Stomach Lavage. This has thrown a new light on the subject, because children always swallow their sputum. The technique is as follows: (1) 2 grains of potassium iodide are given three times a day for two days before the lavage. (2) The child is encouraged to cough first thing in the morning for twenty minutes. (3) He is then given 100 c.cm. of boiled water to drink. (4) Fifteen minutes later a stomach-tube is passed and as much fluid as possible withdrawn from the stomach. (5) This fluid is centrifuged and the deposit is treated with 1/10 antiformin (4 c.cm. diluted antiform being added to 100 c.cm. lavage). Alternatively, a 10 per cent. potassium hydroxide solution is added to the stomach lavage to make a final dilution of 1 per cent. This is allowed to act for an hour and then the whole is centrifuged. This method has the advantage of ensuring that the tubercle bacilli are not destroyed, but has the drawback that it leaves the deposit too thick for direct examination. (6) It is then injected under the skin in the abdominal region of the guinea-pig. (7) The guinea-pig is watched for six weeks, after which it is killed and examined for tuberculosis, both by direct smear of the diseased glands and by culture (**37**).

By this means it has been found that a number of children in the primary and early secondary states have tubercle bacilli in the sputum, *i.e.* have "open" tuberculosis. It is suggested that all patients go through a period of open tuberculosis sometime in this disease. In the late secondary state and in general tuberculosis, tubercle bacilli are found in the majority of cases.

Symptoms and Diagnosis. There is commonly a history of contact with a case of open tuberculosis. In the primary state X-rays may show a primary lesion in the lung. The "early" secondary state is often associated with loss of weight, fever, dry cough, pallor, and disturbances of the alimentary tract, while radiography of the chest may show enlargement of the hilum glands and sometimes "focal" lung reactions. At the same time certain so-called *paratuberculous* conditions, such as erythema nodosum, phlyctenular conjunctivitis, pleurisy and benign infiltration of the lung (epituberculosis) are apt to manifest themselves; the latter is shown by a uniform dense large area on the radiogram, described later, which can be differentiated from a lobar pneumonia by the characteristic shape of the latter and its disappearance in a week or so. Further progress into the late secondary stage of general tuberculosis is dealt with in the next section.

If healing takes place, the symptoms disappear and the only evidence left may be hilum shadows on the radiogram with *enlarged* and partly calcified *bronchial glands*—a combination known as hilum phthisis. Very occasionally these may press on surrounding parts, imitating an intrathoracic tumour, or suppurate, discharging into a bronchus with danger of causing asphyxia or broncho-pneumonia.

The **Prognosis** is favourable with proper treatment, even though tubercle bacilli have been found.

Treatment. This must be conducted on the same principles as that of tuberculosis in general. Rest in bed so long as the temperature is raised, good food, fresh air are the main requisites. Tonics, such as the syrup of iron iodide or of iron phosphate, Parrish's food, or cod-liver oil, may be given. The question arises as to whether these children should be regarded as infectious. Since tubercle bacilli only appear intermittently and are thus always swallowed, these children can quite well be treated with others in a convalescent home.

GENERAL OR MILIARY TUBERCULOSIS AND TUBERCULOUS MENINGITIS

Ætiology. This disease occurs at all ages, but is most frequent in children under two. So far as its causation is concerned, it is constantly associated with and secondary to more advanced tubercle elsewhere in the body. It may arise in the course of phthisis, hip joint disease, caries of the spine, or other tuberculous complaints. In many cases, especially in young children, the tuberculosis has been latent, as already described, and caseous bronchial glands resulting from a primary localised tuberculous affection in the lung, less commonly caseous mesenteric glands, are found at autopsy. Miliary tuberculosis is due to general dissemination of the infection by the blood stream, with the formation of miliary tubercles or minute tuberculous foci in any organ of the body. Such a spread may be due in a few cases to tuberculosis of the thoracic duct; but in the great majority a vein has been found eroded by an enlarged tuberculous gland, so that caseous material has been discharged into it, and quite suddenly the body has been flooded with numerous tubercle bacilli. These have been found in the blood after death and during life. This invasion is characterised by severe constitutional symptoms, presumably due to intoxication, particularly high temperature and rapid pulse. Sometimes several of these invasions may occur in a case, and this will be shown after death by the different sizes of the miliary tubercles in the various organs. Miliary tubercles are not large enough to interfere obviously with the functions of most organs. There are, however, two notable exceptions. Miliary tuberculosis of the meninges leads to interference with the functions of the brain, and to a less extent the same condition of the lungs interferes with its functions. The consequence is that, unless these organs are affected, miliary tubercle cannot be diagnosed with any certainty. It may be found accidentally at post mortem in a case where the symptoms have been ascribed solely to the primary lesion, whether in the lungs, as in phthisis, or in the kidneys, etc. For this reason it will be best to describe miliary tuberculosis and tuberculous meningitis together, the distinction between the two being noted in the appropriate places.

Morbid Anatomy. Through the *lungs* the tubercles are, as a rule, uniformly scattered more or less thickly. Every form of tubercle may be seen, from small grey dots to larger caseating tubercles; and sometimes these last may be breaking down in the centre, forming minute cavities. Definite patches of pneumonic consolidation occur, but are not common. Some inflammation of the bronchi, especially the smallest, is always present. Tubercles are sometimes found on the pleuræ, and pleurisy is often the result. In cases grafted on a former phthisis consolidation and cavities will also be present.

The characteristic appearances seen in the *meninges* consist of the presence of tubercles and of the effusion of lymph between the pia mater and the arachnoid. The lymph, which is gelatinous and translucent, or opaque and grey, or greyish yellow, but never purulent, consists of exuded fluid, fibrin, and lymphocytes in varying proportion. It is seen especially at the base of the brain, over the optic chiasma, the diamond-shaped space behind it, and the adjacent crura and pons. From this central point it commonly extends into the Sylvian fissure on each side, along the course of the middle cerebral artery, where it may be very abundant. The surface of the hemispheres is commonly free from lymph, or is at most a little dull or sticky, so that tuberculous meningitis is often called a *basal* meningitis; but it is common to find a small patch of lymph at the top of the cerebellum, at the anterior part. With the lymph are commonly mixed tubercles, varying from mere points up to the size of millet seeds, and occasionally beginning to caseate. The tubercles are especially abundant on the pia mater in the fissures of Sylvius. Under the microscope the smaller tubercles present aggregations of lymphoid corpuscles in the perivascular sheath; the larger tubercles may present all the characteristic features; but usually giant cells are absent.

The relation of the inflammatory lymph to the tubercles is very variable. There may be abundant lymph in the characteristic situations, with few, if any, tubercles discoverable; there may be a good number of tubercles with very little lymph. The ventricles of the brain are commonly distended with fluid (whence the old name *acute hydrocephalus*); the convolutions are flattened against the skull; the brain tissue is soft and often obviously congested. The cranial dura mater is not usually affected, but the spinal dura mater sometimes shows minute tubercles, and the lymph in the pia mater may extend to the cervical region of the spinal cord.

Miliary tubercles are also usually seen in and on the surface of the liver, kidneys, and spleen; while less often the choroid of the eye, the heart, thyroid, bone marrow, and peritoneum are involved. Any organ of the body may be affected, and no organ is invariably so. Sometimes the meninges may be apparently to the naked eye alone affected, but it is probable that microscopic examination would in such cases disclose evidence of infection in other organs as well.

Symptoms. There is often a prodromal stage, during which the child is out of health, restless, loses appetite, gets thin, may be occasionally sick, and has constipation. The illness begins more definitely by headache or vomiting, or perhaps a convulsion. The headache is severe and continuous, with exacerbations from time to time; the child puts its hand to its head, and may be often crying, "Oh, my head!" or simply whining, or moaning, or occasionally uttering a sudden short shriek. With this there is a moderate degree of fever, quick pulse, excessive sensibility to light and sound, so that the child shuts the eyes, and desires to be left alone in bed; it resents being disturbed, and often curls itself up in bed away from intruding friends. The vomiting does not generally last long. If the illness begins with a fit, this is not often repeated. Occasionally there is squint, and there may be diplopia quite early.

After a few days, still with severe headache, there may be slight delirium, and the patient becomes drowsy. The head is sometimes retracted, and the neck is stiff; the abdomen becomes hollowed or retracted, the outlines of the muscles are obvious through the skin, and the margins of the ribs and the iliac crests are prominent. For this the terms *carinated* and *boat-shaped* are sometimes used. Kernig's sign is sometimes present. The pulse may be slow, and is often irregular; the respirations are slow, sighing, and irregular; the temperature is still generally high, or oscillates between 101° and 103°, but it may be extremely irregular, and sometimes the *typus inversus* is present, the morning temperature being high and the evening low. When the finger is drawn sharply across the skin of the forehead or abdomen, a broad red line quickly appears, and may persist five minutes or more. This condition, which is not peculiar to, but only more marked in, meningitis, is called *tache cérébrale*. Even as early as this, changes may often be observed in the optic disc, which at first becomes highly vascular, and then shows definite optic neuritis. Tubercles are seen in the choroid in a small proportion of cases. Usually some pulmonary symptoms are present; there is cough, and râles may be heard in the chest. Yet it is remarkable how full of minute tubercles the lungs may be without producing any physical signs.

From this point the case may steadily go on to a fatal termination without any fresh symptom. Food is taken badly, and the bowels are constipated. The drowsiness increases to coma, optic neuritis is more pronounced, the abdomen becomes more and more hollowed, the pulse more irregular, feebler, and generally quicker, and Biot's respiration may be seen (*see* p. 121), and the temperature may fall more or less rapidly, or just before death go up quickly to 106° or 107°. Mucus accumulates in the bronchial tubes, and with failing pulse death takes place. But often the last few days are marked by local symptoms, paralysis of a limb, squinting, or ptosis. The pupils are frequently unequal, and one or both may be insensitive to light. Frequently this stage is marked by convulsions, and

these may recur several times before death. Sugar is sometimes found in the urine in the last few days. The illness lasts from ten days to four, five, or six weeks. The above course of the disease has been divided into three stages: a stage of *irritation*, one of *compression*, and the last a *paralytic stage*. But it is not always easy to distinguish between them, and in some cases the more typical symptoms may be very little marked, coma alone being prominent.

In the tuberculous meningitis of adults the symptoms are often much more rapidly developed. The onset may, of course, be masked by those of the disease already existing, *e.g.* phthisis. The patient may, with very little warning, become delirious, and have paralysis of a limb or of the face, or have a fit, quickly becoming comatose, and dying within a few days. Retention of urine has sometimes been observed as the first sign of meningitis in such cases.

The cerebro-spinal fluid in the early stages is quite clear, though it may be under considerable pressure; a "spider" clot may form in the tube. Later it is faintly turbid, but never purulent. It contains an excess of lymphocytes, and sometimes tubercle bacilli may be detected. For other features, *see* Cerebro-spinal Fluid.

In cases of general tuberculosis without involvement of the meninges, or when this occurs only in the last stages, the symptoms may be very obscure most of the time. The patient complains of weakness, inability to do his work, loss of flesh, anorexia, nausea or sickness, and headache. The bowels may be constipated or occasionally loose for a few days. Irregular pyrexia is present. The pulse is rapid and feeble and the tongue dry. In proportion as the course is prolonged the tubercles in the lungs grow, break down and produce prominent symptoms. There are cough, dyspnœa, scanty mucous expectoration, tinged, it may be, with blood, and sometimes pain in the side. The physical signs are at first suggestive of bronchitis, and later broncho-pneumonia. When this is well marked the patient presents a high degree of cyanosis, the face, lips, nose, ears, and cheeks being livid, and the fingers shrunken and blue. Death at length takes place, after from three to eight or ten weeks, with increasing dyspnœa, lividity, prostration, and drowsiness. Meningitic symptoms may supervene at any time.

The characteristic features in tuberculous meningitis are, the insidious onset, pulmonary symptoms when present, headache, irritability leading on to drowsiness and coma, and the early involvement of the cranial nerves; choroidal tubercles when present are pathognomonic. The disease must be distinguished from other forms of meningitis and so-called meningism and other forms of intra-cranial disease, such as tumour, abscess and thrombosis of the cerebral sinuses. There is no real difficulty, because the clear cerebro-spinal fluid in tuberculous meningitis, with its increase of lymphocytes, is quite characteristic; the sugar disappears and the chloride content is lowered. In many other types of meningitis the onset is abrupt, as in cerebro-spinal fever, or there is an obvious primary focus, as in suppurative meningitis following otitis media or other condition; the cerebro-spinal fluid is definitely turbid and contains polymorphonuclear leucocytes. Pronounced opisthotonus and a marked Kernig's sign are more in favour of cerebro-spinal than of tuberculous meningitis. Acute poliomyelitis or encephalitis lethargica might cause a difficulty; in the former disease the onset is abrupt. In cerebral tumour and abscess the temperature is not usually much raised, and the pulse may be slow.

Prognosis. Tuberculous meningitis is a very fatal disease, but undoubtedly a few cases in which tubercle bacilli have been found in the cerebro-spinal fluid have recovered. But these few cases do not alter the absolutely unfavourable prognosis that should be given when once the nature of the disease is known. On occasions there may be for a time a remission of symptoms. Much the same thing applies to miliary tuberculosis without meningitis.

Treatment. This should be directed to the relief of symptoms. Lumbar puncture is the most effective measure; it relieves the headache, and temporarily

alleviates the symptoms, and may be performed daily. Owing to photophobia the rooms should be darkened.

GLANDERS

(*Equinia, Malleus, Farcy*)

Glanders is a disease which affects chiefly horses, mules, and asses, though sometimes other domestic animals, and is occasionally transmitted accidentally to man. Grooms, stablemen, and others in charge of horses are most liable to contract the disease, which in its acute forms is a febrile disorder, characterised by special lesions of the nasal and respiratory mucous membranes, by the formation of subcutaneous nodes and the implication of the lymphatic vessels and glands, and by a cutaneous eruption. It also occurs in a chronic form. The term *farcy* was given to cases in which the subcutaneous nodules (farcy buds) with the lymphatic lesion were prominent features; but it is not desirable to have two names for one disease, and glanders is now the appellation generally adopted.

The disease is mostly transmitted to man by accidental inoculation of wounds, cuts, or abrasions, either in grooming a glandered animal or in skinning one dead of the disease, or a horse may bite its groom and convey the disease by means of its saliva, or may sneeze and discharge some nasal mucus into the eye, nose, or mouth of any one standing near. It is stated that it may be conveyed by eating the raw flesh of a glandered animal, and that it has been caught in this way in menageries. It may also be communicated from man to man. The bacillus of glanders (*B. mallei*) is found in the nodules; it is about the size of the tubercle bacillus, but is thicker and is decolorised in Gram's method.

Pathology. On post-mortem examination in acute glanders the changes characteristic of pyæmia are often found: increased fluidity of the blood and abscesses of the lungs, the pyæmia being secondary to the local lesions.

The characteristic lesions of glanders are found in the mucous membranes, the skin, and the lungs. In the nasal mucous membrane, subepithelial nodules occur, from the size of a millet seed to that of a pea, consisting of lymphoid corpuscles or pus corpuscles. In a later stage these nodules have suppurated, and left ulcers with yellowish bases. Around these fresh nodules of infiltration have formed, which go through the same process. The septum may be perforated. If recovery takes place, irregular puckered scars are left. In the lungs, similar nodes form, the centres of which break down into a caseous detritus. These are accompanied by patches of broncho-pneumonia, which may form abscesses. Similar nodes form in the conjunctivæ, frontal sinuses, pharynx, larynx, intestines, skin, subcutaneous tissue, and muscles.

Symptoms. *Acute Glanders.* The disease begins with malaise, headache, lassitude, loss of appetite, and pains in the joints and limbs. For a time there is often a resemblance to rheumatic fever or enteric fever, or there may be pain in the side or dyspnœa. If a wound or scratch has been infected directly, it becomes inflamed, tense, and painful; and the skin around has the appearance of erysipelas. The sore ulcerates, and discharges a sanious fluid, and the lymphatics in the neighbourhood may become enlarged. The more characteristic features of the disease may not appear for a week or more after its commencement, though sometimes earlier. The *eruption* consists of small red papules, upon which vesicles appear; these soon form bullæ, or pustules, of different sizes, up to ½ or ¾ inch in diameter, hemispherical, flat or depressed in the centre, with serous, purulent, or blood-stained contents. The base of the pustule is inflamed, and infiltrated for some distance round. After a time the discharge escapes, and an ulcer covered with scab or slough remains. The *nodes* which form under the skin are at first hard and painful, and generally suppurate. The lymphatic glands are not always inflamed. The implication of the mucous membranes is shown

by a discharge from the nose, which is at first a thin mucus, but afterwards becomes thick, viscid, purulent, fœtid, and often blood-stained. It is connected with the formation of the tubercle-like nodules already described.

Usually the disease progresses steadily, with symptoms of a pyæmic character. The temperature is high, but may oscillate; the pulse is quick, and the tongue dry and brown. Albumin appears in the urine, low delirium with tremor is succeeded by coma, the breathing becomes more rapid, and death finally ensues, generally in two or three weeks from the commencement.

Chronic Glanders. Here the local lesions predominate. They consist of ulcers with thick and hard edges, or abscesses about the joints, or inflammatory swelling beneath the skin or in the muscles. A pustular eruption may also occur, but it develops more slowly than in the acute form. The nasal mucous membrane may also be involved, and in some cases emaciation occurs, with hoarseness and pulmonary symptoms, such as cough and hæmoptysis. The average duration of the chronic cases is stated to be four months.

Diagnosis. In early stages the disease may be mistaken for rheumatism or typhoid fever, and later for pyæmia. In chronic cases, syphilis, scrofula, and phthisis may be simulated. In veterinary surgery, the diagnosis is made by the injection into suspected animals of *mallein*, which consists of the chemical substances present in the artificial cultures of the glanders bacilli. If the animal is diseased, a definite "reaction" with rise of temperature occurs, similar to that produced in man by Koch's *tuberculin* (*see* Diagnosis of Phthisis).

Prognosis is very unfavourable. Only a few recoveries from acute glanders are recorded, and only about half of the chronic cases get well.

The **Treatment** must be supporting and stimulating. Quinine should be given internally; the nasal lesion should be treated with antiseptic injections, such as creosote, carbolic acid, iodine or potassium permanganate lotion. Abscesses of the skin should be opened when ready. For chronic cases carbolic acid, potassium iodide, arsenic, strychnine, and sodium benzoate have been recommended.

ANTHRAX

This term, formerly the Latin equivalent of *carbuncle*, is now generally used to designate a disease which affects various animals, and is communicated from them to man. In animals it is known as *splenic fever;* in man it includes *charbon* of the French, and *malignant pustule* of English writers. Its distinguishing feature is the presence of a bacillus (*B. anthracis*), which can be found in the local lesions, the blood, viscera, and secretions. This is a non-motile, Gram-positive bacillus, varying from 5μ to 20μ in length—that is, considerably longer than the diameter of a blood corpuscle. The bacilli multiply by elongating and dividing. Outside the body they may produce spores within themselves, which subsequently become free. The spores have great vitality, and resist considerable changes of temperature; they reproduce bacilli in a favourable environment.

Infection in man occurs from the living animal, as in drovers, shepherds, and farmers, or from the carcase, and this is much more common. Thus slaughterers, butchers, and those who have to do with the hides may be infected through a scratch or wound, and rarely it may be contracted in eating the flesh of diseased animals. Most frequently, however, in England it occurs amongst tanners and those who have to handle the skins and hides that come from abroad, and among those who deal with wool and hair from the same animals. Thus wool-sorters, furriers, tanners, and others in like occupations may contract the disease either by direct inoculation through the broken skin, or by inhalation of dust or wool particles proceeding from the goods. It is twice as common in the winter as the summer months (**58**). Some cases have arisen from the use of shaving brushes, especially those of Japanese manufacture, made of animal hair infected with anthrax. Rarely it is transmitted from man to man by direct

contact. Rag-sorters engaged in paper manufactories are subject to pulmonary anthrax, and the bacillus of anthrax has been found in the viscera.

Morbid Anatomy. In all fatal cases there may be found the changes indicative of acute septic disease: ecchymoses in the submucous and subserous tissues, in the substance of the heart, or in other muscles; hæmorrhage or œdema of the lungs; congestion and softening of the liver and kidneys. The spleen is not always enlarged. When the special *pulmonary* symptoms have been present, there are congestion of the mucous membrane of the trachea and bronchi, hæmorrhages into the lungs or under the pleura, swelling of the cervical and bronchial glands with hæmorrhage into or around them, fluid in the pleural cavities, and ecchymosis and gelatinous exudation in the neck and mediastinum surrounding the trachea and mediastinal glands.

In the *intestinal* form the peritoneum contains serum, which is often blood-stained; there is semi-gelatinous infiltration of the mesentery and retroperitoneal connective tissue; congestion and swelling of the mucous membrane and submucous tissues of the stomach and intestines in patches of $\frac{1}{4}$ inch to 1 or 2 inches in diameter, which are pink and fleshy on section, but on the surface discoloured, or excoriated, or covered with an adherent layer of blood. There are also submucous and subserous hæmorrhages, and the spleen and the mesenteric and lumbar glands are often enlarged.

Some cases of hæmorrhagic *meningitis* have also occurred.

Symptoms. The different forms of the disease are local or external anthrax —*malignant pustule* proper—and *anthrax septicæmia*, which includes a pulmonary and a gastro-intestinal form. Either of the last two may be combined with the local variety.

Malignant Pustule. Infection generally occurs through a scratch or abrasion on the face, neck, hands, or arms. After an *incubation* of a few days, or it may be only some hours, the spot itches or burns, and a small patch of erythema appears, a little larger than an ordinary flea-bite with a minute vesicle on top. This gradually enlarges and bursts, discharging a thin fluid. The base of the vesicle then forms a brown or black eschar, and the skin around becomes red, swollen, and indurated, forming a prominence from $1\frac{1}{2}$ to 2 inches or more in diameter. Around the central eschar there is often a ring of small vesicles containing serum, and the skin for some distance round may be œdematous, and the nearest lymphatic glands enlarged and tender. However, in most cases the pustule has not this characteristic appearance, but resembles vaccinia. For three, four, or five days the patient may feel in his usual health and continue at work; he then becomes feverish, with prostration, delirium, sweating, or diarrhœa; and finally, in many cases, death occurs, preceded by collapse. In *malignant anthrax œdema* no definite pustule forms, but an œdematous swelling, usually affecting the eyelids. It is otherwise like malignant pustule, and is mostly soon fatal.

Anthrax septicæmia varies in different cases. The early symptoms are generally restlessness, a sense of depression and exhaustion, and vague sensations in the limbs; then acute fever suddenly sets in with the usual symptoms, and, in addition, great prostration, embarrassed respiration, and rapid collapse. In the cerebro-spinal fever epidemic of 1915–16, the symptoms of this disease were simulated by five cases of anthrax septicæmia, the bacilli being found in the cerebro-spinal fluid (Reece).

In the *pulmonary* form difficult and laboured breathing with a sense of constriction, cyanosis, and great prostration, are the main features, without much cough or physical signs other than a few rhonchi and râles. The expectoration, if there is any, may be bloody. Delirium and coma may precede death, or the mind may be clear to the last. This is the *wool-sorters' disease* observed at Bradford and elsewhere.

In the *gastro-intestinal* form there are vomiting, abdominal pain, and diarrhœa, often with blood in the fæces, sometimes dysphagia and bleeding from the

pharynx and mouth. Fever is slight, but dyspnœa and lividity, restlessness and convulsions of epileptic or tetanic character, precede the invariably fatal end.

Diagnosis. The diagnosis of cutaneous anthrax is easy in quite an early stage, if only the practitioner thinks of the possibility of anthrax. All that is necessary is to examine a stained smear from the vesicle under the microscope. But it may be missed, because the lesion may be thought to be just a pimple. In a later stage it resembles vaccinia. In pulmonary and gastro-intestinal anthrax the diagnosis is much more difficult. But an unusual combination of symptoms, such as vomiting and joint pains, may arouse suspicion. Bacilli may be detected in the blood, vomit, expectoration, urine or cerebro-spinal fluid. But they are not generally to be found in the blood for some days. The diagnosis may be confirmed by inoculation of a rabbit, guinea-pig, or mouse with the secretions or with blood. The animal dies within two or three days with dyspnœa, dilated pupils, and, perhaps, convulsions; and the blood contains the characteristic bacilli.

Prognosis. In Bradford, where special precautions have been taken to make an early diagnosis, the mortality has been lowered from 16 to 5 per cent. A localised pustule indicates resistance to the bacillus; a widespread œdema suggests that resistance has broken down.

Treatment. In malignant pustule the correct treatment is complete surgical excision in the early stages; but this should not be carried out if the lesion has progressed much beyond the "flea-bite" stage, as is usually the case when the diagnosis is made. The part must be rested by means of splints or sand-bags and antiseptic dressings applied. It is also important to administer anti-anthrax serum, such as Sclavo's, at the earliest possible moment: 150 to 300 c.c. are injected intravenously, to be repeated on the day following, if there has been no reaction (shown by a rise of temperature) and the general condition has not improved; 10 c.c. serum are injected locally just outside the blanched zone every four hours. In default of serum, novarseno-benzol should be used, 0·6 to 0·9 gram on the first and second day, and again on the fourth day if necessary; the worse the case the larger the dose given. The temperature may remain high even though the bacilli have disappeared from the wound.

TETANUS

In this disease, of which the name is derived from τείνω, I stretch, the essential condition is the occurrence of tonic contractions of most of the muscles of the body with paroxysms of increased contraction from time to time. It is due to a bacillus (*B. tetani*), which exists in different forms of earth or garden mould, and which will cause tetanus in animals when such earth is inoculated under the skin.

The bacillus measures 4μ to 5μ in length, and 0·4μ in thickness, is flagellated, and stains with the usual dyes and with Gram's method. It produces spores which are developed at one end, and, having a diameter larger than that of the bacillus, give it the appearance of a drumstick. It grows anaerobically.

Ætiology. The disease occurs in quite young infants (*tetanus neonatorum*), and after that age at all periods of life from five years upwards. It is more common in hot countries, and the dark-skinned races seem especially liable to it. A very frequent antecedent is injury (*traumatic tetanus*), by which an entrance is provided for the bacillus. This may be of any kind, from a mere scratch with a pin or nail to the most serious compound fracture or lacerated wound; but infection is especially liable to take place when the wound has been contaminated by contact with earth, dirt from the road, garden mould, stable straw, or similar materials. In fact, a suspension of washed tetanus bacilli or their spores can be injected into animals without harm; but if calcium chloride or hydrated soluble silica, both of them common constituents of soil, be injected at the same time, the organisms grow and produce the disease. Tetanus has

followed the subcutaneous injection of gelatin for aneurysms and of quinine for malaria. In new-born infants the organism enters by the cut surface of the umbilical cord. Probably, in all cases formerly called *idiopathic*, some means of local infection was overlooked. For instance, a stableman with otorrhœa acquired tetanus, no doubt, because he infected the meatus and tympanum with his finger soiled with stable dirt. The disease is sometimes epidemic.

Morbid Anatomy. Many cases present after death no pathological lesions whatever. The organs most commonly affected are the lungs, which may be the seat of pneumonia, bronchitis, œdema, or hæmorrhages. The central nervous system, as a rule, looks normal to the naked eye, or at most shows some hyperæmia of the grey matter. Microscopical examination may also show slight degenerative changes in the nerve cells. Both these conditions are referable to the action of toxins, or to the vascular disturbance during the spasms. The muscles of the trunk, especially the abdominal muscles, are sometimes ruptured or the seat of hæmorrhages. In traumatic cases the state of the wound bears no relation to the final result—it may be healing, or healed, or suppurating, or sloughing.

Pathology. The bacillus multiplies chiefly in the neighbourhood of the wound, and produces poisons which have an affinity for the central nervous system, especially the spinal cord. They have, however, been found in the lymphatic glands.

Experiments on animals also show that such toxins are absorbed into the blood; but they are also taken up by the end plates of the nerves in the muscles, and are transmitted by the axons of motor nerve fibres, or by the lymphatic vessels accompanying them, to the cells of the corresponding anterior cornu; and this appears to be the chief means by which the nerve centres are infected. If the toxins are sufficient, they are carried to the opposite cornu, and to other parts of the cord. Nevertheless in unprotected man the muscles first attacked by spasms are not generally determined by the seat of injury, but are usually those of the back of the neck and of the jaw. Tetanus has also been transmitted from man to animals by the inoculation of materials from the wound, and by the injection of urine which contains the toxin.

Symptoms. There are two distinct clinical types of tetanus: (1) the classical type of "pre-serum" days, characterised by trismus being the initial symptom; (2) modified tetanus, a discovery of the recent war, which may occur in patients who have had a prophylactic injection of anti-tetanus serum.

The Classical or Generalised Type. The period of *incubation* between the infliction of the wound and the onset of symptoms is from one to thirty days, about half the total number of cases developing during the second week and one-third during the first week. It is found that the incubation period is delayed in prophylactically immunised patients who contract this type of disease. The patient feels stiffness first in the jaws, so that he is unable to open his mouth wide, or to masticate properly. There is also stiffness at the back of the neck. He may continue like this for a day or two, or may rapidly pass on to the next stage, in which there is rigidity of the muscles of the trunk and to a less extent of those of the extremities. The back becomes rigid, and is slightly arched, with the concavity backwards (*opisthotonus*); the muscles of the trunk and abdomen become quite hard from constant contraction; the movements of the chest are limited from the same cause; the legs are generally rigid, but the arms are only rather stiff about the shoulders and elbows, and the fingers may be moved freely. By this time the jaw is generally firmly fixed by contraction of the masseters, and the teeth cannot be separated for more than ¼ inch (*trismus*, or lockjaw, by which last name the disease itself is popularly known); the angles of the mouth are drawn outwards, and the lips are slightly separated; the eyebrows are drawn up by the frontal muscles, and together by the corrugators, so that the facial expression is that of a painful grin, known as the *risus sardonicus*. When this stage has

been reached, the so-called "spasms" or paroxysms of increased and even violent muscular action begin. These consist of sudden contractions involving the whole of the muscles hitherto in tonic rigidity. The teeth are clenched more violently, the *risus* becomes more marked, the head is thrown back and the back arched more strongly, the chest is fixed, and the respiratory process is checked; a groan may escape from the patient, either elicited by pain or the result of expiratory spasm. The paroxysm is often of momentary duration, scarcely to be counted in seconds, and the patient relapses into his former condition of tonic contraction, or it may last several seconds, the face and hands become more and more livid and swollen, and there is imminent danger to life from the hindrance of respiration. It is always intensely painful; it is brought on by external impulses, by touching the patient, jerking his bed, by passing a catheter or giving a subcutaneous injection. The paroxysms occur at first at intervals of half an hour, an hour, or more, but as the disease progresses unfavourably they become more violent, and occur at shorter and shorter intervals. Between the spasms there is still some pain from tonic contraction, respiration is not entirely free, and the voice is feeble. The reflexes are increased. The pulse is small and quick, and becomes quicker during the paroxysms. The temperature generally at first remains normal, and may continue so to the end, though it sometimes rises a little before death; sometimes the temperature is constantly above normal; in other cases a hyperpyrexia of 107° or 108° occurs just before death, and the temperature has been observed to continue rising even after death to 110°. The urine is often retained, so as to require the use of the catheter. Sensation is generally unaffected, and the cerebral functions are mostly quite normal until near the end, when delirium may occur. In a great number of cases the disease progresses to a fatal termination in from one to twelve days: the paroxysms become more violent and frequent; and death takes place from exhaustion, or from spasm of the glottis, or from fixation of the respiratory muscles; or pneumonia or bronchitis adds its influence against the patient. As happens both in fatal chorea and in hydrophobia, the muscular contractions sometimes entirely cease for eighteen or twenty-four hours before death. In a few cases life is prolonged to the third or fourth week. On the other hand, recovery may take place: the spasms, having reached their height, gradually become less frequent; the constant rigidity of the muscles subsides, and the patient is convalescent in from three to six or eight weeks. Occasionally a case runs its whole course to a fatal termination with general rigidity, but without any paroxysms in addition; and very rarely there are paroxysms without the continuous spasm.

Modified or Local Tetanus. In this form the incubation period is lengthened, being over three weeks in about half the cases. The disease is limited to the muscles which are close to the wound. Thus one arm may be affected, or one or both legs, or the abdominal muscles when the wound is in the abdomen. The affected muscles may show tonic or clonic spasms, or there may be rigidity and hardness of the muscles, with inability to move them. The contractions may be extremely painful. Local tetanus may spread after some days. Thus if one limb is affected the disease may later on involve the other one. It may also become generalised, causing trismus and reproducing the classical form of the disease.

Some special types of local tetanus are described. Thus the name *splanchnic* tetanus has been given to cases which arise after lesions of the viscera, such as penetrating wounds of the abdomen or thorax. It is nearly always rapidly fatal: the spasms are confined to the muscles of deglutition and respiration; and the difficulty of swallowing may be so great that the case closely resembles one of hydrophobia in the liability to pharyngeal spasms at the sight, or even mention, of a glass of water. This is usually accompanied by dyspnœa.

The name *cephalic* tetanus is given to cases which arise from injuries to the head or face. Of this variety four forms are described: (*a*) one in which there

is no paralysis, but in which dysphagia and dyspnœa may be present, and the dysphagia may reach such a degree as to resemble closely hydrophobia; (*b*) another, ophthalmic tetanus, in which the oculomotor nerve is involved, causing ptosis, or paralysis of the ocular muscles, extrinsic or intrinsic; (*c*) a third rare form, in which the hypoglossal nerve is concerned; and (*d*) the fourth, in which the facial nerve is affected, facial paralysis occurs, and spasms take place in the paralysed muscles.

Diagnosis. Tetanus may have to be distinguished from strychnine poisoning, hydrophobia, spinal meningitis, tetany, muscular rheumatism, and hysteria. In *strychnine poisoning* the extremities are involved to a much greater extent than in tetanus, and the paroxysms are excited by external stimuli; but in the intervals the muscles are relaxed. The symptoms develop very rapidly, but do not begin with trismus. In *hydrophobia* there is no continuous rigidity; the spasms involve the respiratory muscles, and are excited by the attempt to drink or the sight of fluids. Mental agitation or even maniacal excitement is generally present. In *spinal meningitis*, again, trismus is not an early symptom, nor is there constant rigidity; muscular spasms are excited by attempts to move, and the temperature is high from the first. The early occurrence of cerebral symptoms would be opposed to tetanus. The peculiar distribution of the spasm in *tetany* makes it easy to distinguish it from tetanus. *Muscular rheumatism* may cause stiffness of the back of the neck, which might, under certain circumstances, cause alarm; but trismus is never present. In severe forms of *hysteria* opisthotonus is often a prominent feature, but it occurs as part of a series of convulsive movements, which cannot be mistaken. The local form of tetanus affecting one limb must be distinguished from a hysterical paralysis.

Prognosis. The shorter the incubation period the greater the mortality. In pre-serum days the mortality was between 80 and 90 per cent. of all cases as judged by several independent series of observations. During the late war the average mortality of all the English cases was 50·8 per cent., this reduced rate being accompanied by a considerable increase in the incubation period. This was due to the introduction of prophylactic serum injections. Analysis of the whole series of cases indicated that there was no evidence that curative serum injections had any effect in reducing the mortality (Golla). The mortality of purely local tetanus was practically *nil*.

Prevention. All wounds should be promptly cleansed or excised; antiseptics, even strong carbolic acid, may be usefully employed to diminish the chance of infection. In warfare and in civil life, if the wound is deep or lacerated or contaminated with mud or earth, 500 units of tetanus antitoxin should be injected subcutaneously as early as possible: and as the protection conferred by this dose seems not to last more than ten days, a second injection should be given after seven days in cases of septic wounds, and in exceptional cases a third or even fourth at the same interval. The antitoxin has been applied locally to wounds in similar circumstances. In the event of secondary operations having to be performed, Leishman and Smallman recommend injections of antitoxin around the site of the operation, if possible, forty-eight hours before the operation, and to the extent of about 1,500 units. They suggest also injection into the sheaths of the prominent nerves.

Treatment. The patient should be kept at rest, and is best placed in a darkened and perfectly quiet room, so as to avoid all impressions of sight and sound. The closure of the jaws may necessitate food being given by a nasal tube. If a wound is present, it should not be actively interfered with until the tetanic symptoms have subsided, as fresh toxin may be liberated.

The curative action of serum has been much discussed. Statistics suggest that serum is not of much use; but these are not very satisfactory, as the matter is complicated by the very favourable influence prophylactic injection has upon the mortality. Experimental evidence points strongly to the fact that serum

may do good if given early, and further that the correct route is by the spinal canal. Thus Sherrington found that there were fourteen recoveries out of twenty-five monkeys which had been injected with tetanus toxin and received an intrathecal injection of antitoxin forty-seven to seventy-eight hours later, *i.e.* after the first symptoms of tetanus had shown themselves. When the same dose of antitoxin was given subcutaneously the recovery rate was two out of twenty-five; when given intramuscularly it was three out of twenty-five; when given intravenously it was seven out of twenty-five; when given subdurally through the skull it was none out of ten. On the other hand, when it was given intrathecally through the atlanto-occipital membrane the recovery rate was thirteen out of twenty. In view of the uncertainty attaching to the results of serum treatment in the war, it will be safest to take these experiments as the guide to treatment. They point to the importance of intrathecal injection of serum in the first place, and of intravenous injection in the second place. These must be carried out at the earliest possible moment, and a general anæsthetic must be given to prevent anaphylaxis. The serum should be allowed to run slowly into the theca under gravity through a funnel after withdrawing some cerebro-spinal fluid. The present tendency is to give large doses of serum intrathecally (cisternal puncture has been used), intravenously and intramuscularly; as many as 700,000 units have been advocated for a case (**32**). Intrathecal injections of magnesium sulphate (1 c.c. of a 25 per cent. solution for every 10 kilogrammes of body weight) have also been used. The contractions may be abolished, but it is doubtful if the injections reduce the mortality. Curare has recently been used and the results are promising. If necessary, the patient should receive sedatives, *i.e.* avertin; chloral hydrate, 30 to 60 grains by mouth; chloretone, 10 to 15 grains by mouth or 30 to 40 grains dissolved in olive oil *per rectum*. In a case of generalised tetanus treated successfully by A. Taylor at Lewisham Hospital 214,000 units were given intramuscularly between the sixth and 17th days after the wound, and 120,000 intravenously on the sixth, seventh and eighth days, 334,000 units in all. In addition the boy had 60 grains of chloral and 120 grains of potassium bromide in twenty-four hours.

If respiration ceases owing to spasm of the respiratory muscles Drinker's respirator or the Bragg and Paul apparatus or rocking method should be used as described under Acute Poliomyelitis.

GAS GANGRENE

This is an infection of the tissues by certain gas-forming anaerobic bacteria.

Ætiology. Gas gangrene was common in the pre-antiseptic days. It became very rare in hospitals after antisepsis and asepsis were firmly established, but was met with again frequently during the recent war, where the bacteria which are often present in dirt gained access to the tissues through gunshot and, particularly, shell wounds. Several different bacteria are found, but the most important are *Bacillus perfringens*, which is the same as the *B. aerogenes capsulatus* of Welch, *B. œdematiens* and *Vibrion septique*.

Symptoms. In the early stages the skin looks normal. Then the limb swells and the skin becomes tense. As gas accumulates a resonant note is obtained on percussion and there are crepitations. Areas of purple staining appear and coalesce, and there are blebs containing fluid, stained by altered blood. Finally, the purple gives place to a dark yellow-green tint.

Diagnosis. X-rays provide the earliest means of diagnosis. Clear areas corresponding to collections of gas are seen in radiograms. They tend to be arranged along the muscle fibres.

Prognosis. This is practically hopeless, unless early energetic treatment is adopted.

Prevention. This consists in the excision of contaminated wounds, and in the prophylactic injection of specific anti-serum.

Treatment. This is chiefly surgical, and consists in the excision of the affected muscles or amputation. Good results have been obtained experimentally with serum injections (Bull).

Diseases Due to Fungi (Mycoses)

Fungi are filamentous plants of simple cellular structure composed of two distinct parts—mycelia and spores. Their classification is at present very difficult (**59**). The parasitic dermatomycoses are described elsewhere.

ACTINOMYCOSIS

Actinomycosis is the name given to a granulomatous lesion from which typical "sulphur granules," visible to the naked eye, are obtained. It is due to the ray fungus, which belongs to the streptothrix group, and is known as *Actinomyces bovis* (Wolff-Israel). In 1877 Israel, of Berlin, described the first cases in man, and in 1878 Ponfick showed the identity of the human cases with the cases occurring in cattle.

The actinomyces form masses which are visible to the naked eye as yellow, greenish-yellow, or grey, glistening, spherical, granular bodies, the "sulphur granules," mostly about ½ to 1 mm. in diameter, and consisting, under the microscope, of a central mass of closely woven mycelial threads and an outer layer of "club"-shaped bodies arranged radially and giving the appearance of "rays," from which the organism gets its name. The whole is encased with leucocytes. The organism grows anaerobically and is non-acid fast.

The *Actinomyces bovis* is a saprophyte in the mouth, growing, in particular, round septic teeth. It gains entrance owing to injury of the mucous membrane, and this may be caused by a foreign body, such as a barley corn or piece of straw. Further, there is clinical evidence that actinomycosis has followed the extraction of a septic tooth. Thoracic actinomycosis has followed the accidental disappearance of a tooth down the trachea, and in one case the knuckles have become infected in a patient who had knocked out an opponent's tooth with his fist. The organism always grows in association with the Gram-negative *Bacillus actinomycetum comitans.*

Once introduced, the organism adheres to some point of the surface of the alimentary or respiratory passages, penetrates then to deeper parts, and forms local lesions in different parts of the body. These consist mainly of inflammatory changes, of more or less intensity, set up around the granules, so as to form slowly growing tumours, which ultimately suppurate, break down, and discharge. From the continued growth and multiplication of the parasite at one spot—as, for instance, in the liver—large tumours may be formed, three or more inches in diameter, consisting of a kind of cavernous tissue, the trabeculæ of which are fibroid, while the spaces contain pus, in which the yellow granular masses of fungus lie loose. A remarkable feature of the disease is the way in which lesions extend by contiguity from one tissue to the next over long periods of time; but occasionally the parasite is conveyed by the vessels to remote parts, and a more widespread deposit by *metastasis* occurs. It is characteristic that the lymphatic glands are rarely involved.

Symptoms and Course. These depend on the seat of the primary invasion.

In the superficial type a tumour is generally first noticed under the skin in the submaxillary, parotid or sterno-mastoid regions, and sometimes elsewhere on the surface of the body. It is hard, does not affect the skin, is chronic in its course, varies in size from time to time, and tends to spread, leaving for a time a narrow band of firm tissue in its track. Ultimately the skin becomes involved,

obscure fluctuation is felt, and a thin, sero-purulent, odourless fluid, containing the sulphur granules, is discharged. A sinus is formed, which rarely closes, but continues patent with slight secretion. In the cervico-facial region trismus is a characteristic symptom; the lesion may resemble an alveolar abscess (**38**). It may form in the substance of the lower jaw, and expand the bone. An extension to the base of the skull or the mediastinum by means of the pharynx is a possibility. Penetration of the *œsophagus* has led to mediastinal abscesses and erosion of the vertebræ.

In *intestinal* actinomycosis, which involves most frequently the cæcum or the appendix, the mucous membrane presents on its surface patches of whitish material, covered with yellow and brown granules. The patches are about two-fifths of an inch in diameter and one-fifth of an inch thick, and adhere firmly to the membrane. The disease may also cause swellings in the substance of the intestinal wall, from which it may perforate into the peritoneal cavity, or, by means of adhesions, invade adjacent viscera or the abdominal wall at almost any point. The *liver* is often secondarily infected in intestinal cases, and then contains large prominent masses, having the structure above described. Clinically

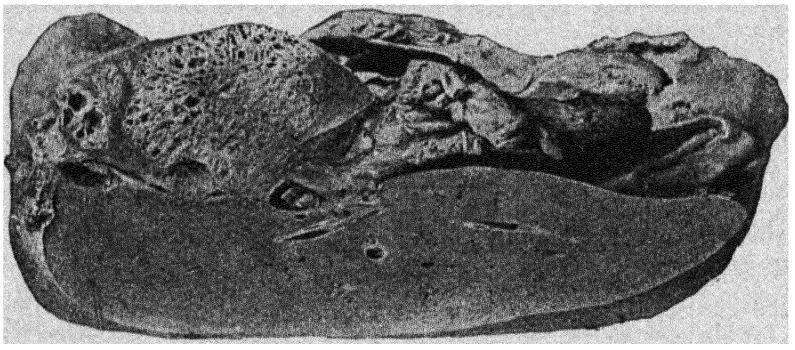


FIG. 7.—Sagittal section of a Liver showing the Lobulus Spigelii honeycombed by Actinomycosis.

such tumours may present the characteristics of hepatic abscesses, with local pain, tenderness, remitting fever and rigors.

When actinomycosis affects the *lungs* the symptoms may be bronchitic or pneumonic. In the former case there may be a close resemblance to putrid bronchitis, the sputum separating into two layers, the upper clear and the lower turbid, the latter containing the ray fungus. When the substance of the lung is affected, pneumonia occurs in patches, the patients cough and lose flesh, and the expectoration is either thick and muco-purulent, containing the typical granules, or it may be viscid, translucent, and rusty, like pneumonic sputa. There is often a close resemblance to phthisis, but the posterior and lateral portions of the lungs are involved, not the apices; and the sputum is, of course, free from tubercle bacilli. If the inflammatory lesions reach the surface, they set up pleurisy or pericarditis. Effusion takes place, or the lung becomes adherent to the chest wall, which then becomes involved, and ultimately soft diffused inflammatory swellings appear on the chest, which may fluctuate, break, and discharge purulent fluid containing the fungus. From the lung also the inflammatory track of the organism may stretch through the diaphragm into the abdomen, or behind the diaphragm to the psoas and iliacus muscles, or between the ribs to the surface of the chest. In a case of this kind recorded by Pringle, in which the skin was secondarily involved, there were large, soft, fleshy, sarcoma-like growths on the back of the chest, of mottled, purplish-red and yellow colour, covered by very thin skin, and presenting small ulcerative openings, from which a sticky fluid oozed, and in which lay a purulent fluid containing actinomyces granules. These processes are commonly very slow, and are accompanied with varying amounts of fever in different cases. A primary infection of the *skin* is

much rarer. The actinomyces is the cause of one of the white varieties of madura foot (*see* p. 1028). Infection by the *female genital tract* with extension to the ovaries and Fallopian tubes is also recorded, and actinomycotic cerebro-spinal meningitis is known (**39**).

Diagnosis. The diagnosis may be suggested by the presence of indurated lesions which are nearly painless and slowly progressive, while surrounding tissue presents to palpation a special "wooden" resistance. The disease can only be positively identified by finding the sulphur granules in the pus, or on the granulating surface of the sinuses, or in the sputum and urine. Some care is required in looking for them. A few drops of pus may be shaken up vigorously in half a test-tubeful of water, fitted with a cork, when the granules will be seen on holding the tube up to the light. One of these may be then placed on a slide and lightly crushed with a cover glass, when a low power will show the characteristic radiating structure. On crushing further the mycelial filaments may be seen; they are stained rather irregularly by Gram's method. Finally, anaerobic cultures of the organism should be made.

Prognosis. Death takes place from direct extension to vital structures, generalised pyæmia or by amyloid disease. There were nine recoveries out of ten cases in which the face or neck was affected, but the prognosis is bad in thoracic and abdominal cases (Colebrook).

Treatment. Surgical measures should be adopted in the first place if possible, multiple incisions being made into the tumours and the granulating surfaces being thoroughly cleaned by rubbing with dry gauze swabs, in preference to a sharp curette, which injures the surrounding healthy tissue. Potassium iodide has a powerful influence in the treatment of actinomycosis, and very remarkable results have been obtained under its use. It should be given to the extent of 2, 3, or 4 drachms daily, and better at short intervals of two or three hours during the twenty-four hours than in two or three doses or at longer intervals. Vaccines and arsenobenzol are other remedies which have been employed. Deep X-ray therapy is of value. As the organism is anaerobic oxygen by local injection or continuous inhalation might be tried.

Sporotrichosis. A number of different species of Sporotrichum have been described and their classification is by no means complete. *S. schencki* is one of the best known. In pus the parasites appear as oval bodies, 2 to 4 microns long by 1 to 3 microns broad, often situated within the large mononuclear leucocytes; after treatment with two or three drops of potassium hydroxide (20 per cent.) they appear microscopically as a tangled mass of fine, septate mycelia with oval spores on the ends of the filaments. Sporothricha may gain access to the tissues through the abraded skin from infected soil, pricks from the barberry shrub, biting insects or from the ingestion of contaminated food.

Symptoms. In localised *lymphangitic* sporotrichosis the primary lesion generally involves the hand and is the result of some infected abrasion of the epidermis or cutis. After a variable period of weeks to months a painless, cord-like thickening of the lymphatic vessels appears with multiple subcutaneous gummas along its course. General dissemination is rare. In the *cutaneous* type the onset is insidious and the local lesions generally painless. Months may elapse between the appearance of single, subcutaneous gummas or they may occur in crops or in rapid succession. Ulceration with the formation of cup-shaped ulcers may or may not result. Pyrexia and other manifestations of toxæmia are generally lacking. Where the *mucous membrane* of the upper alimentary tract is affected ulceration of the larynx may end fatally, while involvement of the intestinal mucosa may or may not lead to a diarrhœa accompanying blood and mucus in the stools.

Systemic involvement, whether associated with cutaneous, mucosal or osseous lesions, is generally characterised by fever of sudden onset, chills, rigors, digestive disturbances, secondary anæmia and loss of weight. A neutrophile leucocytosis

is marked, the total count varying from 15,000 to 30,000 cells per centimetre. *Leptomeningitis* is rare.

Diagnosis. The diagnosis depends on demonstrating the sporothricha in the pus or cerebro-spinal fluid or reproducing the disease in laboratory animals by inoculation. **Prognosis.** Early diagnosis and treatment is most important. Chronic cases with localised skin lesions generally recover, but those with systemic manifestations and severe fever, and cases with involvement of the pharynx and upper respiratory tract do badly. **Treatment.** Potassium iodide in increasing dosage to the limit of tolerance should be administered, and continued for at least six weeks after all signs of the disease have disappeared (Jacobson), while local abscesses should be aspirated and irrigated with Lugol's solution. X-rays may also be of assistance.

Blastomycosis. (*Chicago Disease : Gilchrist's Disease*). Males of the industrial classes are mainly affected though people of any age or either sex are susceptible. It may occur in any part of the world, but is specially prevalent in Chicago. Some observers hold there is only one *Blastomyces* which causes blastomycosis, other authorities state there are two, *B. immitis* and *B. dermatitides*. When blastomycotic pus is treated with a drop or two of 20 per cent. potassium hydroxide they appear microscopically as oval or round highly refractile bodies, measuring 5 to 20 microns in diameter and containing vacuoles and granules. Budding forms are frequently observed.

Symptoms. The clinical picture is very variable and any organ or tissue in the body may be involved. Primary cutaneous lesions may be subdivided into papulo-ulcerative, papillomatous and gummatous types which cause discomfort and pain locally, but no generalised features in the absence of systemic involvement. Secondary cutaneous lesions generally manifest themselves as ragged superficial ulcers with soft granulating bases covered by crusts which may heal spontaneously : deeper abscesses may also form leading to ulceration or the formation of fistulæ and sometimes they communicate with destructive lesions in the muscles and bones.

In systemic blastomycosis widespread visceral involvement occurs with chills, fever and a clinical picture resembling acute or sub-acute pyæmia. The mode of onset varies, sometimes being very sudden and acute, in other cases mild or insidious. The lungs are involved in 95 per cent. of cases with signs and symptoms of pleurisy and pneumonia, while renal involvement gives rise to nephritis or pyelonephritic features. Involvement of the central nervous system leads to meningitic symptoms, while blastomycotic osteomyelitis, periostitis and arthritis may ensue. Involvements of the tongue, larynx and mammary glands have been recorded.

Diagnosis. The diagnosis in either cutaneous or systemic blastomycosis is dependent on the demonstration of this budding yeast fungus in pus, pulmonary exudate or cerebro-spinal fluid. A marked leucocytosis varying from 15,000 to 40,000 cells per centimetre with an absolute and relative increase in the neutrophile granulocytes is characteristic. **Prognosis.** The course is variable and is generally benign in the localised, cutaneous varieties, but if improperly treated the condition may last with periods of remission and relapses for years. The systemic types are always of grave significance. **Treatment.** Local types of blastomycosis should, if feasible, be treated by total resection with the cautery or carbon dioxide snow and potassium iodide given internally to the point of tolerance. Local treatment with radium and X-rays when combined with iodides have in some cases yielded good results.

Systemic blastomycosis is always difficult to treat. Fresh air, adequate rest, and a nourishing dietary are important and iodides should be administered in full dosage in all cases. Tincture of iodine, minims v t.d.s., increasing by 1 minim per day up to the point of tolerance, is also advised. Vaccines of the blastomyces killed at 110° C. have been employed with promising results (**60**).

Torulosis. Age and race exert no influence on the incidence of the disease which, however, is more common in males than in females. The fungus (*Torula histolytica*) is a yeast-like organism which reproduces only by budding, produces neither mycelia nor ascospores, ferments none of the sugars, and has a predeliction for the central nervous system and lungs (Jacobson). In sputum, pus, or cerebro-spinal fluid they appear as spherical or oval bodies 3 to 15 microns in diameter with an enveloping cell wall. The parasites may be mistaken for lymphocytes and for this reason it is always advisable to make cultures from cerebro-spinal fluid in suspected cases, examining the cultures for a period of at least ten days (Jacobson).

Symptoms. The incubation period is unknown. The manifestations may be local or systemic, the cerebro-spinal system and the lungs being most frequently involved. More rarely other organs such as the lungs, liver, spleen, kidneys, small intestine and mesenteric glands may be involved. There is a moderate leucocytosis and fever generally accompanies the systemic disease. (1) *Local torulosis.* This is a rare manifestation, but abscesses involving the spinous processes, pelvic bones, nasal septum and tongue have been described. (2) *Cerebro-spinal torulosis* is characterised by moderate fever, headache, visual disturbances, mental symptoms and paresis and paralysis of different kinds. The cerebro-spinal fluid is under increased pressure, contains globulin, an excess of leucocytes and *Torula histolytica.* (3) *Pulmonary torulosis* is a sub-acute or chronic disease with pulmonary manifestations and may be confused with tuberculosis, syphilis, neoplasm and other pulmonary mycoses ; *Torula histolytica* may be found in the sputum.

Diagnosis. The diagnosis can only be made by demonstrating the infective agent. **Prognosis.** The course of the disease is essentially sub-acute or chronic, its duration varying from a few weeks to two years. In localised torulosis the prognosis is good if radical surgery be adopted, but cases with systemic involvement almost always die. **Treatment.** Resection of the local lesion preferably with the electric cautery is essential. No known treatment is successful, but Jacobson advises colloidal copper as worthy of trial.

Aspergillosis. Aspergillosis is largely an occupational disease and is common amongst those dealing with birds such as pigeons and parrots, handlers of grain, house cleaners and hair sorters who use rye flour to free the hair from grease. Most species of *Aspergillus* are entirely saprophytic. *A. fumigatus* is definitely pathogenic and has fulfilled Koch's postulates : it is found in quantity in soil and dust originating from agricultural products. A number of other species such as *A. repens, A. versicolar* etc., have been isolated from the external ears, skin lesions and sputa, but their claim to pathogenicity is not so clear. To demonstrate the organism which appears as a stalk or conidiophone with a spore-bearing head, pathological exudate such as sputum or pus should be mixed with a drop of 20 per cent. caustic soda to make a thin film. They grow readily on potato and bread and may be cultured on any laboratory medium. The condition was produced experimentally in animals (**45**).

Symptoms. Three groups have been described clinically with cutaneous, middle ear and pulmonary lesions. The status of cutaneous aspergillosis is very doubtful, and in the vast majority of cases aspergilli isolated from the skin are pure saprophytes. They probably contribute to inflammatory conditions and ulceration of the external auditory meatus (otomycosis). Examination reveals the lining membrane and tympanum to be covered with black, powdery granules or a greenish-white layer containing clumps of black granules. Pulmonary aspergillosis presents a variable clinical picture and may simulate acute bronchopneumonia, the patient being gravely ill, with identical signs and symptoms and X-ray picture. In the more chronic types hæmoptysis is common, and cough, loss of weight, blood-stained sputum, night sweats and an evening rise in temperature lead to the suspicion or diagnosis of tuberculosis ; as a general rule,

however, these patients are well nourished and maintain a fair standard of health (Jacobson).

Diagnosis. The occupation of the patient, his well-nourished condition, and the absence of tubercle bacilli may lead to suspicion, but the diagnosis can only be definitely made by demonstrating *A. fumigatus* in the sputum by microscopic examination and cultural methods. **Prognosis.** Generally dermal and interstitial pulmonary aspergillosis run a chronic course lasting many months or even years, and the outlook is good, but the acute form terminates fatally—sometimes in a few weeks. **Treatment.** Local treatment for dermal lesions consists in the application of dressings with 1 per cent. copper sulphate solution combined with X-ray treatment or, if desirable, copper ointment. For the pulmonary type, potassium iodide to the point of toleration should be given combined with rest, liberal high vitamin diet and fresh air. Aspergillus vaccines have proved disappointing.

Spirochætal Disease

SYPHILIS

Syphilis, or The Pox, is a specific disease due to infection with an organism either through the skin or mucous membrane (acquired syphilis) or through the umbilical cord (congenital syphilis). The acquired form consists of a lesion at the seat of inoculation (*primary* lesion); lesions of the skin, mucous membranes, and other parts after an interval of a month or more (*secondary* lesions); and, after one or more years, deeper lesions of the skin, bones, muscles, viscera, central nervous system, and arteries (*tertiary* lesions). While the *primary* stage of syphilis means that the visible lesion is localised in the neighbourhood of the site of inoculation, the separation of the *secondary* from the *tertiary* stage is distinctly artificial, as both are due to essentially the same pathological process attacking different parts of the body after generalisation of the infection. However, the distinction is useful in the clinical description, and so it will be retained. Syphilis is also the cause of locomotor ataxy and general paralysis of the insane, two diseases of the central nervous system that are sometimes classified together under the term *parenchymatous syphilis*.

The micro-organism of syphilis is the *Treponema pallidum* or *Spirochæta pallida*, first described in 1905 by Schaudinn and Hoffman. It is a long thin filament, of spiral shape, with from six to fourteen coils, and tapering at the ends to a sharp point. The length is from 4μ to 20μ, the breadth about 0·27μ, and it is stained a rose-pink with Giemsa's stain. It has been found at the seat of infection before there is any evidence of a sore, in chancres, in the lymphatic glands associated with them, in the skin papules of primary and secondary syphilis, in mucous patches and condylomas, and in the blood and spleen. In the gumma of tertiary syphilis, the spirochætes often occupy the peripheral parts. In congenital syphilis, the organisms are found in great numbers in the blood, and in the internal organs, viz. the liver, spleen, lungs, and suprarenal bodies. Noguchi and others have found spirochætes in the cortex of the brain of general paralytics; they have also been demonstrated in the walls of the aorta in syphilitic aortitis (*see* Fig. 99, p. 1035).

ACQUIRED SYPHILIS

Infection. Syphilis is, as a rule, communicated during sexual intercourse, the delicate epithelium of the mucous membranes brought into contact allowing of the easy transmission of the virus. Cracks or abrasions of the mucous membrane do not seem to be necessary for the reception of the virus, though they must undoubtedly favour it. Inoculation by sexual intercourse takes place commonly in the *male* on the glans penis, prepuce, in the sulcus behind the glans or on the side of the frenum, and occasionally on the scrotum or in the pubic

area, or at the urinary meatus. In the *female* inoculation most commonly occurs on the labia, the fourchette, clitoris and the urinary meatus, and occasionally on the cervix uteri, but rarely on the vaginal wall. Syphilis may also be transmitted in other ways—for instance, in the act of kissing, by smoking pipes previously used by syphilitic persons, or by contact of syphilitic sores or secretions with the abraded finger of the medical man. After inoculation there is usually a period of *incubation*, varying from three to five weeks; the extreme limits are from ten days to three months.

Primary Lesion. The first sign is a small red itching papule, which gradually enlarges in all directions like a flat button; the surface is dry, or scaly, or superficially ulcerated and covered with a crust of dry secretion. The surrounding tissue becomes indurated in a week or ten days from the first appearance of the papule; and the lesion is known as the *hard, indurated,* or *Hunterian chancre.* On the mucous membrane the lesion may be scarcely so well marked; it begins as a vesicle with a red base; the vesicle breaks, and forms a shallow ulcer, the floor of which becomes indurated. In the course of time, and it may be some months, the induration gradually disappears, the ulcer heals, and a patch of pigment is left behind for a while. In a very early stage of the infection —even before the appearance of the primary sore—the spirochætes are transmitted to the *glands* of the groin; and from seven to fourteen days after the appearance of the hard chancre a single large indurated gland, the *primary bubo,* may be felt, with occasional small shotty glands beside it. These remain freely movable upon one another, without adhesion to or reddening of the skin, and they do not suppurate.

Extragenital sores mostly occur on the lips, finger, face, breast, tongue, or eyelid. They are usually larger than genital chancres, and the associated glands are always large and hard. On the lip or tongue ulceration begins early, and the base is often covered with a thick pseudo-diphtheritic membrane.

Secondary Lesions. The appearance of these lesions from five to eight weeks after the appearance of the primary sore indicates the generalisation of the infection throughout the body. Such lesions may continue to appear at any time up to twelve months or more. The most constant are certain eruptions on the skin (*syphilodermia, syphilide*), faucial inflammation, and enlargement or induration of lymphatic glands; others are febrile reaction, anæmia, pains in the temples, back, or limbs, swelling of the joints, iritis, and falling of the hair. Albuminuria may occur.

Eruptions. There are four main characteristics in secondary syphilitic skin eruptions:—

1. Lesions of different types are present together (*polymorphism*), but the size of the spots does not vary much. Large diffuse lesions are not seen.
2. The eruption is widely spread and copious.
3. Itching is uncommon; but this feature is not constant, and there may be concomitant lesions, such as scabies or pediculosis.
4. The shape of the lesions tends to be round, and the spots may be grouped or in rings. Except in the case of the macular eruption, the colour resembles raw ham.

The different types of secondary lesion and their differential diagnosis are as follows:—

1. The *macular* syphilide, or *roseola,* which forms rose-coloured round or oval spots about the size of a threepenny bit, rather thickly grouped. The trunk, neck, limbs, palms and soles are affected. There is no infiltration or scaling. It lasts from three weeks to two months, and may recur. It does not itch. It must be distinguished from measles and rubella and *pityriasis rosea.* The latter consists of pink spots of varying size covered with fine scales, and there is frequently a history of a "herald" spot, seen first of all, which is of larger size than the other lesions, and the patient often complains of itching.
2. A *follicular* syphilide, consisting of small dull red papular elevations, with

a hair in the centre of each; they are often capped with a dry scale, and sometimes become pustular. They must be distinguished from *acne vulgaris*, which usually has a long history.

3. The *papular* syphilide consists of hard elevations, flat or hemispherical, or more prominent still, so as to form nodules or tubercles, which come out in crops irregularly over the whole body, like the macular syphilide, or grouped in clusters; the papules are red or ham-coloured, and have a shiny surface, often with a ring of fine scales round the edge; they may occur on the rose spots of the macular syphilide. This variety must be distinguished from *lichen planus*, where the lesions are polygonal, flat-topped and shiny, with lilac or violet tint, and usually itch. In half the cases of lichen planus there are white papules, streaks or patches in the mouth; but there is no ulceration of the fauces or enlargement of the lymphatic glands, as in syphilis.

4. The *squamous* syphilide consists of infiltrated coppery or ham-coloured papules capped with scales, and is common in the flexures. It must be distinguished from *psoriasis*, where the lesion is not infiltrated, and the scales are of a bright silvery type. Further, psoriasis occurs particularly on the extensor surfaces of the knees and elbows. *Seborrhœic* lesions must also be distinguished. These consist of round spots or circinate lesions with greasy scales; the scalp and margin of the forehead are commonly affected, and they also occur particularly in the middle line over the sternum, between the scapulæ and in the submammary regions. Itching is common.

5. *Rupia* is a comparatively rare lesion, occurring in debilitated subjects. It consists of a round or oval ulcer with a purplish edge and soft base, exuding blood-stained pus, which dries to form a characteristic limpet-shell crust. On healing it forms a deep scar. It must be distinguished from neglected patches of *psoriasis* which are covered with masses of brown scales. In the latter case on removing the scale a number of bleeding points are seen, but no ulcer, as in rupia.

Other forms are—(6) *syphilitic keratodermia*, in which there is thickening of the horny layer of the epidermis of the palms and soles, which may be mistaken for chronic eczema or psoriasis.

7. *Syphilitic alopecia*, which may take the form of general thinning or small patches of baldness about the size of a sixpence. The latter must be distinguished from *alopecia areata*, where the bald areas are round or ovoid and quite smooth, with club-shaped hairs at the spreading edge.

8. The *pigmentary syphilide* on the sides of the neck, consisting of an ill-defined area studded with white spots, occurring almost exclusively in women during the first two years of the disease. Arsenical pigmentation resembles it closely; but the latter is found on covered parts, *i.e.* on the trunk.

9. *Mucous patches* are moist papules and *condylomas* are broad warty vegetations, which occur commonly about the genitals, perineum, and anus, in the axillæ, groins, and under the breasts, and at the angles of the mouth—in any place, indeed, where the skin is thin and constantly moist. These lesions are extremely infectious. They are often rather extensive, with well-defined edge, moist surface, and dirty grey secretion. They are to be distinguished from venereal warts, described among the diseases of the skin.

Sore Throat. Coincidentally with the rash, or even before it, the throat becomes affected; there is a diffused redness of the fauces, with enlargement and excoriation of the follicles; but the most characteristic feature is the swelling and symmetrical ulceration of the tonsils. The ulcers are often kidney-shaped, superficial, with grey borders, painless, and not of very long duration. Sometimes, however, the tonsillar ulcers are much more persistent, extend to the soft palate and uvula, have bright red edges, and are covered with a yellowish-grey secretion, the removal of which is followed by bleeding. Other changes in the mouth in the secondary stage are white spots, like those produced by the application of nitrate of silver, mucous patches on the tongue, or faucial pillars or inside

the cheeks, bald patches on the tongue from the destruction of the papillæ, or enlargement of the tongue, which is of bright red colour, with hypertrophied papillæ, or irregular prominences and deep sulci between them ; this last condition is aggravated, or in part caused, by excessive smoking. The lesions in the mouth must be distinguished from aphthæ, which are rounded yellow, painful superficial lesions, from herpes, which is also painful, and occasionally from erythema multiforme with extensive lesions in the mouth. The lesions on the fauces must be distinguished from Vincent's angina.

The *lymphatic glands* are enlarged, especially in the groins, above the inner condyles of the humerus, and at the back of the neck. The *fever* of secondary syphilis is often entirely absent, or it is represented by no more than a slight malaise or indisposition preceding or during the outbreak on the skin. In a small number of cases there is very distinct intermittent or remittent *pyrexia*, the temperature highest in the evening ; and it may last for some weeks. The *periostitis* of secondary syphilis is slight ; pains and tenderness are felt in the tibiæ, skull bones or clavicles, but they are of short duration, and nodes do not generally form, as in the tertiary stage. The *joints* are not often affected ; but there may be synovial effusion, which is sometimes excessive (hydrarthrosis), and is liable to vary from time to time in the same joint.

The most common affection of the eye is *iritis ;* it usually affects one eye before the other ; the symptoms are photophobia and pain, with ciliary congestion, irregular pupil, obscured iris, and, in severer cases, nodules of rust-coloured lymph and blocking of the pupils. Iritis occurs from three to six months after contagion ; at a later period still, but within the limits of secondary symptoms, there may be diffuse retinitis or choroiditis.

Various nervous affections, especially paralysis of cranial nerves and myelitis, are apt to occur within a few months or a year of infection, and thus fall within the category of secondary results. Such disorders show a considerable proportion of recoveries under antisyphilitic treatment.

Some other lesions occur at a time which is intermediate between the second and tertiary periods, such as scaly or peeling patches on the palms of the hands (*psoriasis palmaris*) ; enlargement of the testis with perhaps nodular deposit in the epididymis ; choroiditis and retinitis ; and transitory visceral changes not due to gumma—for instance, enlargement or tenderness of the liver and spleen, with failure in the blood-making process, slight and temporary albuminuria, and symptoms of impending pulmonary mischief. And, indeed, no hard-and-fast line can be drawn between the end of the secondary and the beginning of the tertiary stage.

Tertiary or Late Lesions. These are first observed from one to two years after contagion, and may recur at intervals for ten or fifteen years, or more. They are certain eruptions on the skin, periostitis and nodes on the bones, and lumps in the subcutaneous tissue, muscles, meninges, liver, spleen, testis, and other viscera.

Late Syphilides. The skin rashes of the tertiary period are variable, and may consist of maculæ or scaly patches. But the most characteristic is a dusky red, infiltrated patch, forming a circle or broad band curved in a half-circle or horseshoe ; part of the surface is covered with a brown or greenish scab, beneath which are deep ulcers with sharply cut edges. The lesion spreads in serpiginous lines, being made up of small gummas of the skin set in circles or segments of circles, which in turn ulcerate, while the old ulcers heal and leave scars surrounded by deeply pigmented skin. Sometimes such nodules will subside and leave scars even without ulceration, and altogether there is a general resemblance to lupus. Ultimately large, irregular patches, of several inches in diameter, may form, and they are frequent on the knee, thigh, shoulder, forearm, face, and neck. Sometimes much deeper infiltrations of the subcutaneous tissues occur.

Gummas. The lesion in the viscera and other parts which is so characteristic

of the later stages of syphilis is known as a *gumma*. This is a mass of granulation tissue which may very closely resemble tuberculous granulation tissue; but giant cells are not so commonly seen, and the smaller arteries often show *endarteritis*. In the early stages it is grey, gelatinous and transparent; but the cells undergo fatty changes, and caseation takes place, so that the centre becomes yellow, and the circumference develops into fibrous tissue, which contracts like that of a scar. Sometimes gummas break down completely, and suppuration, with destruction of the tissue in which they are situated, takes place; thus caries and necrosis not infrequently follow nodes on the bones. In the liver gummas form large, more or less uniform, yellow nodules; or a yellow caseous mass lies in the centre of a fibrous cicatrix; or nothing is left but the fibrous cicatrix, with consequent depression and puckering of the organ. In the testis gummas also occur; but this organ is often enlarged by a diffuse gummatous infiltration of its substance generally, and may afterwards atrophy from the formation of a dense fibrous tissue without any local nodular growth. For the clinical results of these lesions the reader is referred to the diseases of different organs. It will be sufficient here to say that gummatous periostitis, or nodes, occur especially along the anterior surface of the tibia, on the frontal and parietal bones, and on the clavicles. The patient suffers from pains, which are worse at night, and there may be found on the affected part flat, round prominences, from ½ inch to 1 inch in diameter, soft, or even fluctuating, and very tender. This is not necessarily a sign of pus being present, as quite distinctly fluctuating nodes may entirely disappear under treatment. Gummas are sometimes found involving the synovial or perisynovial tissues of joints. A very definite *pyrexia* with the temperature rising to 101° or 102° in the evening, and falling to 98° or 99° in the morning, may accompany a gumma apart from suppuration. Syphilis attacks arteries, producing in the case of the larger vessels *arteritis* and *atheroma*, which may lead on to aneurysm, and in the case of the smaller ones syphilitic *endarteritis* (arteritis obliterans), leading on to myocarditis. There is a consensus of opinion that the cardio-vascular system is more commonly attacked than formerly. Several disorders of the nervous system are referable to syphilis; some, like hemiplegia, are due to syphilitic endarteritis, leading to thrombosis and consequent softening of the nervous tissue; when this occurs in the brain, it gives rise to hemiplegia, or in the spinal cord to acute or chronic paraplegia, including Erb's *syphilitic spastic paraplegia*; another is probably a true infective myelitis; others, like localised paralyses and convulsions, are due to gummas or meningeal thickenings on the surface of the brain and the roots of nerves. The mucous membranes are affected with deep-seated destructive ulcerations, such as are seen in the mouth, destroying the uvula and soft palate, with adhesion of the remainder to the pharynx, or in the trachea, bronchus or rectum, leading to stricture or stenosis of these passages. Late syphilis is also one of the causes of the lardaceous degeneration, even without the existence of any suppuration.

Parenchymatous Neurosyphilis. The latest results of this disease are certain pathological conditions, with accompanying symptoms, the association of which with syphilis was first determined by statistical evidence. These affections are tabes dorsalis and general paralysis of the insane, in which it is found that a history of syphilis is obtained in 70 to 80 per cent. of cases; while some forms of ophthalmoplegia, optic atrophy, loss of pupil light reflex, show similar relations. This view is supported by the results of investigation of such cases by the Wassermann test, which is positive in the blood-serum in nearly 100 per cent. of cases of general paralysis and somewhat less in tabes, and by the discovery of spirochætes in the brains of general paralytics. These diseases are much less amenable to treatment than other forms of syphilis.

Course and Termination. In all stages of syphilis there is a tendency for lesions to appear at sites of injury. As examples may be cited the mucous patches and glossitis of smokers, squamous syphilides on the palms of manual workers,

the gummatous bursitis affecting the pre-patellar bursæ of charwomen, and gumma of the frontal bone in Mohammedans, arising from the practice of striking the forehead during religious worship. Thorough treatment in the early stages may entirely prevent the occurrence of late symptoms, and the secondary symptoms may be avoided or rendered extremely mild by diligent treatment when the primary lesion is first recognised. The disease has no fatal tendency in the first two stages, but in late syphilis the gumma may act like other tumours, and cause death by direct interference with function, especially in the brain and meninges. Death also results from syphilitic disease of the arteries, from bronchial, tracheal, or rectal stenosis, from periostitis with necrosis of bone and pyæmia from lardaceous disease of the liver, spleen and kidneys, and from the disorders classed as parenchymatous syphilis.

Diagnosis. In the *primary* stage it is important to make the diagnosis as soon as possible, so that treatment may be carried out before generalisation of the infection has occurred. The chancre is distinguished by its induration, and by the presence of the hard primary bubo from: (1) *soft sore*, which is usually multiple and causes soft and tender enlargement of the glands; (2) *herpes genitalis*, where the lesions are superficial; (3) very rarely *lichen planus;* (4) traumatic ulceration. In addition, when the lesion has been untreated spirochætæ should be looked for. Some serum is obtained from the lesion or from the neighbouring gland and is mixed on a slide with a few drops of normal saline. The slide is examined with a $\frac{1}{12}$-inch oil immersion objective by the dark-ground illumination. The spirochætæ, which appear white, are seen moving in the field.

From a medical point of view it is the recognition of the late syphilitic lesions that is most frequently required, and help is commonly sought in the former history of the patient. The points likely to be remembered are the occurrence of a definite sore other than mere gonorrhœa, the rash, the sore throat and the falling of the hair. Whether the sore was of the hard or soft variety may be unknown to the patient. The patient may be able to give consistent accounts of the rash, or of the ulcerated sore throat. In married women some reliance is placed upon the previous occurrence of still-births and deaths in infancy, and of eye troubles, etc., in the older children.

Search should be made for scars of the original sores on the penis in men, for scars of tertiary lesions on the skin and in the throat, for nodes on the tibiæ and skull, for hardness or atrophy of the testes, and for evidences of lardaceous disease, in the size of the liver and spleen and in the existence of albuminuria.

The diagnosis is sometimes assisted or confirmed by therapeutic measures, when, for instance, a suspected lesion yields rapidly to the treatment mentioned below.

By serological methods it is now possible to detect in the blood serum a specific result of syphilitic infection. Bordet and Gengou showed that if any *antigen* (*i.e.* a substance that has the power of calling into existence *anti-bodies* on being injected into an animal) is mixed and incubated at 37° C. with serum containing such anti-bodies, the two combine together and at the same time fix *complement*, an enzyme normally present in the blood. This phenomenon has been applied to the diagnosis of syphilis, and is known as the *Wassermann reaction.* The antigen originally consisted of an extract of syphilitic liver, and this was added to serum taken from the patient to be investigated. If complement is fixed, the patient is to be regarded as syphilitic. This fixation is determined by means of a special hæmolysis test. If red cells from some animal, like a sheep, are injected into another animal, such as a rabbit, they behave as antigen, so that the corresponding anti-body, or hæmolysin, is formed. If the red cells and serum containing the hæmolysin are mixed, hæmolysis occurs so long as complement is present, but does not occur in the absence of complement. For the test the suspected serum believed to contain syphilitic anti-body is heated to destroy complement and then mixed with the extract of syphilitic liver, and with normal guinea-pig's serum

containing complement. These are kept for an hour at a temperature of 37° C. and the mixture of rabbit's serum containing hæmolysin (but deprived of complement by previous heating to 56° C.) and the washed sheep corpuscles is then added, and the whole mixture further submitted to 37° C. for two hours. If the serum in question contains anti-body of syphilis, the complement will be bound, or fixed, by it in the first incubation, and the hæmolysin in the rabbit's serum, not meeting with free complement in the second incubation, will not destroy the corpuscles—*i.e.* there will be no hæmolysis. This event is called, in regard to complement fixation and to the presence of syphilis, a *positive reaction*. If, on the other hand, the anti-body of syphilis is not present, the complement will not be bound in the first incubation ; it will co-operate with the hæmolysin in the second incubation, and hæmolysis will take place. This is a *negative reaction*. By carrying out the whole process on quantitative lines it is possible to judge from the amount of hæmolysis that occurs the amount of syphilitic anti-body present in the patient's serum.

As a matter of fact, the reaction as carried out at the present day has been modified in one particular way. For some unexplained reason it has been found unnecessary to use a syphilitic liver to prepare the antigen. Certain other substances will do, and an extract of human heart mixed with cholesterin answers the purpose, so that this is always used now as antigen, because it is easier to obtain. These facts indicate that the original explanation of the Wassermann reaction no longer holds good.

The Wassermann test gives a positive reaction in primary cases in from five to eight weeks after infection, in 95 per cent. of secondary cases, in 75 per cent. of tertiary cases, and in 50 per cent. of cases where syphilis is latent (D'Arcy Power). It is very frequently found (70 per cent. or more) in the case of apparently healthy mothers of children congenitally syphilitic. The child itself may give a negative reaction in spite of the mother's positive result, or a positive reaction may appear with the outbreak of definite symptoms. Conditions other than syphilis that give a positive Wassermann reaction are rarely met with in practice.

The Kahn reaction is another serum reaction which is used extensively in diagnosing syphilis. It depends on the fact that serum from a syphilitic patient can flocculate a saline suspension of a mixture of alcoholic heart extract and cholesterin.

In patients under treatment the reaction may become negative, and yet in many cases, if a small dose of salvarsan (*see* below) is injected, the reaction again becomes positive, showing that the syphilitic infection is still present; and freedom cannot be pronounced until the negative reaction persists in spite of this so-called " provocative injection " of salvarsan.

Prevention. As syphilis is rarely conveyed otherwise than by direct contact it should be easy to prevent its spread, if those who are known to be infected could be made to abstain from contact, sexual or otherwise, with healthy persons ; but those who are infected do not always know that they are so.

Legislation has many difficulties to contend with. Following the report of the Royal Commission in 1916, the State has made grants of money for the purpose of providing means of bacterial diagnosis, of promoting the establishment of treatment centres all over the country free to all who apply, of educating practitioners in the use of newer methods of treatment, and of supplying salvarsan or its substitutes free to medical practitioners. In the vast majority of cases which have been exposed to infection, immediate disinfection—thoroughly washing the parts and rubbing in the 30 per cent. calomel ointment mentioned on p. 114—will prevent the primary sore; but in spite of this there may be generalised infection, so that observation by blood tests is necessary after disinfection. A solution of mercury cyanide (1 in 1,000) is an even better antiseptic.

Pregnant women known to be syphilitic, or demonstrated to be so by the

Wassermann test, should be promptly treated, to secure the health of the offspring.

The following facts may guide the medical man in advising patients. Both primary and secondary lesions are contagious, and the blood during these periods contains the virus. During the latent and tertiary stages the infectivity usually becomes progressively less but the disease may be transmitted many years after acquisition. It will be seen that syphilis of the fœtus is probably always due to maternal infection (*see* p. 115).

As a rule, syphilis confers upon the sufferer immunity from fresh infection, though by some it is stated that the immune person is only an *uncured* syphilitic. Instances are recorded in which, after a long interval, a fresh primary sore and fresh secondaries have appeared, and here we must suppose that the protective influence, if it ever existed apart from the spirochæte and its toxins, has died out, as it does rarely in the exanthems.

Treatment. The extraordinary tenacity of the spirochæte of syphilis and its possible influence for years after infection upon the bodily structures makes it essential that treatment should be prompt and persistent over a long period of time. The following have a pronounced effect upon the disease: (1) mercury and its compounds; (2) certain arsenical compounds; (3) bismuth, which all act by destroying the spirochæte; (4) potassium iodide, which stimulates a tissue reaction, to absorb exudates.

(1) Mercury can be given in a variety of ways. For *intramuscular injections* a soluble preparation may be used such as the perchloride, $\frac{1}{10}$ to $\frac{1}{5}$ grain, dissolved in 0·9 per cent. salt solution, every day or every other day, or an insoluble one such as mercury in fine subdivision, calomel, or the salicylate suspended in a fatty medium of which there are a number of formulæ. The method of *inunction* with mercurial ointment is undoubtedly a very thorough way of introducing mercury into the system, but it requires to be done by expert attendants, and in view of other methods of treatment is rarely used now, except in cases of congenital syphilis in infants. *Oral* administration of mercury, the simplest method, is commonly used. The more usual preparations are the perchloride in doses of $\frac{1}{16}$ to $\frac{1}{12}$ grain (60 to 80 minims of the liquor) three or four times a day, and hydrargyrum cum creta (grey powder) in doses of 1 or 2 grains with the same frequency. Hutchinson advised 1 grain of grey powder with 1 grain of Dover's powder, if necessary, to be given every six, four, three, or two hours. During the use of mercury the patient should abstain from smoking and from stimulants, frequently clean the teeth and mouth, and live in every way as healthy a life as possible. Excessive treatment causes salivation (*see also* Chronic Mercurial Poisoning). Mercury has a very mild spirochæticidal action, but it acts persistently.

(2) Salvarsan was introduced by Ehrlich (1909), and was known later as arsenobenzol. As its method of administration is complicated, it is no longer included in the British Pharmacopæia; but the names may be conveniently used for this group of compounds.

Neo-salvarsan, or "914," is an allied drug, also known as novarsenobenzol, novarsenobillon, neokharsivan, novarsan, neoarsphenamine (the official name). It is soluble in water, and so can be injected directly into a vein by means of a needle and syringe. The solution must not be kept, but must be injected immediately it is made. It must not be allowed to run outside the vein, as it is irritating; to avoid this a little blood is first sucked into the syringe so as to be sure the needle is properly in the vein, before pushing the plunger home. The injection should not be made on a full stomach and it is often advisable to give glucose beforehand.

Sulfarsenol, closely allied to "914," can be given intramuscularly or just over the gluteal fascia without undue discomfort, and is of value when the Wassermann reaction continues to be positive. It can be given without reference to

meals. Kharsulphan, metarsenobillon, sulphostab and myosalvarsan are all chemically like sulfarsenol and have all been devised for intramuscular injection. Silver salvarsan is a combination of sodium salvarsan with silver and has been found very useful in neuro-syphilis.

Arsenic preparations act rapidly in destroying the spirochæte; but not thoroughly. In fact, it is suggested that a strain of arsenic resistant spirochætes is being produced from insufficient treatment.

(3) Bismuth was introduced into the treatment of syphilis by Sézary and Levaditi after numerous animal experiments had shown that it has a powerful curative effect. It has a stronger spirochæticidal effect than mercury and is persistent in its action, differing in this way from the arsenic compounds. The majority opinion to-day places it in therapeutic power between the salvarsan preparations and the mercurial. It is always administered by injection, intramuscularly, or over the fascia covering the glutei. The preparations for intramuscular injection are very numerous. They may be divided into the soluble and the insoluble. An example of the soluble is a preparation of iodo-bismuthate of quinine (Solubyl), used by Fournier, when a quick effect is desired. The disadvantage of the soluble preparations is that, like the preparations used for intravenous injection, they quickly provoke the general signs of poisoning mentioned below. The insoluble preparations, such as the insoluble basic tartrate, the oxychloride, salicylate, or the metal itself in fine subdivision, are suspended in an oily or in a watery medium such as glucose solution, and of these probably the watery medium is better, as it is absorbed more evenly. For the same reason probably a compound is preferable to the metal in fine subdivision. Usually intramuscular injections cause little or no discomfort, and in this respect they have a great advantage over mercury. Treatment by bismuth alone is used for elderly patients, and in cases of intolerance to salvarsan preparations. The signs of bismuth poisoning are somewhat similar to those of poisoning by mercury. The more common are aphthous stomatitis, which is usually preceded by the formation of a slaty-blue line on the margins of the gums, albuminuria, colitis, vague aching in the back and limbs, insomnia, general depression and occasionally skin rashes rather similar to those provoked by arsenobenzol preparations.

(4) *Iodide of potassium* is especially useful in the treatment of later manifestations, but in other stages it may be used in combination with the perchloride of mercury. Under its use the most serious and alarming nervous symptoms, due to syphilitic gummatous lesions, rapidly subside, ulcerating skin lesions quickly heal, pains in the bones subside, and periosteal nodes disappear. Five or 7 grains three times a day are often sufficient, but in serious cases it should be pushed to ½-drachm or drachm doses three times daily; or as much as 20 grains may be given in a little milk every two hours through the whole day and night. The advantage of this, no doubt, lies in the thorough saturation of the system; otherwise, as the salt passes away rapidly by the kidneys, the amount in the body may fall very low in a long night interval. If iodide, in any dose, causes coryza, it should be taken much diluted—*e.g.* in half a tumblerful of water; arsenic may be added if it causes eruptions (*see* Medicinal Eruptions). General tonics, good food and sea air are desirable if it causes much depression, or the iodide of sodium may be given instead in corresponding doses, or a mixture of the iodides of potassium, sodium and ammonium in equal parts. If these fail, recourse may be had to mercury, either alone or with a tolerable dose of potassium iodide.

It is now generally recognised that a prolonged course of treatment is desirable, and this depends on the stage of the disease and the Wassermann reaction. In Harrison's table (**33**) the dose of the salvarsan preparation is stated in grammes of "914" or of Stabilarsan. An equivalent dose of silver salvarsan would be one-third. All these preparations are given intravenously. The dosage of the preparations which can be given intramuscularly, such as sulfarsenol, etc., is the same as that of "914." Hg means an insoluble preparation of mercury given

intramuscularly, and the dosage below is that of mercury in fine subdivision. If calomel is used the dosage is usually three-quarters of that stated in the table, and that of the salicylate is 50 per cent. greater. Bi means a good preparation of bismuth, preferably an insoluble compound, such as the oxychloride or the salicylate suspended in a glucose solution and injected intramuscularly or over the gluteal fascia. Mercury and bismuth are alternatives, and either (preferably bismuth) is administered at the same time as the arsenobenzol. The dosage in the tables is that recommended for males of average build and weight without clinical manifestations of disease of the central nervous system or of any viscus. For women the dosage is lower, according to weight.

A. Primary Cases with Negative Serum Reactions

Day of Treatment.	Neoarsphenamine, grm.	Hg with grain.	Bi or with grain.
1st	0·45	—	—
8th	0·45	i	iii
15th	0·45	i	iii
29th	0·60	i	iii
36th	0·60	i	iii
50th	0·75	i	iii
57th	0·75	i	iii
78th	0·75	i	iii
85th	0·75	i	iii
92nd	0·75	i	iii

Potassium iodide is given from the 58th to 77th days, and from the 127th to 147th day in a dosage increasing in each period from 15 to 30 grains a day.

A blood test is taken on the 92nd day. Whatever the reaction, a second course similar to the above is commenced on the 148th day. After this the patient is put under observation for two years, testing the blood serum every three months in the first year and every six months in the second. The tests at the end of the first and of the second years respectively are preceded a week previously by a provocative injection of 0·3 gram "914." If at all practicable, the cerebro-spinal fluid is examined at the end of the first and second years.

B. Primary with Positive Serum Reactions

(1) As for sero-negative primary, followed by
(2) No treatment for ten weeks.
(3) Potassium iodide for three weeks.
(4) A course of five injections as from the 29th to 78th days, but with only two weeks between the 3rd and 4th injections.
(5) Assuming that the blood was negative on the 92nd day and at the end of each subsequent course, suspend treatment and observe as above. If not negative on the 92nd day or at any time later, proceed as for secondary cases.

C. Cases with Clinical Signs of Secondary Syphilis

(1) As for sero-positive primary, followed by
(2) A repetition of the procedure shown in B (2) to (5).

D. Tertiary and Latent

(1) A course of 7 injections as from the 1st to 57th day in A.
(2) Potassium iodide for three weeks.
(3) No treatment for ten weeks.
(4) Course of 5 as in B (4).
(5) Potassium iodide for three weeks.
(6) Repeat (1) to (5) twice.
(7) No treatment for sixteen weeks.
(8) Repeat (4) and (5).
(9) No treatment for eighteen weeks.
(10) Repeat (4).

This series of courses lasts over two years, and even then the serum reactions may still be positive. The question of persistence with treatment is debated. Harrison advocates keeping the patient under treatment with intervals of rest so long as the reactions are positive, believing that this is the best preventive of late effects. Others would not treat these " Wassermann-fast " cases for so long. Recently there has grown up the practice of combining the injection treatment of such cases and even earlier ones with the artificial induction of malarial fever. This arises from the good results obtained by such treatment in general paralysis. Finger advocates 3 grams of " 914 " in doses of 0·3 to 0·45 at five-day intervals followed by malarial inoculation and ten paroxysms of fever, which is then stopped by quinine, and on the day of the last paroxysm another course of ten injections of " 914 " is commenced. By this method the serum reactions are said to be converted to negative in a much higher percentage of cases than by purely drug treatment given in a very much higher total dosage. A milder procedure than the malarial treatment is to provoke a series of rises of temperature by injections of such foreign substances as anti-typhoid vaccine, milk and turpentine.

The treatment of syphilitic myocarditis and aneurysm (*see* p. 279), of hepatic syphilis (*see* p. 398), of syphilitic myelitis (*see* p. 666), and neuro-syphilis (*see* p. 681), are dealt with in the appropriate places.

The only contra-indications to treatment along these lines are intolerance on the part of the patient. Intolerance to arsenobenzol is fully discussed on p. 117, and it is essential to take the precautions mentioned there, since many deaths from poisoning have been reported.

The destruction of the primary sore will not prevent generalised infection, but, in view of the presence of organisms therein, it is advocated by some as an additional measure. Excision, cauterisation, and the application of an ointment—calomel 33 parts, lanoline 67, and vaseline 10—have been tried. Infiltration of the area with hectine, " 914," or similar preparations, is probably more effective than applications.

CONGENITAL SYPHILIS

Children born of parents suffering from syphilis in any stage may themselves be infected with the disease. This transmission is less frequent in the tertiary stage. Congenital syphilis is due to infection of the fœtus by the mother, who may herself have been the subject of syphilis before conception or may contract the disease during pregnancy. Fœtal infection may occur through the placenta at any time during the pregnancy, and the later it occurs the better chance there is of the fœtus surviving. Infection may occur during parturition. In this case a primary chancre develops at the site of an abrasion (*e.g.* from forceps), as the result of infection from primary or secondary lesions in the maternal passages.

It was formerly stated that a child might be infected with congenital syphilis

from the father, the mother being healthy. Further, under these circumstances, the syphilitic infant might infect a wet-nurse—*e.g.* causing a chancre on the nipple—but would not infect its own mother, thereby showing that the mother was in some way protected against infection, though she might manifest no lesions whatever. This is called *Colles' law.* The now generally accepted explanation is that the father has really infected the mother, who however shows no signs of the disease, and she passes on the infection to the fœtus, and this is proved by the fact that the Wassermann reaction has been found to be positive in 95 per cent. of mothers of syphilitic children when they have been examined soon after the birth of the child.

Infection *in utero* does not always occur when there is maternal syphilis, and sometimes its transmission is irregular, as is shown by the fact that the same parents may have children showing a positive Wassermann reaction alternately with children showing a negative reaction, and one child may be badly affected, another not at all.

Death of the Fœtus. One effect of syphilis in the parent is the early death of the fœtus, with resulting miscarriage or premature birth. In fact, 15–20 per cent. of all miscarriages and still-births are due to syphilis. The fact of miscarriages having occurred in the history of a married woman may be important evidence as to syphilis in herself or her husband. It is not so easy to say the exact cause of the fœtal death, whether from the immediate effects of the syphilitic virus or from some disease of the placenta. Hard yellow masses have been found in this structure, but usually there are no naked-eye characteristics. Microscopically the villi show increase in size and vascularity. Endarteritis is absent. On the other hand, the fœtus not infrequently presents lesions of the bones, viscera, and skin which show that it may be profoundly diseased. In the bones there is irregularity and deepening of the line of calcification at the junction of the epiphysial cartilages and the shaft. This is described as osteochondritis or *epiphysitis,* and resembles the changes in rickets, except that in syphilis the calcification is more evident. The cartilage may be separated from the bone by soft granulation tissue or pus. The changes in the liver are described on p. 397. The lungs show increase in the interalveolar tissue, with compression of the alveoli and capillaries and sometimes gumma. Increase of connective tissue is present in the thyroid, thymus and pancreas, and ulcers in the intestines. Spirochætes may be found where the lesions are marked.

Early Symptoms. Epiphysitis, which occurs in about 16 per cent. of cases, is sometimes present in children born alive, the principal epiphyses being separated from their bones, and the limbs consequently lying useless, so as to give the appearance of paralysis. Occasionally also the child is born with a bullous eruption on the skin, or the rash comes out very soon after birth. The palms and the soles are always affected. This is a syphilitic rash, and must be distinguished from *Pemphigus neonatorum,* which is a bullous impetigo due to sepsis usually at the umbilicus. But in a large majority of cases the child is born not only alive, but healthy, fat, and plump, and remains so for three or four weeks after birth. Then it acquires a nasal catarrh, *rhinitis,* causing the symptom commonly known as *snuffles,* with a discharge, at first thin and serous, afterwards thicker, purulent, and drying up into crusts, which obstruct the nostrils, so that sucking is difficult. At the same time a *rash* appears, most commonly on the buttocks and adjacent parts of the thigh, back, and abdomen. It consists most often of circular patches, brownish red like the lean of ham, dry, shiny, and inelastic; the patches run together, and form larger areas of irregular shape, but mostly with a well-defined edge. This is to be distinguished from intertrigo, which occurs in the flexures, and from the "napkin rash," a bright shiny red inflammation affecting the convex surfaces over the area which comes in contact with a dirty napkin (*see* later); and the two conditions probably sometimes co-exist. Less frequently the rash is papular, pustular, and bullous.

Other lesions occurring in early infancy are stomatitis, ulcerations about the lips and angles of the mouth, rapidly forming cutaneous abscesses, and periostitis; and the spleen is enlarged in very many cases. With all this the nutrition of the child may be little affected, but sometimes wasting results, and the face acquires a withered and shrunken appearance like that of an old man. In this stage death may occur; but under treatment, or otherwise, all the symptoms may subside, and the child may show no indications of the taint for many years, when, often about the time of puberty, symptoms appear which are more or less comparable with those of the third stage of the acquired disease. The Wassermann reaction is positive in 90 per cent. of the cases, and the mortality may be as much as 40 per cent.

Later Symptoms. These are—periostitis with the formation of nodes; synovitis, especially a chronic synovial effusion into both knees; scaly or lupoid skin eruptions, which are not very common; bilateral deafness coming on with noises in the ears, but without pain or discharge; disseminated choroiditis; dark brown punctate pigmentation of the *fundus oculi;* iritis; and keratitis. The last is common in inherited syphilis, not so in the acquired disease; it causes opacity of the cornea, which gradually increases till the cornea looks like ground glass. It is associated with ciliary congestion, and in late stages vessels may encroach upon the cornea, producing a "salmon patch." Its tendency is to recover. But, in addition to these fresh lesions, inherited syphilis may be recognised by some permanent deformities, the result mostly of those changes which took place in infancy. Such persons present a broad forehead, with unusual prominence of the two halves of the frontal bone; the bridge of the nose is broad and sunken; around the mouth are numerous linear cicatrices radiating from the orifice as a centre; and the permanent teeth, as was first pointed out by Hutchinson, show features from which alone an absolute diagnosis of the condition may be made. It is only the upper central incisors that can be relied upon for this purpose, though other teeth may be similarly affected: they are short, narrower at the edge than near the gum, and the edge presents a single central cleft or notch. This notch is at first, soon after the eruption of the tooth, filled by a notched edge of exposed dentine, which soon breaks away. This change in the teeth must be distinguished from the simple transverse marking, which may result from the excessive use of mercury in infancy, causing stomatitis, and interfering with the proper development of the tooth sacs. Periosteal changes in the tibia may result in a convexity of the anterior border, the so-called *sabre-shaped tibia.* Visceral changes are also not uncommon, such as enlargement of the spleen, cerebral inflammation or degeneration (*see* Cerebral Diplegia), occasionally orchitis, interstitial hepatitis (*see* Cirrhosis of the Liver), anæmia with or without splenic enlargement, and gummas revealing themselves in adult life.

Prevention. This may be considered under two heads:

(1) *Prevention of Infection of the Mother.* Men with syphilis should not marry until there is no danger of transmitting the disease. They should have had adequate antisyphilitic treatment and be free from all clinical evidence of the disease, and the blood should have given a negative Wassermann for at least three years. Sometimes the blood remains persistently positive. In such cases there can be no certainty, and the risk, though slight, must be explained to the patient. Not uncommonly a husband becomes infected from irregular sexual intercourse during the later months of pregnancy or the puerperium. Adequate and prompt treatment must be undertaken and he must abstain from sexual relations until free from infection.

(2) *Treatment of the Syphilitic Mother before and during Pregnancy.* The Wassermann reaction is of great value in diagnosing maternal syphilis, because many women suffer from syphilis without knowing it. The primary lesion may be hidden away and cause very little discomfort. Often there is additional

evidence of syphilis, *i.e.* a history of still-births, etc., or a positive Wassermann reaction obtained from the husband's blood, which should always be tested. Antisyphilitic treatment with arsenobenzol compounds and bismuth may be given throughout pregnancy, and should be continued afterwards.

Treatment. Mercury is rapidly effective in infantile syphilis. A grain of grey powder three times a day or liq. hydrarg. perchlor. 10 to 20 minims, will quickly disperse the rash, snuffles or other symptoms, and improve the nutrition. An excellent method is by mercurial ununction, $\frac{1}{4}$ drachm of ung. hydrargyri being rubbed into the abdomen daily. Calomel powder may be applied to mucous patches or ulcerations of the skin. Bismuth is even more effective but must be administered by intramuscular injection. While such treatment is usually effective in the treatment of symptoms, to effect the complete eradication of syphilis it is essential to administer neo-salvarsan compounds and bismuth over several years. Intramuscular injections of sulphostab may be given to an infant a few weeks old, increasing from an initial dose of 0·05 to 0·15 gram at two months of age. The toleration of salvarsan by infants is high. Bismuth preparations are also well tolerated and may be given by intramuscular injections of 0·25 c.c. of a 10 per cent. suspension of bismuth oxychloride at weekly intervals. Even with apparently satisfactory results the child should be kept under periodical clinical observation and repeated Wassermann reactions done until after puberty. Any clinical or serological relapse of syphilis will indicate further prolonged treatment.

POISONING BY ARSENOBENZOL

On account of a wide variation in the tolerance of patients to the intravenous and intramuscular injections of arsenobenzol compounds symptoms of poisoning are not uncommon. In the early years of the use of salvarsan, before this danger was recognised, there were many fatalities. The toxic symptoms may appear either at an early stage of treatment or they may be greatly delayed and bear no apparent relation to the injections.

Early Toxic Effects (1) *Vasomotor reaction.* This is a sudden syncope with rapid cyanosis and œdema of the face and extremities during or immediately after one of the first few intravenous injections. Although alarming the condition is rarely fatal and usually reacts promptly to the injection of adrenaline. Treatment may be resumed with intramuscular injections. (2) *Jarisch-Herxheimer Reaction.* This is a general reaction with malaise and fever and exacerbation of the existing syphilitic lesion, *e.g.* in the skin or meninges, and it is probably due to the stimulation of spirochætes by a dose of drug insufficient to destroy them. It is usually seen after arsenobenzol preparations, but may be caused by mercury or bismuth. The phenomenon has been called *biotropism*, and similar exacerbations have been observed with streptococcal focal lesions and malaria. (3) Mild *gastro-intestinal* irritation with vomiting and diarrhœa, occasionally followed by transient jaundice, may occur from twelve to forty-eight hours after an injection, particularly in constipated patients. (4) *Cutaneous eruptions*, urticarial, erythematous and papular are not uncommon. Further treatment must be delayed and administered with caution. Purpura is rare but denotes a dangerous idiosyncrasy ; it may be followed by severe or fatal aplastic anæmia. (5) *Encephalitis Hæmorrhagica.* This serious condition is characterised by drowsiness with intense headaches for a few days, followed by epileptiform convulsions and rapidly deepening coma. The majority of the patients are young adults, and this condition, which follows the first two or three injections, is usually fatal.

Delayed Toxic Effects. (1) *Jaundice* of more prolonged duration may occur after one or more courses of treatment, and may be delayed until some months after treatment has ceased. There are no characteristic signs of the toxic

origin of the jaundice, and the differentiation from catarrhal jaundice is difficult. Pyrexia and pruritus are usually absent and the patient suffers little if at all from depression. Very rarely acute necrosis of the liver ensues with fatal result. (2) *Dermatitis.* Severe *exfoliative dermatitis* may occur after a series of injections, and is often preceded by transient erythema or urticaria. In the acute stage there is generalised erythema with œdema of the skin. Irritation is very marked. Vesicular formation and gradual exfoliation follow. Recovery is slow but septic infection may occur with fatal result from broncho-pneumonia and toxæmia. (3) *Neuritis.* Peripheral neuritis and optic neuritis are rare complications. The tolerance of infants and children for arsenobenzol preparations is excellent; toxic effects are rarely seen.

Prevention. At present all commercial samples of arsenobenzol and its derivatives are tested by the Medical Research Council so as to exclude impurities and to estimate toxicity. Patients must be carefully examined before treatment for signs of liver or kidney disease and must be watched during treatment for any signs of intolerance. In doubtful cases the hepatic efficiency may be determined (*see* p. 383), the levulose and van den Bergh tests being specially valuable. Urobilinogen in the urine is an early sign of hepatic insufficiency.

Treatment. Any sign of mild intolerance should warrant caution during further treatment. The doses must be reduced and the intervals between the injections lengthened. Sodium thiosulphate, 15 grains, t.d.s., is given for the milder toxic effects, and 0·6 to 0·9 grams intravenously daily for the more severe cases. Injections of calcium gluconate or calcium thiosulphate are of value in toxic hepatitis. No further arsenobenzol therapy should be given after a severe toxic reaction.

REFERENCES

1	H. H. Dale and C. H. Kellaway	1923	*Phil. Trans. Roy. Soc.*, B. 211, p. 273.
2	Wanklyn	1924	*Brit. Med. Journ.*, **ii.**, p. 309.
3	Widal, Abrami and Brissand ..	1920	*Presse Méd.*, **28**, p. 181.
4	E. Dubois (Basal Metabolism in Health and Disease)	1924	Lea & Febiger, New York.
5	G. Graham and E. P. Poulton ..	1912	*Quart. Journ. Med.*, **6**, p. 82.
6	Discussion on Scarlet Fever ..	1926	*Brit. Med. Journ.*, **ii.**, p. 513.
7	J. A. Glover and F. Griffith ..	1930	*Lancet*, **ii.**, p. 815.
8	S. P. Bedson	1929	*Lancet*, **ii.**, p. 920.
9	A. D. Gardner and P. H. Leslie	1932	*Lancet*, **i.**, p. 9.
10	G. Evans and W. A. Robb ..	1930	*Brit. Med. Journ.*, **i.**, p. 1039.
11	H. S. Banks and J. C. H. Makenzie	1929	*Lancet*, **i.**, p. 381.
12	P. Stocks	1931	*Brit. Med. Journ.*, **i.**, p. 157.
13	C. J. MacSweeney	1931	*Quart. J. Med.*, **24**, p. 487.
14	D. McClean	1927	*Lancet*, **i.**, p. 483.
15	C. C. Okell	1932	*Lancet*, **i.**, pp. 761, 816, 867.
16	J. A. Ryle	1930	*Guy's Hosp. Reps.*, **80**, p. 137.
17	P. N. Panton and Others ..	1931	*Lancet*, **ii.**, p. 1180.
18	S. W. Patterson and Williams..	1922	*Lancet*, **ii.**, p. 806.
19	J. Torrens	1934	*Brit. Med. Journ.*, **i.**, p. 274.
20	M. Gordon	1922	*Brit. Med. Journ.*, **ii.**, p. 299.
21	Bunting (Review on Influenza)..	1922	*Med. Sci.*, **6**, p. 366.
22	C. F. Brockington	1931	*Lancet*, **i.**, p. 1387.
23	R. A. O'Brien	1929	*Lancet*, **ii.**, p. 241.
24	R. R. Armstrong and R. S. Johnson	1932	*Brit. Med. Journ.*, **ii.**, p. 662.
25	T. E. Dickinson	1922	*Lancet*, **i.**, p. 312.
26	H. L. Tidy and E. C. Daniel ..	1923	*Lancet*, **i.**, p. 9.
27	S. P. Bedson and G. T. Western	1930	*Brit. Med. Journ.*, **i.**, p. 882.
28	K. Lewkowicz	1924	*Lancet*, **ii.**, p. 487.

29	J. A. GLOVER	1931	*Lancet*, **i.**, p. 497.
30	H. S. BANKS	1931	*Lancet*, **i.**, p. 747.
31	F. M. R. WALSHE	1933	*Brit. Med. Journ.*, **ii.**, p. 1197.
32	B. B. YODH..	1932	*Brit. Med. Journ.*, **ii.**, p. 589.
33	L. W. HARRISON	1922	*Brit. Med. Journ.*, **ii.**, p. 1.
34	L. COBBETT (Review)	1922	*Lancet*, **i.**, p. 979.
35	A. S. GRIFFITH and W. T. MUNRO	1933	*Brit. Med. Journ.*, **i.**, p. 399.
36	T. [illegible]UMSDEN	1930	*Lancet*, **ii.**, p. 136.
37	W. [illegible]. F. COLLIS and C. F. BROCKINGTON	1933	*Lancet*, **i.**, p. 127.
38	R. [illegible]ATES	1933	*Lancet*, **i.**, p. 571.
39	L. [illegible] CANN and G. F. HOLLIS ..	1931	*Lancet*, **i.**, p. 130.
40	E. [illegible]UIR	1924	*Lancet*, **i.**, p. 277.
41	F. [illegible] KLEINE	1924	*Lancet*, **i.**, p. 384.
42	C. M. WENYON	1928	*Brit. Med. Journ.*, **ii.**, p. 558.
43	Sir LEONARD ROGERS	1922	*Lancet*, **i.**, pp. 463, 569, 677.
44	P. MANSON-BAHR, G. C. LOW, J. J. PRATT and A. L. GREGG ..	1923	*Lancet*, **i.**, p. 941.
45	Sir P. W. BASSETT-SMITH	1922	*Brit. Med. Journ.*, **ii.**, p. 902.
46	H. C. BROWN and L. I. DAVIS ..	1927	*Brit. Journ. Exper. Path.*, 1927, **8**, p. 397.
47	R. SASERAC and Others	1927	*Bull. Acad. Med.*, **97**, p. 774.
48	J. E. MCCARTNEY	1927	*Lancet*, **i.**, p. 93.
49	W. GLEN LISTON	1924	*Brit. Med. Journ.*, **i.**, pp. 950, 997.
50	J. C. G. LEDINGHAM and F. R. FRASER	1924	*Quart. Journ. Med.*, **17**, p. 365.
51	R. A. ANDERSON, O. T. SCHULTZ and T. F. STEIN	1923	*Journ. Infec. Dis.*, **32**, p. 444.
52	R. P. GARROW	1925	*Lancet*, **i.**, p. 225.
53	J. A. RYLE	1921	*Guy's Hosp. Gaz.*, **35**, p. 422.
54	T. H. G. SHORE	1927	*Lancet*, **i.**, p. 252.
55	S. A. KINNIER WILSON	1928	*Lancet*, **i.**, p. 11.
56	E. L. OPIE	1927	*Brit. Med. Journ.*, **ii.**, p. 1130.
57	DEEKS	1924	Proc. Internat. Conf. on Health Problems in Trop. America.
58	S. G. BRENTNALL	1930	*Lancet*, **i.**, p. 1174.
59	H. P. JACOBSON	1932	Fungous Diseases, London.
60	A. M. HOBER	1914	*Arch. Int. Med.* **13**, p. 704.
61	M. MACAIGNE and P. NICAUD ..	1926	*Presse. Méd.* **26**, p. 403.

DISEASES OF THE ORGANS OF RESPIRATION

EXAMINATION OF THE CHEST

Inspection. By looking at the chest in front, behind, and from above, abnormalities such as various skin eruptions, scars from old empyema operations or gunshot wounds, and enlarged veins may be noticed, and any alteration in its shape and movements can be detected. As regards enlargement of the veins, it is important to distinguish between those that are distended, which may suggest obstruction to the venæ cavæ internally, and those that happen to be more superficial than usual and are of no pathological significance. The chief points to be noticed in a healthy adult chest are as follows: It has a somewhat flat oval form—that is, the antero-posterior diameter is much less than the transverse; its greater breadth is at the lower part; the clavicles are only slightly prominent with but little depression above, and scarcely any below them; the position of the nipple is on the fourth rib, or on its upper or lower border; the angle (*epigastric angle*), which has its apex at the ensiform cartilage, and is bounded on each side by the seventh and eighth costal cartilages, is from 95 to 105 degrees; the scapula is closely adapted to the posterior part of the thorax; and the spine is straight. In inspiration the chest should expand from 2 to 3 inches in circumference, the two sides should move symmetrically, the epigastric angle should be widened, the sternum thrown forwards, and the lower ribs lifted; and there should be only very slight recession of the lowest intercostal spaces on deep breathing.

By inspection abnormalities in the shape of the chest are noted, and these may be due to the following causes: (*a*) Disease of the *lungs*. In emphysema the chest is more capacious and the epigastric angle wider than normal. In fibrosis of the lung, as in phthisis, the chest is asymmetrical, owing to local contraction, usually at one or other apex. (*b*) Disease of the *bones*, such as deformities due to rickets and angular and lateral curvatures of the spine. The chest may become asymmetrical, or still show bilateral symmetry although abnormal in shape. Bronchitis and broncho-pneumonia have usually played a part in producing the deformities due to rickets. (*c*) Hypertrophy of the *heart* in young subjects may lead to a local bulging of the chest wall on the left side.

The circumference of the chest is obtained by a tape measure, the transverse and antero-posterior diameters by *callipers*. The actual shape can be obtained by a *cyrtometer*, consisting of two long pieces of soft metal, joined loosely together by one end of each.

By inspection also, apart from changes in the shape and symmetry of the thorax, we may note the character of the respiratory movements. The normal frequency of respiration in adults is from about fifteen to eighteen in the minute; in children it is much more rapid; it may be thirty or more and varies with the age. In different forms of disease, both pulmonary and of other origin, the movements may be slower or more rapid, shallower or deeper, feebler or stronger than is normal, and they may be irregular. *Dyspnœa* is a clinical term used to indicate "shortness of breath"; it is the patient's own realisation that increased respiratory effort is necessary; there may be (*a*) increase in the respiratory rate (*polypnœa*); (*b*) increase in the respiratory volume (*hyperpnœa*); (*c*) obstruction to

sternum, the first costal cartilages at their junction with the sternum, and a diamond-shaped space at the back in the middle line, including the seventh cervical and first dorsal spines. Elsewhere the vesicular murmur is always present as long as the lung is healthy and the air passages are pervious. In children the vesicular murmur is louder and harsher than in adults (puerile breathing). In adults the vesicular murmur over a healthy lung may be harsh and exaggerated when the other one is put out of action (*compensatory breathing*). The breath sounds may be weak in shallow breathing, in emphysema, and when the chest wall is thick. *Interrupted* or *cog-wheel breathing* is where the inspiratory murmur is jerky or wavy, from irregular expansion of the lung, of which the cause may be mechanical obstruction to the entry of air or irregular muscular action from nervousness. It is not of much diagnostic significance.

Diminished vesicular murmur, deficient entry of air, or absence of breath-sounds, occurs if the air vesicles are obliterated or if the bronchus communicating with them is obstructed or obliterated, or if the air vesicles are displaced from the surface of the chest as is commonly the case in pleural effusion. In the latter case the absence of breath sounds depends on the principle that when sound travelling in one medium, such as air, reaches the boundary surface of another medium, such as a pleural effusion, it is badly transmitted across it, most of it being reflected back again. This is a sign of great diagnostic importance when the breath sounds are normal at the corresponding point of the opposite lung.

Bronchial breathing is a double sound produced in the glottis during respiration, modified by resonance in the mouth, pharynx and bronchial tubes. It can be heard by listening over the trachea. The inspiratory and expiratory sounds are of equal lengths; they are distinctly separate from one another, and are harsh in quality. They may be imitated by placing the mouth and tongue in the position to pronounce the German "ch," and then blowing in and out. As heard over the lung bronchial breathing may be high-pitched (*tubular*), medium-pitched or low-pitched (*cavernous*). The loudness of the sounds is unimportant. Tubular breathing which is heard particularly over hepatised lung has a special blowing or "whiffing" quality. Cavernous breathing has a hollow quality. It is often heard over cavities in the lung, but it does not always indicate that there is a cavity. Bronchial breathing when heard over the chest means that the lung tissue has been modified, mostly by a conversion of the spongy tissue into solid tissue, either by filling up or destruction of the air cells (pneumonia, phthisis), or sometimes by compression from without (pleuritic effusion), if the air passages are not entirely obliterated. The necessary condition is patency of the bronchial tubes with consolidation of the surrounding lung, so that the glottic sound is conducted to the surface, instead of becoming diffused, while the alveolar part of the ordinary respiratory murmur is absent.

Amphoric breathing. This is a double sound heard during inspiration and expiration, more musical than bronchial breathing. It may have a peculiar metallic or ringing character. It may be imitated by blowing softly into the mouth of a narrow-necked glass jar or vase. It is heard over large cavities or a pneumothorax in open communication with a bronchus, and is due to the resonance of the cavity. The pitch and loudness of amphoric breathing are variable.

Stridor is a loud sound rather similar to tubular breathing, but it has a characteristic whistling or hissing quality. It is produced by constriction of the glottis, trachea, or one main bronchus. It is audible over the greater part of the chest, and can sometimes be heard by those near the patient without the aid of the stethoscope.

Adventitious Sounds are heard in addition to, and at the same time as, the ordinary breath sounds or the breath sounds modified as above. If they are not heard with tranquil breathing, the patient should inspire deeply, when they

may become audible. The adventitious sounds are *rhonchi*, *râles*, and *friction sounds*.

Rhonchi are more or less musical sounds, due to obstruction of the bronchial tubes by accumulation of mucus, swelling of the mucous membrane, or spasmodic contraction of their muscular fibres. The sounds vary very much according to the size of the bronchial tube and the extent of the narrowing, and are likened to various familiar sounds, such as cooing, groaning, snoring, grunting, or whistling. The lower-pitched, snoring sounds are called *sonorous* rhonchi, and are produced in the larger tubes ; the higher-pitched, whistling sounds are called *sibilant* rhonchi, and are produced in the smaller tubes. They may be heard with expiration or inspiration, and are constantly changing in position and loudness. Loud sonorous rhonchi are often audible to those standing near the patient, and constitute " wheezing."

Râles are various forms of crackling or rattling sounds, which are produced in the large, medium-sized and smaller bronchial tubes, or in pulmonary cavities by the air forcing its way into fluid secretions accumulated there, and thus causing bubbles to form and burst with a slight noise. They are sometimes distinguished as *moist* sounds from rhonchi or *dry* sounds ; but this is undesirable, as rhonchi may themselves be due to the presence of mucus. The râles differ according to the size of the bubbles, and are called *fine*, *medium*, and *coarse*. Râles are also divided into *bubbling* and *crackling ;* the latter have a sharp, clear, ringing, explosive character, which is probably due to their occurrence in the midst of consolidated lung, and to consequent special conditions of resonance ; the former, or bubbling râles, are dull, not ringing or explosive, and occur mostly in tubes surrounded by normal spongy tissue. Crackling râles are sometimes called *consonating* from their supposed acoustic origin, and bubbling râles *non-consonating* in contrast. A *gurgling* râle is a coarse râle which is produced in the largest tubes.

Crepitation is a term which has been used indiscriminately for all râles, but is now generally confined to a very fine râle, so fine as to be suggestive of an origin in dry materials (rubbing of hair close to the ear, or rustling of silk). It is heard in the early stage of pneumonia, in œdema of the lung, and in lung that is forcibly expanded after prolonged collapse. It is probably due to the opening up of respiratory bronchioles, atria and air-sacs, which have been adherent by sticky fluid or from simple disuse. Crepitations and the finer râles are heard only during inspiration ; medium-sized and coarser râles may be heard during expiration also. In phthisis râles may be revealed during the deep inspiration that follows a cough.

Metallic tinkling is applied to sounds of a tinkling or ringing character, sometimes heard when a patient with a large cavity breathes, or speaks, or coughs. It is usually a musical râle.

Post-tussive suction is a sucking sound heard over a cavity (tuberculous or bronchiectatic) following a cough ; it is due to the air being suddenly sucked back into the cavity with a hissing sound at the beginning of the succeeding deep inspiration.

In cases of hydro-pneumothorax or pyo-pneumothorax, if the patient be shaken while the physician's ear is applied to the chest, a *splashing* sound will be heard which proceeds from the air and liquid in the pleural cavity (*Hippocratic succussion*).

Friction sound, or *pleuritic rub*, is produced by the rubbing together of two pleural surfaces roughened by inflammation. In its most characteristic form it is a rough, grating, or creaking sound, like that which may be heard on forcibly dragging two pieces of leather over one another, or on rubbing the palmar surface of a finger over a wooden surface. It is best heard during inspiration, but may be heard with expiration also. Some friction sounds resemble râles very closely ; but they are localised to a small part of the chest, and are not influenced by

coughing. Their loudness varies, when the pressure of the stethoscope against the chest wall is altered. When they arise in the pleura overlying the heart, they correspond with the heart beats, but their loudness varies with the phases of respiration (*pleuro-pericardial friction*).

Voice Sounds. The voice sounds heard with a stethoscope over the normal chest have a "blurred" or indistinct quality owing to irregular conduction through the alveolar tissue. It is to this quality of indistinctness that the term *vocal resonance* is applied. *Diminished or absent vocal resonance.*—In children and females with voices of high pitch, the vocal resonance may be slight or absent. In disease its absence is produced by obstruction of the bronchus, or compression of the lung by fluid. *Bronchophony.*—This term is used when the voice sounds are distinct in quality and, at the same time, louder than usual. When the sounds are distinct but faint the term *distant bronchophony* may be used. Bronchophony is obtained in consolidation of the lung, such as occurs in pneumonia and phthisis, and sometimes when there is great compression of the lung. When bronchophony is present whispered sounds will also be conducted through the lung (*pectoriloquy*). *Ægophony* is a peculiar *nasal* or *twanging* modification of the voice when heard through the chest. It derives its name from its resemblance to the bleating of a goat. Its most common cause is undoubtedly the presence in the pleura of a liquid. Sometimes it may occur in pneumonic consolidation. The explanation of ægophony, most generally accepted, is that the spoken voice is not a pure tone, but a mixture of a fundamental notes and its harmonics of higher pitch. It is well known that low notes are not so well transmitted as high notes from air to liquid, and so it is considered likely that the fundamental note fails to get through the liquid and the harmonics are chiefly heard on the surface of the chest. It is best brought out by asking the patient to utter words containing the vowels "e" and "i," such as "three," or "ninety nine," which depend on the presence of the higher harmonics.

Auscultatory Percussion. In this process a stethoscope is placed on the chest, and the surface is percussed around it; its chief value is to elicit the *bell sound* or *bruit d'airain* in cases of pneumothorax. While the physician listens with the stethoscope to one part of the chest, presumed to be the subject of pneumothorax, an assistant lays one coin on the chest and strikes it with another. The noise is resonated in the hollow cavity, and transmitted as a loud ringing musical note through the stethoscope (*see* also p. 191).

TRACHEITIS AND SPECIFIC INFECTIONS

Inflammation of the trachea arises from circumstances similar to those producing laryngitis. Acute catarrhal tracheitis frequently accompanies laryngitis and bronchitis, but is masked by the symptoms which they produce. Occasionally it exists alone. It then produces cough, often hacking, perhaps violent or paroxysmal, with some amount of expectoration. At the beginning of influenza the tracheitis may be accompanied by substernal pain of unknown origin. With the laryngoscope the mucous membrane may be seen to be congested, and ulcers are sometimes observed. With the stethoscope mucous râles may be heard in the trachea, but the swelling of the mucous membrane and the mucous accumulation are not generally sufficient to cause much dyspnœa. The patient requires treatment similar to that used in bronchitis—warm temperature and avoidance of exposure; troublesome cough may be relieved by insufflations of morphia ($\frac{1}{16}$ to $\frac{1}{8}$ grain); and expectorants, such as squill and ipecacuanha, steam or benzoin inhalations, and the application of mustard to the upper part of the sternum, are of service.

The trachea is attacked by *diphtheria*, spreading from the larynx. Croup, which is no other than laryngeal diphtheria, was at one time supposed to be mainly a tracheitis.

Tubercle of the trachea occurs occasionally in association with tubercle of the larynx; ulceration follows the deposit of tubercle in the mucous membrane or submucous tissue. The ulcers are more common on the posterior wall, and usually measure from 2 to 4 mm., but may reach 10 mm. in diameter. The symptoms due to tracheal tubercle are generally masked by those to which simultaneous disease of the larynx or lung gives rise.

Syphilis, in its secondary and tertiary stages, also affects the trachea, producing in different cases congestion, condylomas (rarely), and superficial ulcers. The most important change, however, is stricture. The trachea is affected most often at its lower end, less commonly at its upper end; and the stricture may consist simply of a narrowing at one spot, or a considerable length of the trachea may be reduced in calibre. The mucous membrane is raised into bands and ridges, which have been regarded as cicatrices of former ulcers, possibly preceded by gummas; but German pathologists look upon the thickening as a direct result of the syphilis, and the ulceration as secondary. In later stages the cartilaginous rings have been exposed, necrosed, and expectorated or absorbed. The stricture can be sometimes seen below the glottis by means of the laryngoscope. For the symptoms, diagnosis, and treatment of stricture, *see* below under Tracheal Obstruction.

NEW GROWTHS IN THE TRACHEA

The trachea is remarkably little subject to primary new growths, whether benign or malignant. When present they give rise to dyspnœa, and may be recognised by the use of the laryngoscope or bronchoscope. More frequently carcinoma of the œsophagus or of the mediastinum grows into the adjacent trachea, narrowing its channel and producing symptoms of stricture. When it spreads from the œsophagus, it is preceded by dysphagia; but tracheal symptoms may be the first indication of carcinoma of the mediastinum. Another way in which tumours affect the trachea is by compressing it from outside.

As the chief symptoms in all these cases depend on the reduction of the calibre of the trachea, and as this may be due to other causes besides such tumours, it will be well to consider separately the pathology and clinical features of tracheal obstruction.

TRACHEAL OBSTRUCTION

The causes may be grouped under three heads: (1) compression from without; (2) changes in the walls of the trachea itself (stricture); (3) foreign bodies within it.

Compression of the Trachea. The most common causes are mediastinal new growths, aneurysm of the aorta or large vessels, enlargement of the thyroid body, and malignant tumours in the neck. Carcinoma of the œsophagus may also compress the trachea, but soon invades it, so that perforation takes place between the two tubes. Occasionally in children caseation and suppuration of the bronchial glands may lead to their enlargement, by which the trachea is compressed; and if the abscess bursts into the trachea, pus or portions of caseous glands may be expectorated. A mediastinal abscess arising in any other way (caries of the spine, localised empyema), the dilated left auricle in cases of mitral stenosis, and in children an enlarged thymus, are occasional causes of tracheal compression.

Stricture. The chief cause is syphilis, which has been already considered.

Foreign bodies are rarely retained in the trachea, but commonly fall into one or other bronchus, though they may be driven up and down the trachea by the respiratory currents.

Symptoms. The most important are dyspnœa and stridulous breathing; they are often accompanied by cough and the expectoration of thin frothy mucus. The voice is unaffected, or it is feeble because the obstruction weakens the current of expired air. The chest is resonant, but vesicular murmur is faint, or drowned

by the noise of the stridor. Other symptoms accompanying tracheal stenosis are due to the lesion which causes it, and these may be at first entirely absent in a case of aortic aneurysm or deeply seated mediastinal tumour.

When the tracheal stricture or compression has reached a certain limit, the patient becomes liable to sudden attacks of aggravated dyspnœa with cyanosis. From a few of these paroxysms he may recover, but in the third or fourth or a later one he will probably die.

Diagnosis. This has to be made (1) between obstruction in the trachea and obstruction in the larynx; (2) between the different causes of tracheal obstruction.

The laryngoscope will show at once the absence of laryngeal disease; the presence of tracheal stricture, or of tumour or aneurysm compressing the trachea, may also be demonstrated by the laryngoscope, or, failing that, by the bronchoscope. This point should be determined, if possible, before the occurrence of the paroxysms above mentioned, in which the use of these instruments may be difficult, and which, moreover, may wrongly suggest laryngeal spasm and lead to a hasty and useless tracheotomy. There are some differences in the effects of laryngeal and tracheal obstruction. One is the fact, noticed by Gerhardt, that in laryngeal obstruction the larynx is moved extensively up and down in the neck during respiratory movements, whereas in tracheal obstruction it moves but slightly. In laryngeal obstruction the head is thrown back; in tracheal obstruction it is often bent forward. If the laryngeal obstruction is due to abductor paralysis, the stridor is chiefly inspiratory, whereas in tracheal obstruction there is generally some stridor with expiration. But in other cases of laryngeal obstruction the stridor occurs with both respiratory acts. Auscultation of the trachea is certainly deceptive, as the loudest stridor is heard over the larynx even when the stenosis is in the trachea. The point is of practical importance, because laryngeal obstruction may be relieved by tracheotomy, but tracheal obstruction rarely so; and it is desirable to spare the patient an operation of this nature when it can do no possible good. But a new growth or aneurysm in the neck or upper part of the chest may produce the two obstructions, namely, one directly, by pressure on the trachea, the other indirectly, by pressure on the recurrent laryngeal nerves so as to cause abductor paralysis.

Apart from the assistance rendered by the laryngoscope or the bronchoscope, the recognition of the cause of tracheal obstruction must depend upon collateral symptoms. Any source of compression would probably involve other organs and thus cause dysphagia, obstruction of the veins of the head, neck, or arm, pressure on corresponding nerves, and dulness under the sternum, or at the upper part of the chest on one side. On the other hand, stricture due, as already stated, to syphilis must be free from such symptoms; but an aneurysm of the aorta may compress the trachea without at first any other symptom by which it can be recognised. For the diagnosis of intra-thoracic growth from aneurysm the reader is referred to Intra-thoracic Neoplasms (*see* p. 181). The Röntgen rays may in either case render some assistance.

Prognosis. This is very unfavourable, the commoner causes being little amenable to treatment; but the rare cases of abscess compressing the trachea may recover on the bursting of the abscess.

Treatment. The indications are (1) to remove the cause, if possible; (2) to open the trachea below the obstruction where this is in the upper part; and (3) to relieve symptoms and secondary results. A diseased thyroid or hypertrophied thymus may be removed, and enlarged glands or growths in the neck; and abscesses, where accessible, may possibly be opened; but such opportunities are infrequent. If an aneurysm is diagnosed, the treatment for that condition should be employed, and for obvious stricture active antisyphilitic treatment by means of mercury and potassium iodide or salvarsan, especially if a positive Wassermann reaction is obtained. The iodide may be employed in any case

which does not present sufficient data for a positive diagnosis as to the cause of the obstruction. In the case of a foreign body, tracheotomy should be performed, and then efforts to dislodge it should be made by inversion of the patient or shaking, or by the use of special forceps through a bronchoscope.

BRONCHITIS

Ætiology. Bronchitis may occur as a primary infection, and it is then probably one form of the " common cold " described on p. 195, and the bacteriology and mode of infection are the same. This type of bronchitis is often associated with, or followed by, inflammation of the larynx and nasal mucous membrane, or the inflammation may commence in the latter, and spread downwards to the bronchi. In fact the section on coryza should be read in connection with bronchitis. Another cause is contact of the bronchial mucous membrane with irritating vapours, or air carrying solid particles, such as dust, fog, or cold, damp and changeable climates, or the air of mines and of certain manufactories. Bronchitis may also be set up by the presence of foreign bodies actually in the bronchial tubes ; this is comparatively rare, but blood effused into the tubes may act in this way, and it constantly occurs as a result of the deposit of tubercle or carcinoma in the substance of the lung. Bronchitis may be due to infection by any of the catarrhal organisms which are present in the sputum, such as the pneumococcus, Friedlander's pneumo-bacillus, streptococci, *M. catarrhalis*, staphylococci, *M. tetragenus*, and occasionally *Bacillus coli communis*. Bronchitis may also be secondary to focal infection of any kind, and especially to sinus disease. Certain infectious diseases are frequently accompanied by bronchitis—namely, typhoid fever, measles, diphtheria, influenza and whooping-cough ; and it often occurs in Bright's disease. The relation of bronchitis to asthma is described later.

Bronchitis is especially prevalent amongst infants, young children, and elderly people, whereas young adults and the middle-aged are much less subject to it. Habits of luxury, confinement to warm rooms, and undue wrapping up, render the subject liable to contract bronchitis on comparatively slight exposure ; and those in weakly health, or depressed from insufficient food, exhausting occupations, or bad sanitary conditions, easily acquire it. Heart disease, impeding the circulation in the lungs, is a predisposing cause. Bronchitis is much more common in winter than in summer. Chronic bronchitis may follow a single attack or repeated attacks of acute bronchitis ; and acute bronchitis may supervene on chronic bronchitis.

Pathology. The mucous membrane is the part most affected, but in severe or prolonged cases the submucosa is involved, and rarely the cartilages of the bronchial tubes, and adjacent parts of the lungs. The first effect is increased vascularity and swelling of the mucous membrane, and after a short time a free secretion from the surface takes place. It is a clear fluid containing mucus ; but in it there are also leucocytes and shed epithelial cells. In later stages the secretion becomes more opaque and yellow from the presence of increasing numbers of leucocytes. The secretion may also contain cells in a state of fatty degeneration, or cells containing particles of soot or dirt derived from the inspired air.

In fatal cases the tubes are often seen to be filled with greenish pus (*purulent bronchitis*). Sometimes the smallest tubes are affected. If the superficial part of the lung be sliced off, and the exposed section be squeezed, minute drops of pus will be found to ooze freely from the cut surface. The condition is one of *capillary bronchitis*, or *bronchiolitis*. Fraenkel describes a *bronchiolitis fibrosa obliterans* occurring in workmen exposed to irritating air or dust ; the bronchioles are obstructed by acute or subacute growth of connective tissue.

If, in ordinary catarrhal cases, the inflammatory process persists long enough,

the fibrous coats of the bronchi become thickened, and infiltrated with leucocytes; the muscular fibres are atrophied by pressure; and the cartilages and mucous glands disappear from the same cause. Ultimately, in many cases, the bronchial tubes become dilated, and form fusiform or cylindrical wide channels, often reaching the surface of the lung (*bronchiectasis*).

As a result of bronchitis the lung itself undergoes important structural changes. Acute capillary bronchitis may lead to *lobular collapse* and *broncho-pneumonia*; chronic bronchitis is followed by *vesicular emphysema*, and sometimes by *chronic interstitial pneumonia*. The last three will be spoken of separately.

Lobular collapse occurs in isolated lobules when the bronchial tubes leading to them are blocked with mucus, since when a tube is plugged the retained air, being stagnant in contact with the pulmonary capillaries, undergoes absorption, just as air is absorbed which has escaped into the subcutaneous cellular tissue.

There is experimental evidence (7), obtained by examination of the arterial blood, that the dyspnœa present in severe cases of bronchitis is due to a retention of CO_2 and deficiency of oxygen, probably brought about by bronchial spasm.

Physical Signs. On *inspection* the breathing is seen to be quickened, the chest is symmetrical, and generally in a state of moderate over-distension. The accessory muscles of respiration are seen to be in strong action, and expiration is prolonged. There may be sucking in of the intercostal spaces during inspiration. *Percussion*, as a rule, yields a normally resonant note, but there is occasionally slight hyper-resonance from temporary over-distension of the air vesicles; there may be impairment of resonance at the bases from accumulated secretion or from collapse. *Auscultation* shows that both inspiration and expiration are accompanied by *sibilant* or *sonorous rhonchi*, depending on the size of the tubes affected, or various kinds of *râles*, or both combined. The coarser rhonchi are often felt by the hand placed upon the chest, and may be even heard by the patient himself, or those standing near him. The larger or coarser râles are heard with both expiration and inspiration, the finest râles only with inspiration. These sounds are not equally present in all cases or in all stages of the disease. In many cases rhonchi alone are present. In severe cases the sounds are heard, variously mixed, over the whole chest, and may entirely drown the vesicular murmur. With spasm of the bronchial muscle there is marked prolongation of expiration.

Symptoms of Acute Bronchitis. At the beginning there is malaise, and a sensation of tightness of the chest; and cough occurs with little sputum. In mild cases the general disturbance may be but slight, and the illness is confined to cough. In severe cases there is slight fever, the temperature rising to 100° or 101°, the appetite failing, the tongue furred, the bowels inactive, and the urine scanty. The cough is at first hard and dry, and is often attended with pain behind the sternum and in the muscles of forced expiration from the strain put upon them. The expectoration is then but scanty, consisting of thin, frothy mucus, with possibly an occasional streak of blood. After a few days the cough becomes easier and looser, and the expectoration is more abundant, more opaque, and yellow and green, from the addition of increasing quantities of leucocytes. In slighter cases the expectoration is generally more in the morning, from the accumulation during sleep, and in towns this sputum is frequently black with pigment derived from the atmosphere. Dyspnœa is often considerable, and the patient has to sit upright in bed (orthopnœa), and all the respiratory muscles are called into play. After a time the secretion of muco-pus becomes less, the cough is less frequent, and the symptoms gradually subside. When the smallest bronchial tubes are filled with purulent secretion in the form above described as a capillary bronchitis, the position is one of extreme danger, especially in quite young children. There is severe dyspnœa, great cyanosis or lividity of the face and extremities, and rapid exhaustion. The cough is at first frequent, with abundant expectora-

tion of viscid glairy mucus, or muco-pus, or pus. In later stages the patient becomes livid and drowsy; the pulse is feebler and quicker; inspiratory efforts are less effectual; and the intercostal spaces are more sucked in. Expectoration gradually diminishes; and before death the disturbance of the cerebral circulation is shown in coma, often with a slight amount of delirium.

Symptoms of Chronic Bronchitis. The main features are not essentially different from those of the acute form; but there is an absence of fever and the constitutional disturbance which occur in acute attacks, and after long continuance secondary results of a permanent kind are produced. In the lung itself, emphysema and dilatation of the tubes (*bronchiectasis*) take place, and these will be described later. But the effects are felt beyond the lung; the emphysema (*q.v.*) impedes the pulmonary circulation, and the right heart becomes hypertrophied; it may eventually dilate, and thereupon the general venous system suffers, so that œdema of the lower extremities, congestion of the liver, ascites, and albuminuria occur. Under such circumstances tricuspid regurgitation often takes place, with its characteristic murmur (*see* Diseases of the Heart). Long-continued and severe chronic bronchitis has a serious effect upon the strength of the patient. In consequence of disturbed sleep, abundant expectoration, and impaired digestion, nutrition fails, and there may be considerable emaciation. In some cases also, in this late stage, febrile reaction of a hectic type may set in. The varieties of chronic bronchitis commonly described are the following:

1. By far the larger number of cases come under the head of ordinary *winter cough*, occurring as above mentioned. The cough is variable, sometimes coming on in paroxysms, generally worse at night; and in the morning also there is often severe coughing to expel the secretions which have accumulated during the period of rest. According to the severity or extent of the affection, the expectoration may be slight in amount, thin, mucous, and frothy, and containing black pigment in the morning; or it may be yellow or yellowish green and muco-purulent, with very little air; or it may be entirely airless, liquid, green pus. The sputa in this case generally run together in the vessel, and do not exhibit the *nummular* character common in phthisis. Microscopically, besides the abundant pus cells, there are epithelial cells containing fat, and non-pathogenic micro-organisms. Blood is occasionally present in the expectoration, usually in the form of streaks, but rarely in masses, or in any considerable quantity.

2. *Dry bronchitis*, or *dry catarrh*, is a form of chronic bronchitis in which there is very little secretion. The cough is frequent, violent, and prolonged, so that extreme congestion of the face occurs; but there is either no sputum at all, or only a small quantity of tough mucus. There is much soreness of the chest and considerable dyspnœa from spasm of the smaller tubes.

3. In the rare condition called *bronchorrhœa* or *pituitous catarrh*, the mucous glands bear the chief brunt of the infection. The cough is troublesome and paroxysmal in the endeavour to bring up either a thin or a thick and ropy sputum, which looks like unboiled white of egg streaked with yellowish white plugs from the smaller bronchi, the whole being covered with froth. In a case recently described (8) a pint was expectorated in twenty-four hours, and it was brought up with difficulty in small amounts at a time, each bout of cough ending with the expulsion of one or more of the mucous plugs. But where the total volume measures four or five pints large quantities may be brought up at a time with comparatively trifling effort. The condition may be distinguished from œdema of the lung by the yellow or amber colour and high albuminous content of the fluid in the latter case after removing the froth from the top.

4. *Putrid* or *fœtid bronchitis* is characterised by very offensive sputum, which mostly occurs in cases where the tubes are dilated. The sputum is abundant and rather thin, and in the sputum vessel it often separates into three layers, of which the uppermost is frothy with mucus, the middle a thin sero-mucous fluid, and the lowest a thick layer of pus containing the bodies known as Dittrich's or

Traube's plugs. These are whitish grey or dirty greyish yellow, varying in size from a millet seed to a bean. Under the microscope they are seen to consist of pus corpuscles, detritus, bacteria, bundles of fine acicular crystals of palmitic and stearic acids, and twisted threads of leptothrix. The chemical contents of the sputum are acetic, butyric, and valerianic acids, leucin, tyrosin, sulphuretted hydrogen, and methylamine. The condition is to be distinguished from gangrene of the lung. Very offensive sputum may also proceed from an empyema opening into the lung, and occasionally from an old tuberculous cavity.

5. *Plastic, fibrinous* or *croupous bronchitis.* This rare affection is characterised by the expectoration of casts of the bronchial tubes. The sputum is generally in the form of a rounded mass, covered with mucus or blood, and, when frayed out in water, one sees a more or less perfect branching cast of a portion of the bronchial tube system. The cast is not generally thicker than a goose quill, and varies from 1½ to 2½ inches in length, and only rarely reaches 4 or 5, or even 7 inches. It has a grey or whitish yellow colour, and consists of concentric laminæ, which do not usually fill up the lumen of the tube, so that the casts are not solid, except those from the smallest tubes. Under the microscope the cast has a fibrillated structure, with numerous embedded leucocytes, streptococci and staphylococci, hæmatoidin crystals, Curschmann's spirals and Charcot-Leyden crystals (*see* p. 141). The patient is seized with violent attacks of coughing, often suffocative in character, with more or less pain or oppression at the chest, and attended at first with no sputum, unless perhaps a little mucus. After a time—it may be a few hours, or as long as two or three days—a bronchial cast is brought up. Relief is generally at once afforded : the cough subsides or disappears. But it commonly recurs in a few hours, and casts may continue to be expectorated, at intervals of a day or so, for several days, when the patient gradually gets quite well. Hæmoptysis occurs in some cases, usually after the expulsion of the cast. The physical signs are those of obstruction of a bronchus, with râles as the casts are becoming loosened. Plastic bronchitis is rarely fatal, except from complications ; but it recurs at irregular intervals over a period of several years.

6. Chronic bronchitis associated with *polycythæmia rubra* (Ayerza's Disease) is the result of long-continued oxygen deficiency, and this leads to increase in the hæmoglobin of the blood, the number of red cells may approximate to 10,000,000 per cubic millimetre, and there may be clubbing of the fingers. The patient is very cyanosed, and in one case the arterial blood was found to be only 79 per cent. saturated with oxygen, instead of the normal 95 per cent. However, the actual amount of oxygen carried by the blood was about normal, owing to the great increase in the hæmoglobin and red cells. The arterial CO_2 pressure was also increased, and the patient was very breathless (7). Males are more commonly affected than females, and the Wassermann reaction is often positive. There is great hypertrophy and dilatation of the right ventricle, and this is indicated by the electrocardiogram ; there is dilatation and atheroma of the pulmonary artery with engorgement of the lungs—evidence of high pulmonary blood pressure.

Diagnosis. The diagnosis of bronchitis depends on the presence of rhonchi or râles. The dyspnœa and physical signs in *asthma* are like those of a very acute bronchitis, but the history of its occurrence and of former attacks will help to distinguish it. In the capillary bronchitis rhonchi are generally quite absent, and these cases are recognised by the lividity, drowsiness, and presence of râles. Rarely *obstruction* of one *bronchus* (*see* p. 144) may cause a stridor which is mistaken for a bronchitic rhonchus. Often there is difficulty in excluding chronic phthisis, for phthisis is often accompanied by bronchitis. Here the occurrence of febrile reaction, of hæmoptysis, of rapid wasting, and the greater intensity of the physical signs on one side or at one apex, would be in favour of phthisis, and confirmation may be obtained by examination of the sputum for bacilli, by the use of X-rays, or of tuberculin (*see* Phthisis).

It remains to determine whether an acute bronchitis is a primary infection or secondary to such disorders as whooping-cough, measles, typhoid, or other specific fever. In children acute miliary tuberculosis must be thought of.

Prognosis. *Acute Bronchitis.* The duration is from a few days to three weeks or more. In fatal cases of purulent or capillary bronchitis it is from nine to twelve days. *Chronic bronchitis.* Though it frequently shortens life, many people live to an advanced age in spite of it. It is mostly affected by the season in a marked manner, and patients are often practically well during the summer, and again get ill in the winter; but they are worse with each succeeding winter, and finally may be carried off during an exceptionally severe season, or during the cold fogs of towns, or during east and north-east winds elsewhere. On the other hand, if they can be protected from this unfavourable weather by confinement to the house, or better, by residence in a warmer climate, they may keep their bronchitis within limits, and postpone the fatal termination for years. Its ill effects will, however, vary with the amount of secretion and with the rapidity with which the secondary results—emphysema, dilated tubes, and dilatation of the right heart—are developed.

Prevention. This depends on avoiding sources of infection and the causes predisposing to infection in individual cases. Susceptible people must avoid others suffering from catarrh. If contact is necessary gauze masks may be worn as described for influenza. Various measures described under the prevention of coryza (*see* p. 196) may be used in suitable cases. Stock vaccines or autogenous vaccines are often useful. The latter may be prepared from the sputum, but cultures should also be taken from the nose, where the organism chiefly responsible may often be obtained in pure culture. The English winter climate with its cold and damp is a very common predisposing cause of bronchitis, but residence in places in the south of England such as Bournemouth, Ventnor, Torquay or Penzance may produce favourable results. There are also favourable climates abroad, and Mentone, San Remo, Cannes, Arcachon, Canary Islands, Madeira, and the Nile (Assouan) are the places most frequented by patients.

Treatment. In cases of moderate severity the patient should be placed in bed in a warm room. In less severe cases the patient, though allowed up, must be guarded from exposure, and kept as far as possible in a uniform temperature of 60° or 65° F. In chronic bronchitis removal to a favourable climate may have to be considered (*see* Prevention). If there is much tightness of the chest, counter-irritation by means of antiphlogistine, mustard leaf, or a linseed meal poultice sprinkled with mustard, should be employed. In children, counter-irritants should be used with care, but a thin poultice surrounding the whole chest (jacket poultice) is of great service. The diet should be light and nutritious.

There are three motor mechanisms that keep the air passages free from obstruction, viz., for the larger bronchi the propulsive movement of the ciliæ and the expulsive mechanism of the cough, and for the smaller bronchi muscular peristalsis; but of equal importance is a good flow of bronchial secretion, which acts both as a lubricant and as a diluent of irritating substances. At first, when the cough is dry, sedatives, such as tinct. camph. co, are indicated, and later expectorants. Ammonium carbonate (5 grains every four hours), vinum ipecacuanhæ (5 to 10 minims), and tinct. scillæ (15 minims) irritate the gastric mucous membrane, and by reflex vagal action increase the bronchial secretion. The latter is increased still more if the drugs are pushed to the extent of causing emesis, and this is sometimes made use of in treating children, *i.e.* a drachm of vinum ipecacuanhæ, repeated in fifteen minutes if necessary, is given to get rid of accumulated bronchial secretion. Squill is of particular value in chronic bronchitis owing to its digitalis-like effect on the heart. A second class of expectorants stimulates secretion by being excreted by the bronchial glands. The most important member of this class is potassium iodide in doses of 5 grains; it is particularly valuable in chronic bronchitis. Where the expectoration is abundant, the balsams of Peru (20 minims suspended

with 1½ drachms of honey) and tolu should be given, or ammonium chloride (5 to 20 grains). Where the sputum is fœtid, terebene (5 to 15 minims) may be tried; 5 drops on sugar, taken several times a day, is useful for winter cough. In young children, who have but little power of expectoration, the secretions in capillary bronchitis may be so abundant as to threaten to fill up the tubes and cause suffocation. Tinct. belladonnæ, in doses of 3 to 5 minims, or injections of atropine, $\frac{1}{600}$ grain, are given to paralyse the secretory glands and dry up the tubes. The same treatment may also be useful in adults. When the cough is very irritating, sedatives may be employed—morphia in small doses ($\frac{1}{8}$ grain or $\frac{1}{6}$ grain), compound tincture of camphor (½ drachm), heroin ($\frac{1}{160}$ grain to $\frac{1}{120}$ grain), codeine phosphate (¼ grain), or potassium or ammonium bromide (5 grains). But they must be used with great care if there is much lividity, as they may dangerously depress the respiratory and cardiac centres under these circumstances. Hydrocyanic acid, which is contained in the commonly prescribed syrup of Virginian prune, is a sedative, and probably acts by paralysing the vagal nerve endings in the stomach—the converse of ipecacuanhæ—and is valuable in "stomach cough." Cases accompanied with much spasm of the bronchial tubes may be benefited by tinct. stramonii or tinct. lobeliæ æth. (15 minims), ether (15 minims), or tinct. cannabis ind. (10 minims). Chloral in small doses (5 to 7 grains) has also been recommended. Some of these methods of treatment might appear to be opposed to another. Actually, good results are obtained by combining them, as for instance in the Linctus scillæ co. (B.P.C.) (dose 1 drachm), which contains equal amounts of the sedative tinct. camph. co., and of the expectorants oxymel scillæ and syrup. tolutanus. Again, stramonium or lobelia are commonly prescribed with potassium iodide, while the elixir diamorphinæ et terpini (B.P.C.) (1 drachm) contains terpin hydrate, heroin and syrup of Virginian prune—one expectorant and two sedatives.

In all severe cases with cyanosis (or dyspnœa), oxygen inhalations may render valuable service (*see* p. 156). Good may be derived from keeping the air of the room moist by steam issuing from a "bronchitis kettle," or from medicated inhalations such as vapor benzoini (1 drachm tinct. benzoini co. in 1 pint of hot water to be inhaled from a special inhaler or an ordinary jug). The following preparations are useful when the sputum is abundant or fœtid: Vapour olei abietis (B.P.C.) (1 drachm to ½ pint); the dry inhalations, vapor cresol. co. (B.P.C.), a small quantity of the fluid being poured into a metal vessel and volatilised by heat; vapor iodi. æthereus (B.P.C.), by means of an oro-nasal respirator; vapor ammonii chloridi (B.P.C.) If the bronchitis can be referred to any constitutional disease, this should, of course be treated at the same time—for instance, gout by the exhibition of alkalies and colchicum. Many cases require tonics, such as quinine and cod-liver oil. It is desirable to see that the bowels are freely opened; and in cases of long standing, where the right side of the heart is dilated, the various secretions should be kept free, and the heart's action assisted by digitalis, as under corresponding conditions in valvular disease. Vaccines are of value when the predominating organism is M. catarrhalis or Friedlander's bacillus, or when focal infection is the primary cause.

BRONCHIECTASIS

Ætiology. Bronchiectasis, or dilatation of the bronchi, may occur in connection with many diseases of the lungs. It is often associated with some fibrosis of the surrounding lung tissue (*fibroid lung*), or with *emphysema.*

Any gradually increasing and persistent obstruction of a large bronchial tube is likely to be followed by dilatation of the smaller bronchi proceeding from it. Thus aneurysms pressing on a bronchus, carcinoma pressing on or growing into it, syphilitic stenosis and an impacted foreign body may be the causes of bronchiectasis. But the commonest cause of bronchiectasis is a primary inflammatory

condition, such as bronchitis, long-continued broncho-pneumonia, especially in children, and occasionally lobar pneumonia. Pressure on the lung from the outside by pleural effusions or neglected empyemas may also cause bronchiectasis, associated with fibrosis of the lung. Rarely the condition is congenital; the rare cystic degeneration of the lung may also be mentioned here.

Pathology. In cases of partial obstruction, the tubes beyond become distended, because the inspiratory movements are more effective than the expiratory ones, so that air is sucked in and does not completely escape again. In chronic bronchitis the secretion in the tubes may cause obstruction, and at the same time the walls of the tubes are softened by the inflammation and so readily dilate. Another mode of production has been discovered in severe broncho-pneumonia. The acute bronchitis and peri-bronchial lymphangitis leads to complete destruction of the bronchial wall, which may involve neighbouring alveoli and form a clear-cut activity, which may be *cylindrical* if a length of tube has been destroyed, or *saccular* if only one side of the tube has met this fate. During healing the cavity becomes lined with young fibrous tissue, and a new epithelium of low cubical cells is formed. In ordinary cases the change affects the medium and smaller tubes, and is more common in the lower lobes than in the upper. The cavities are thin-walled and present generally no trace of the muscular tissue or cartilage of the healthy bronchi—"honey-comb lung"; a small bronchus may often be found opening into the cavity. Sometimes there are bands running along the walls; sometimes the surface is ulcerated, though it is usually smooth. These cavities are frequently associated with the extensive fibroid changes in the lungs (**10**) (*see* Plate 1).

Bronchiectasis is often limited to one lung, especially when due to bronchial obstruction, to a foreign body, or to acute pneumonia or pleurisy. If both lungs are affected, either the lesions are not extensive, or one lung is very much more involved than the other.

Symptoms. In cases of moderate cylindrical dilatation associated with bronchitis or emphysema, the symptoms will be lost in those of the primary disease. But in larger dilatations and in the saccular variety the bronchiectasis is the prominent fact in the case, and the secretion from the cavities and the fibrosis and cavitation of large portions of the lung are productive of definite symptoms and physical signs.

The patient need not be emaciated, is generally free from fever, and may be inconvenienced by little besides dyspnœa, cough, and expectoration. But there may be cyanosis and clubbing of the fingers. When there is increased resistance to the pulmonary circulation, failure of the right heart will cause œdema of the feet, enlargement of the liver, and albuminuria.

The sputum is either (1) purulent and airless, or (2) muco-purulent, or (3) fœtid, muco-purulent and frothy, like that of fœtid bronchitis. When there are one or two large saccular cavities the sputum is often expectorated in a characteristic manner. The secretion collects for some time—it may be two or three hours—in the dilated tubes without exciting cough; then either from its quantity, or because the patient moves about, turns over or sits up in bed, the secretion flows over into an adjacent healthier tube, coughing is excited, and some ounces of muco-purulent secretion are all at once expectorated. In some cases, hæmoptysis is both frequent and moderately abundant.

Dry bronchiectasis is a not uncommon variety, discovered by means of X-ray examination after lipiodol. There is a preceding history of broncho-pneumonia, particularly after measles and whooping-cough; the symptoms are cough with but little non-fœtid sputum and hæmoptysis. There is basal impairment with weak breath sounds and râles; there is usually no clubbing. The danger lies in excessive hæmoptysis or the development of wet bronchiestasis (**11**).

Physical Signs. These differ according to the character and size of the dilatations, their distribution in the lung, and the amount of consolidation or

fibrosis of the intervening lung. In some cases, a large portion of one base, or even the whole of one side of the chest, presents coarse, creaking, and crackling râles, obscuring the respiratory murmur, but without dulness or pronounced limitation of movement. In other cases there is, in addition, an area of impairment where bronchial or amphoric breathing, with bronchophony and pectoriloquy are heard, and other rarer signs of a cavity surrounded by condensed lung tissue (p. 127). When the cavity is full up with secretion, there may be impairment and diminished breath sounds, while râles and bronchial breathing only appear after coughing. In extreme cases the condition resembles chronic pneumonia. Retraction of the chest takes place, the heart is drawn in a horizontal direction towards the diseased lung, and the opposite lung becomes compensatorily emphysematous.

Diagnosis. The diagnosis and the extent of cavitation can be determined by X-ray after injecting lipiodol. The overlying skin, etc., is anæsthetised by injecting 1 per cent. novocaine down to the cricothyroid membrane ; 10 minims of 5 per cent. cocaine are injected through the membrane into the trachea, with the patient sitting upright. After three minutes a special curved trocar and cannula are passed through the membrane into the trachea. Air can be drawn through the cannula to make certain that the position is correct. The lipiodol, warmed to 106° F. (30 to 40 c.c. for an adult, 30 c.c. for a child), is drawn into the warmed sterile syringe and injected through the cannula, and then the patient lies on the suspected side. The radiogram is taken in the vertical position (*see* Plates 1 and 2, A, which shows the normal). If coughed up the lipiodol should not be swallowed. In an adult the lipiodol may be administered over the back of the tongue by means of syringe and catheter (**12**) or by nasal catheter directed straight into the larynx after applying cocaine. Bronchoscopy, as described under Abscess of the Lung, may be very useful in diagnosis.

The differential diagnosis from chronic phthisis depends on the absence of tubercle bacilli in the sputum, the history of some antecedent infection, *e.g.* pneumonia, and the site of the cavitation, which is very rarely apical. A basal bronchiectasis may be hard to distinguish from an *empyema* discharging into the bronchi. The history may help, and hæmoptysis is in favour of bronchiectasis. Exploration might yield pus in either case.

Prognosis. As compared with phthisis, it is good ; patients often live for years with but slow advance in the local conditions ; but they are liable to dangerous complications, such as pneumonia, abscess, gangrene, septicæmia, and the occurrence of cerebral abscess and metastatic abscesses elsewhere.

Treatment. Locally the object should be to assist the evacuation. For this purpose the patient lies in bed on the sound side and the foot of the bed is raised one foot by means of blocks. This drainage is carried out for half an hour daily at first, and the time is gradually increased to two hours a day. The buttocks may be kept in place by a wedge-shaped cushion. The modern method of drainage is by *bronchoscopy* (*see* Abscess) ; great improvement may follow, though, as there is structural alteration of the tubes, the patient is liable to later exacerbations. Antisepsis of the bronchi may be tried by giving up to 15 minims of oil of turpentine three times a day by mouth. Inhalations of antiseptics (*see* Bronchitis) are of value, including the daily inhalation for fifteen to sixty minutes of the vapour of creosote in a closed chamber (Chaplin).

Several surgical methods of treatment have been tried, including surgical drainage of a single large cavity, with or without resection of the overlying ribs ; phrenic avulsion, artificial pneumothorax, and subsequently the chest may be filled with olive oil containing 5 per cent. gomenol through a cannula ; this will remain unabsorbed for six months so that refills are required at long intervals ; excision of the diseased lobe (lobectomy) with occlusion of the bronchus proximal to the cut ; resection of ribs overlying the bronchiectatic part of the lung, so that collapse may be allowed to take place.

HAY FEVER; ASTHMA

Hay fever is a very severe catarrh, affecting chiefly the nasal mucous membrane, often the bronchial mucous membrane as well, and causing contractions of the bronchial musculature. *Asthma*, used in its broadest sense, is a term applied to a state of affairs in the smaller bronchi which hinders the exchange of air between the larger bronchi and the alveoli of the lungs. We know little for certain about the nature of the obstruction, but, arguing from the analogy of the plain muscle of the intestine or bladder, we may assume that the bronchial muscle, which possibly contracts slightly during each normal respiration, may in asthma at one time be tonically contracted, and at another time undergo a series of violent rhythmic contractions and relaxations. Œdema or congestion of the mucous membrane also plays a part in the obstruction. From this definition we see that the term asthma is often used to denote a symptom, or perhaps a syndrome, rather than a disease—a syndrome in fact that may be caused by different agents.

The Allergic State. Hay fever and asthma are often different manifestations of the same type of disease, which also includes paroxysmal rhinorrhœa (vasomotor rhinitis); angeio-neurotic œdema; paroxysmal hydrarthrosis; some types of urticaria, eczema, pruritus, prurigo; certain gastro-intestinal disturbances; migraine, and a few cases of epilepsy. The members of the group have been classed together as the *toxic idiopathies*, or the *allergic state*. The patient is sensitised to a particular foreign protein, which acts as a poison, so that a violent reaction is produced. This is very similar to the effect produced by the injection of serum into an individual who has been sensitised to it, and so it has been regarded as of essentially the same nature, *i.e. anaphylactic* (*see* p. 15, where the Prausnitz-Küstner reaction is also described). However, there is this definite fact about anaphylaxis pure and simple, viz., that a preliminary sensitising injection of antigen is always necessary to produce anaphylactic shock, whereas in naturally occurring allergic disease the evidence of such a preliminary sensitisation is not obvious. But it is possible in allergy that the antigen—and only quite small doses are necessary—may have obtained access through an abraded mucous membrane. For instance, during gastro-enteritis, undigested protein, *e.g.* egg protein, may be absorbed from the intestinal tract and so give rise to a permanent state of hyper-sensitiveness to this substance. Also there is reason to believe that gastric digestion and consequently proteolysis are imperfect in these cases, so that proteoses become absorbed directly from the alimentary tract, and that then the liver fails to deal with them as it should (failure of protopexic function), and they enter the general circulation, producing anaphylaxis (**46**). In allergy there are, no doubt, other factors also present, and nervous factors, light sensitisation and even drugs, undoubtedly play a part, in addition to the protein irritation and the original trauma, through which the protein gained access to the body. For instance, 4 per cent. of asthmatics are extremely sensitive to aspirin and have been nearly killed by quite small doses, and in these people the salicylic acid from a dose of aspirin has been found to accumulate in the blood to a much greater extent than normal (**13**). Again, there is a strongly inherited tendency to the toxic idiopathics, although members of an affected family may differ as regards the type of allergic disease they manifest, and may indeed suffer from more than one of these.

In the section on anaphylaxis it was pointed out that anaphylactic shock resulted from the interaction of antigen and anti-body in the tissues of the body, and that this interaction caused a breakdown of protein molecules. It is very interesting that in allergic diseases certain biochemical changes have been discovered which favour the theory that the allergic attack is also associated with an excess of proteose in the blood and a resulting anaphylactic shock, causing increased protein catabolism (**14**). During the attack the liver deficiency is shown

by the blood giving a positive indirect van den Bergh reaction in the blood by the blood sugar being low (**45**), while at the same time there is a "hæmoclasic crisis," which consists in a fall of blood pressure, a leucopenia, a change in clotting time and in the refractive index of the serum to light. Following from this the content of amino-acid, uric acid and creatinine in the blood rises; there is an increased excretion of these bodies in the urine. Less water is excreted by the kidneys and the urine becomes highly acid; there is a retention of chloride, while the chloride in the red corpuscles is diminished. But most important of all, there appears in the urine a "proteose" (*see* p. 512), which often produces a specific "skin reaction" when tested on the patient (*see* later); positive results have been obtained in 50 per cent. of asthmatics whose skins are sensitive to proteins derived from foods or inhalants, but in only 15 per cent. of other asthmatics. Healthy men rarely react to their own proteose, though 32 per cent. react to asthmatic proteose, which is clearly toxic (**47**). After the attack the blood becomes normal; there is also a marked diuresis, so that the urine may become actually alkaline. The writer would suggest that the protein catabolism resulting from the anaphylactic shock liberates many smaller amino acid molecules which increase the osmotic pressure of the tissues (which depends on the number of molecules and not on their size), so that water is retained. This is very obvious in urticaria and angeio-neurotic œdema. HCl will be required to neutralise the free amino groups (and presumably NaOH to neutralise the —COOH groups), so that not only will chloride be retained, but even the corpuscles will give up part of their store.

Hay fever occurs to a preponderating extent in the months of May, June and July, because dry grass pollen, which is the toxic agent, is plentiful at this time; but attacks can be produced artificially in susceptible individuals by dried pollen at any time in the year. It is found that hay fever patients react in varying degree to pollens of different plants; but in this country grass pollen is the only important agent; in the summer there is plenty of it, and it can be carried long distances by wind. In America the pollen of certain *Compositæ* may also cause trouble. The pollen normally produces its effect on the nasal and bronchial mucous membrane after inhalation. If experimentally swallowed by the patient it causes indigestion and diarrhœa.

Asthma. The animal asthmas form another type of toxic idiopathy. Here the patient may be sensitised to the dandruff of a horse, and gets an attack of asthma if horses are in the neighbourhood, or even if he is in the company of ostlers; in such individuals gastro-intestinal attacks have been described after eating sausages containing horse meat. "Cat" asthma is well known; and there is sensitiveness to sheep, cows, pigs, rabbits, goats, and the feathers of birds, so that an attack may start as the result of sleeping on an ordinary pillow. In Holland it has been found recently that grain infected with mites, much used for feeding animals, is a potent source of asthma.

Sensitiveness to foodstuffs is another toxic idiopathy, and eating the specific foodstuff may cause asthma or gastro-intestinal disturbances. Asthmatic patients can be tested by inoculation with the proteins of different foods. Positive skin reactions have been obtained with cereals, such as wheat, maize, rice, rye, barley or oats. Eggs, potatoes, casein, lobster, oyster and various kinds of fish, meat of different kinds, spinach, strawberries, apples, and other vegetables and fruit, have all produced positive reactions in different cases.

There are two methods of testing for "skin reactions" in allergic patients. (1) By scarification; a drop of N/10 or N/20 solution of NaOH is put on the skin of the forearm after cleaning it, and a small quantity of the protein in powder form is applied on the point of a small knife and dissolved in the liquid, and then a superficial cut one-eighth of an inch long is made through the mixture. A positive result appears in twenty to thirty minutes, consisting of an urticarial wheal half a centimetre in diameter with a surrounding zone of erythema. Results

even less than this are recorded, as they may point to the ætiological factor. The control, of course, must be completely negative. (2) By intracutaneous injection; 0·05 c.c. of the required solution is injected into the skin by means of a very fine needle held nearly parallel to the surface. A small button of fluid must be seen, and a control injection with normal saline should be carried out. The front of the forearm is the best place to choose. An inflammatory areola indicates a positive reaction. The intracutaneous reaction is much the most sensitive of the two, and positive reactions have been obtained with various protein extracts (animals' hairs, foodstuffs, pollens) in a proportion of asthmatics, which varies in different countries, but is not large in England.

In the great majority of asthma cases the poisonous substance is unknown. It appears to be air-borne, and in some cases may be a mould. The dust from the house of an asthmatic patient often contains it. It is present in one locality more than another. Thus, in Zeeland there are villages in which 1 per cent. of the population suffers from asthma, and these individuals lose their asthma when journeying up the Rhine. Again, most asthmatics avoid attacks altogether in mountainous regions such as the Alps, though by living there for a time they lose such immunity as they have obtained lower down, and when they return home their attacks may at first be more severe than usual. The freedom from attacks in the Alps is due to the absence of the poison, and attacks may be artificially produced by making the patient inhale dust, etc., specially brought there (**15**).

In predisposed individuals there are several factors that may actually cause an attack,—irritation of the nasal mucous membrane, constipation, uterine troubles, distension of the stomach with food, over smoking and the dyspepsia that often accompanies it, milk foods, the lead present in hair wash, and even the smell of paint, and especially various psychic conditions. Attacks may occur because the patient expects that they will. Thus a patient sensitised to roses had an attack on seeing an artificial rose which was thought to be real. On the other hand, violent excitement may arrest an attack completely. Attacks are more liable to come on when patients are fatigued, *i.e.* towards the end of the day.

Asthma—Infective and Reflex. This group of cases, which includes the majority of asthmatics in this country, appears to differ from the group just described, though there is overlapping. The asthma often begins at puberty or the climacteric. The immediate precursor may be acute bronchitis or pneumonia, such as may occur in whooping-cough or measles, or the asthma may be due to infection in other parts of the body. The asthma may be due to (1) sensitisation to substances which gain access to the body at the actual site of the infection in the lungs or elsewhere, or (2) to reflex irritation. (1) There is evidence particularly in adults that Gram-negative bacilli of the Friedlander group produce histamine-like substances on culture, and these substances produced locally in the bronchi may be responsible for the attacks (**48**). Focal infection is dealt with below. (2) That reflex asthma may arise from the nose is quite easy to understand from Brodie's and Dixon's work, which definitely proved that stimulating the nasal mucous membrane produces a reflex bronchial constriction. In fact, asthma has occasionally followed the removal of nasal polypi and other extensive operations on the nose.

The focal infection in this group may be situated in the maxillary antrum; there may be ethmoiditis, nasal polypi, septal deviation, ridges, or spurs, hypertrophy of the turbinates, all tending to obstruct the airway and to favour infection. Tonsils and adenoids do, in a small number of cases, play an important *rôle*. Certainly the usual history is that these have been operated upon at least once without relief. However, after other avenues have been explored, operation may be called for. The teeth and intestines are other possible sources. There still remain some patients whose asthma starts or is associated with "colds in the head," in whom no cause is demonstrable other than an apparent lack of resistance in the nasal mucous membrane. They are always worse in the winter

months, or rather in the late autumn and early spring, when the weather is most capricious, and the changes sudden and disturbing. Cases of infective and reflex asthma met with in this country do not usually react when tested with proteins like some of the cases of the previous group.

Asthma and Bronchitis. The relation of asthma to bronchitis is three-fold. In the first place, as just described, asthma commonly follows a *primary* bronchitis. In the second place a condition of asthma may gradually supervene when a patient suffers from recurrent attacks of bronchitis, and the asthma may only come on when the bronchitis is at its worst and clear up again when the bronchitis is better. This condition is known as *asthmatic bronchitis* and is not allergic at all. It results because the bronchial inflammation irritates the nerve endings in the mucous membrane, so as to produce a reflex local contraction of the muscles. Asthma also occurs with phthisis. In the third place, repeated attacks of true allergic asthma may lead to a *secondary* chronic bronchitis, as described later in the symptomatology.

Breathless Attacks in Elderly Subjects. This condition is described on p. 255, and is sometimes known as *cardiac asthma*, or as *renal asthma* if the kidneys are affected, as in *arteriosclerotic kidney*. *Uræmic asthma* is sometimes applied to breathlessness in uræmia.

Symptoms. In *hay fever* there are acute rhinitis and conjunctivitis with œdema of the mucous membrane, lachrymation and sneezing; in thin-skinned people there are erythema, urticaria, with severe itching. There may be asthma and constitutional effects such as lassitude, mental depression, irritability and headaches. Paroxysmal rhinorrhœa, in which the patient suddenly has a profuse watery discharge from the nose, is probably allied to hay fever.

Asthma. Sometimes there are *premonitory* indications, such as a general sense of discomfort, drowsiness, gaping, itching under the chin, sneezing and coryza, or the passage of much pale limpid urine. But the attack is often quite sudden, commencing in the early morning between two and four o'clock, though the patient may have gone to bed apparently quite well. He wakes up with a sense of dyspnœa, so that he has to sit up inbed, or gets out and opens the window to let in more air. The breathing is soon so difficult that he has to call in the aid of all the accessory muscles of respiration; he grasps with his hands the sides of his bed, the arms of a chair, the mantelpiece, or the edge of a table, to give a firm support for the muscles which pass from the upper extremities to the chest. At first the chest is nearly fixed in a condition of inspiration, and there is very slight movement, and practically no breath sounds are heard on auscultation; later, when the movements are beginning to get somewhat more free, the most noticeable feature is the extraordinary length of expiration, which is accompanied with a loud wheezing, audible at a distance, while the respiration rate is slow. The chest is somewhat over-resonant; the inspiratory murmur is scarcely audible, or accompanied with a little sibilant rhonchus, while with expiration is heard the loud rhonchus just mentioned. With this the patient's distress is very great; the face gets cyanosed, the eyes are prominent, the conjunctivæ suffused and the whole attention of the patient is absorbed in the attempt to expel the air from the chest. Usually there is no pyrexia. After a time—it may be two or three hours—he begins to cough, and expectorates some thin, transparent mucus, which may be mixed with a little blood; then the breathing becomes easier, the cyanosis is less, gradually the whole trouble subsides, and the patient falls asleep.

The sputum often contains, besides cylindrical or ciliated epithelium, bodies known as Curschmann's spirals. These are yellowish-green or grey particles, made up of threads of mucus. Under the microscope they are seen to be spirally twisted fine or coarse fibres mixed with eosinophil leucocytes, and there is often in the middle one transparent fibre; they are probably formed in the finer bronchial tubes. Two kinds of crystals are also often found, viz., cubic crystals consisting of calcium carbonate (17) and elongated hexahedral crystals known as

Charcot-Leyden crystals, which consist of calcium phosphate and are sometimes found in the spirals. The eosinophil leucocytes of the blood are increased in number.

Each attack of asthma may last from two or three hours to as many days; their recurrence, at longer or shorter intervals, is a good deal determined by the exciting causes—that is, a careful patient, who knows how to avoid what will bring on his attacks, may escape for long periods. The duration of the illness is also very variable. Many of those who have it in childhood recover in adult age. The attacks themselves are rarely fatal, and the occasional occurrence of not very severe attacks is not prejudicial to health; but frequent paroxysms induce emphysema of the lungs, and ultimately attendant bronchitis, so that there is constantly more or less lividity, with the round shoulders, barrel-shaped chest, and laboured respiration which are observed in the midst of the paroxysms themselves. Life is thereby shortened, and the tendency to suffer from the severer forms of bronchitis is increased.

Diagnosis. The diagnosis of *hay fever* will be helped by remembering that it occurs in the first half of the summer. The diagnosis in the case of *asthma* is easy, if the history and the character of the breathing and its onset be carefully studied. Sudden attacks of dyspnœa in cardiac disease, thoracic aneurysm, and laryngeal obstruction are those which are likely to resemble asthma most closely. Hysterical attacks may also simulate it. The skin reactions are widely used to determine whether the patient is sensitive to a particular foreign protein. It is very important to make this test for horse serum before injecting antitoxic serum as many asthmatics have died from this. Asthma may be due to organic disease, and *bronchoscopy* will be useful in determining this.

Prevention. In both hay fever and asthma prevention of the attacks is the main object of treatment. In *hay fever* residence in the country during the hay-time should be avoided; if the sufferer goes out, he may wear a veil over the eyes or nose. Susceptibility to hay fever is said to be diminished by the internal use of calcium lactate. Stimulation of certain spots on the turbinals by lightly touching with the electric cautery after cocainisation has been used.

Much work has been done on the lines of vaccine therapy (**18**). Alleviation of symptoms and reduction of sensitiveness may be effected in most cases by the subcutaneous injection of dilute extracts of the pollen to which the person is sensitive. An aqueous solution of 1 part in 1,000,000 has been taken as one unit, 1 part in 500,000 as two units, 1 part in 100,000 as ten units, and so on. Preferably two or three weeks before the expected attack 1 c.c. of a very weak solution is injected, and increasing doses, or rather the same dose, 1 c.c., of solutions of increasing strength, are injected every three or four days until twelve or more doses have been given. Freeman tests the sensitiveness of the individual by ascertaining the strength of solution in units which will give the ophthalmic reaction, and checks his later doses by the same test. A solution of 1 in 1,000 appears to be the maximum strength that is advisable.

As regards *asthma*, the most important thing is to keep in as perfect a state of health as possible. In particular, overwork is to be avoided. Regular exercise and adequate holidays should be taken. Some people can live in London and large cities free from paroxysms who have them at once if they attempt to live in the country. Conversely others can only live in the country, and have asthmatic attacks in town. In the same way sea air may excite attacks in some and cure others. The facts with regard to any patient can only be ascertained by experiment. Patients usually do better on high ground.

Moderation and care in diet are the next points to consider. Food should be light and easily digestible; a heavy supper should not be taken; and particular food should be excluded from time to time, such as cheese, pastry, pork, beer, to see if there is any one offender in this respect. Toasted bread and well-baked biscuits should be taken. Farinaceous foods should be boiled in water and not

milk; other milk foods, such as Benger's, should be avoided. An ounce of dextrose three times a day may be prescribed with lemon or orange to help the liver. When the patient is fat a low calorie diet is indicated. If it is found that a patient is sensitised to a particular protein, that substance should be avoided, or if this is difficult, desensitisation with the specific protein may be carried out. A capoc pillow is prescribed for patients reacting to feathers. Good results have been obtained by means of non-specific protein therapy. Weekly subcutaneous injections of 1 c.c. of a 1 in 100,000 Koch's T.D.A. tuberculin have been used (**19**). Peptone injections in the form of a 5 per cent. solution of Armour's No. 2 peptone are injected twice weekly intramuscularly or intravenously. The first dose is 0·3 c.c. and this is gradually increased by 0·2 c.c., the maximum dose being 2 or 2·5 c.c. The maximum dose is that which just fails to give a reaction, and the temperature should be taken four or five hours after the injection to see whether it is raised (**20**). Peptone (0·5 gram) by mouth exactly three-quarters of an hour before every meal is sometimes successful. Injections of the patient's own proteose prepared from the urine have been tried with varying success. Other methods of the most diverse kind may be described which perhaps act by causing some general reaction which temporarily desensitises the patient. A hot bath, with the temperature rising from 98° to 106° F., of twenty minutes duration before going to bed may ward off nocturnal attacks. An "erythema dose" of ultra-violet light on an area of skin or an exposure to X-rays may act in the same way (**21**). Exposure to a hot, moist atmosphere is used at Mont Dore. Lightly stroking the nasal septum with the electric cautery will sometimes stop attacks, and this is of most value when the nose is free from deformity and polypi and the systolic blood pressure is on the high side (120 to 160 mm.). In no circumstances should polypi be removed in asthma (**16**). Airtight chambers have been constructed in which the patient sleeps. They are ventilated by air drawn from a height of 100 feet, which may be further purified from moulds by refrigeration. It is suggested that the patient remains free from attacks because for a large part of the twenty-four hours he is protected from these atmospheric substances (**22**). Liquor arsenicalis in 5 mm. doses, bromides, and particularly potassium iodide in doses up to 30 gr. a day are the most valuable drugs to prevent the onset of attacks. Mild purgation with calomel in small doses is also of value, and salol and other intestinal disinfectants have been used.

When asthma is associated with infection other additional methods are available. Coryza should be treated with the paraffin and vaseline mixture described on p. 196. Autogenous vaccines may be prepared from the sputum or nasal secretions, or a stock vaccine may be used. They are best given *intracutaneously*, and the amount of the local reaction is a guide to the dose. Septic foci should be looked for and dealt with.

Treatment. For *hay fever* Morell Mackenzie recommended a spray of a 4 to 6 per cent. solution of cocaine to the eyes and nose. In the case of the nose this was followed by the daily introduction along the floor of the nose of a bougie, smeared with vaseline or oil, and left in for ten minutes at first, and for gradually increasing periods up to half an hour or longer. Adrenin hydrochloride may be sprayed into nose or throat from a solution of 1 to 5,000. Where there is chronic hypertrophic rhinitis, the application of the galvano-cautery to the swollen mucous membrane, after the preliminary use of a 2 per cent. solution of cocaine, seems to be quickly curative.

To stop an attack of *asthma* an injection of 1 to 2 minims of 1 in 1,000 adrenin hydrochloride is the most certain treatment, though 10 and even 15 mm. have been injected intramuscularly. A convenient method of administration is by a spray of 1 in 1,000 adrenaline containing 10 per cent. glycerine, 0·5 per cent. chloretone and 2 drops of sulphurous acid per oz. The spray may be worked by hand or by a pump, or oxygen from a cylinder may be used as the motive force. Synthetic crystallised adrenine (1 mgm.) may be absorbed by keeping it under

the tongue. Caffeine iodide (7½ gr.) or pyramidon (4½ gr.) and ephedrin (½ gr.) may be taken by mouth. Amyl nitrite is also commonly inhaled, or maximal pharmacopœial doses of Tr. lobeliæ aeth., Tr. stramonii, Tr. belladonnæ, chloral hydrate, the nitrites, or nitroglycerine may be given by mouth. A very common method of treatment is to inhale the fumes from burning a paper saturated with nitre solution and dried, or to smoke cigarettes made of chopped stramonium leaves, or to use other preparations containing stramonium. Inhalation is a bad method of regular treatment, because the bronchial mucous membrane is irritated, with resulting bronchitis.

Status asthmaticus has been averted by treating the patient with oxygen and carbon dioxide in an oxygen tent (**49**). The author has arrested some attacks by increasing the intra-pulmonary pressure (*see* Pulmonary Œdema). The oxygen tent without CO_2 causes relief if there is much bronchitis.

OBSTRUCTION OF THE LARGE BRONCHI

In their relation to the various causes of compression, the two main bronchi closely resemble the trachea, and much that has been said under the head of tracheal obstruction might be repeated here. Obstruction, due either to compression or stricture, may result from pulmonary carcinoma, aneurysm, foreign bodies and bronchial glands enlarged by malignant growth or by caseation and suppuration; less commonly epithelioma of the œsophagus, gumma, and even a dilated left auricle may press upon the bronchus. The special liability of the left bronchus to compression by an aneurysm of the arch of the aorta, under which it passes, is of importance. Foreign bodies more frequently fall into the right bronchus, because it is the larger; and the dividing ridge between the two bronchi is somewhat to the left of the middle line, and hence objects falling down the centre of the trachea are directed into its right branch. They may be driven into the trachea during coughing, and fall back into the same or the opposite bronchus.

The obstruction of a bronchus is followed by important changes in the corresponding portion of the lung, and the distal divisions of the bronchus. Ultimately in every case the *lung becomes collapsed*, because, when the interchange of air completely ceases, what remains is absorbed by the pulmonary vessels; ultimately there is pulmonary fibrosis. In a rapidly complete obstruction, as from impaction of a foreign body, this collapse occurs very early; but when the compression takes place slowly, as in the case of an aneurysmal sac, there is at first *distension* of the lung with air, such that the heart may be pushed out of place, and the diaphragm forced downwards (Newton Pitt). A loose foreign body, acting like a ball and socket valve, produces a similar effect.

Another result is *bronchiectasis*, which may develop in the course of two or three months. The most serious inflammation is to be expected quite early when the foreign body is a pea-nut. Other complications caused by foreign bodies are abscess, and occasionally pneumothorax or pyo-pnumothorax in acute cases, and empyema or profuse hæmoptysis in long-established cases (**23**).

Symptoms and Physical Signs. These vary with the degree of obstruction and rapidity of its production; and since the opposite tube is often free, and thus only half the respiratory area is interfered with, the bronchus is often much more completely obstructed, before death occurs, than ever the trachea can be.

Dyspnœa at rest or on exertion is the only constant symptom at first, and occasionally there are stridor and slight hæmoptysis; but obstruction of either main bronchus may lead to the same paroxysms of asphyxia as occur in tracheal obstruction. When bronchiectasis has developed, cough, expectoration of offensive sputum, and febrile reaction become prominent symptoms.

The chief physical sign is the absence or extreme weakness of the vesicular murmur, which is in strong contrast with the increased breath sounds on the opposite side. This, in some cases for a time, may be the only physical sign, for the resonance may be perfectly normal. But in the cases in which distension of the lung takes place there will be hyper-resonance on percussion, with extension of resonance over the cardiac area and evidence of displacement of the heart, so that the resemblance to pneumothorax may be very close. In these cases eventually, and in other cases much sooner, as the air becomes absorbed, there is dulness at the affected base, with diminished tactile vibration. This may go on to complete absence of breath sounds, voice sounds, tactile vibration, and percussion resonance. If considerable bronchiectatic cavities should be formed, the above physical signs may be, over one or other small area, replaced by tympanitic percussion note, cavernous breathing, crackling, gurgling râles, bronchophony and pectoriloquy.

Diagnosis. The combination of good resonance with nearly complete absence of respiratory sounds on one side of the chest is very characteristic of obstruction of the corresponding bronchus. When the obstruction is accompanied by stridor, it may be mistaken for bronchitis. Stridor from the above cause is persistent and uniform in character, arising from a single point of obstruction, whereas the rhonchi of bronchitis vary constantly in loudness, pitch, and position.

In compression of the bronchus with a distended lung, pneumothorax has been wrongly diagnosed on account of the hyper-resonance with absence of breath sounds. In these cases a radiogram may show the presence of aneurysm in the case of compression, or the lung retracted towards the spine in the case of pneumothorax.

When, on the other hand, the stenosis causes, as eventually it must do, more or less complete collapse of the lung, the physical signs resemble those due to a partially absorbed pleuritic effusion, and the exploring syringe may be necessary for a final decision.

Where foreign bodies are in question, the history must, of course, be carefully considered. Many are opaque to the X-rays. In suitable cases the *bronchoscope* may be employed.

Prognosis. This depends on the nature of the obstruction and the degree of inflammatory reaction. The lung may become extremely tolerant to a foreign body, as is shown by the fact that cases have lasted for thirty-six years, with persistent bronchiectasis and fibrosis of the lung (**23**).

Treatment is similar to that of obstruction of the trachea.

EMPHYSEMA OF THE LUNGS

The term *emphysema* (from ἐν, in, and φῦσα, wind) is rightly used to denote the extravasation of air into the subcutaneous or other tissues of the body (*surgical emphysema*), and into the interlobular or interstitial tissue of the lungs (*interstitial emphysema*). It is much less applicable to the disease of the lung now under consideration, for which, however, in medical parlance it is usually reserved. The alveoli of the lung naturally contain air ; in this disease they are abnormally distended, and may be said to contain too much. So far the name *emphysema* (*vesicular emphysema*) may be justifiable ; but the name *alveolar ectasis*, which has been suggested, is more correct.

Ætiology and Pathology. Several factors are concerned in the production of emphysema. Some of these operate in chronic bronchitis, one of the commonest causes of the condition. (1) Just before the action of coughing there is a high pressure in the lungs behind a closed glottis. This interferes with the blood supply, since the pulmonary blood pressure is low, so that, in course of time,

degeneration of the lung tissue takes place. (2) At the end of coughing a deep inspiration is taken, causing distension of the alveoli, stretching of their walls, and narrowing of the capillaries, with interference with the blood supply again. (3) The force exerted by the muscles during inspiration is greater than during expiration, because the latter action is largely due to the elastic recoil of the lungs. Where the bronchi are partially obstructed with secretion, air may be drawn into the alveoli against the obstruction during inspiration, but cannot get out again during expiration, so that the alveoli are permanently distended. This is the factor that operates in asthma, the obstruction being due to contraction of the bronchial muscles. The obstruction acts as a valve, allowing air to enter, but not to come out again. (4) Prolonged stretching of the alveolar walls has been thought to occur in glass-blowers, and in players of wind instruments, and in those engaged in laborious occupations, who are continually keeping their chests expanded, either to supply a slow regulated stream of air or to serve as a *point d'appui* for the use of the arms. Recent observation makes this doubtful (**24**). (5) In the course of years the elastic tissue of the lungs gradually wears out, producing the *small-lunged emphysema* of elderly people. (6) When a portion of the lung shrinks from disease or becomes infiltrated with inflammatory products or a neoplasm, it cannot expand during inspiration. Consequently the expansion of neighbouring alveoli must be increased so as to fill up the vacant space. This is known as *compensatory emphysema*. By such various means do the septa between adjacent alveoli become atrophied in emphysema. Soon a perforation is established through the septum; then the whole septum is destroyed, and the two alveoli become one. In this process not only the elastic tissue, but also the whole network of pulmonary capillaries contained in the septum, disappear. If this is repeated extensively throughout the lungs, first, all the air spaces are much enlarged, and in many places great blebs of lung tissue simply containing air are formed; secondly, the elasticity of the lung necessary for expiration is reduced much below the normal; thirdly, the vascular area available for aerating the blood is greatly diminished; and fourthly, in most cases the lungs themselves are considerably enlarged.

In consequence of the loss of elasticity, expiration becomes more difficult. Parallel with the increase in size of the lungs, the chest enlarges in width and depth, assuming permanently the shape and position which are characteristic of full inspiration; the mobility of the chest is much diminished, since it ranges only between different degrees of inspiration, instead of between full inspiration and full expiration. The interchange of gases is less complete. This is shown by the values found for the pressure of CO_2 in the arterial blood, which are much above the normal. There is, in fact, a CO_2 acidæmia, which causes severe dyspnœa. The saturation of the arterial blood with oxygen may also be below normal (**7**); there is commonly an increase in the alkali reserve, which tends to compensate for the CO_2 retention.

Another important factor is the *loss of capillary area* in the lungs. From this there results an obstruction to the pulmonary circulation. The tension in the pulmonary artery and right ventricle is increased, the right ventricle hypertrophies, and later there is dilatation of the right side of the heart, so that the venous system becomes engorged, producing congestion and enlargement of the liver, œdema of the feet, legs, and trunk, and albuminuria. In elderly people there is usually also left-sided dilatation of the heart with myocardial degeneration.

Morbid Anatomy. A lung affected with *large-lunged emphysema* does not collapse when the chest is opened at the post-mortem examination, but even bulges out through the aperture. It is soft and inelastic, and yields to the pressure of the finger ("pitting"). In different parts of it, especially along the inner and lower edges, may be seen large blebs the size of peas or nuts; and the lung is unusually pale and bloodless, and of a mottled grey colour. On section the large

blebs collapse; and the whole organ is much drier than usual, except in some parts, such as the bases, which may have been the seat of a complicating bronchitis or œdema.

A second variety (*small-lunged emphysema*) occurs in old people as a senile atrophic change; the lung is not enlarged, and blebs are not numerous. The septa have atrophied so that alveoli have joined together, and the lung is shrunken, inelastic, dry, and pale, and presents a less perfectly spongy structure than normal.

The greater development of emphysema in certain parts of the lungs, specially the apices, anterior margins and lower edges, may be accounted for on Jenner's view—that when air is retained in the chest under great pressure, as when coughing or making any great muscular effort, it is the parts of the lung which are least supported by the surrounding structures which will bulge out owing to the air pressure from within.

Symptoms and Physical Signs. The symptoms of emphysema are at first only shortness of breath; the cough and expectoration which are commonly present result from a co-existing bronchitis. The dyspnœa is especially seen on exertion in early stages, when the breathing is quickened and the patient readily pants; later on it may be always present, producing orthopnœa at night. In its worst forms the extraordinary muscles of respiration are in constant use; the clavicles are lifted; and the sterno-mastoids and scaleni stand out at each inspiration, striving to increase the tidal air; expiration is prolonged, laboured, and aided to their utmost by the muscles of the abdomen. The *physical signs* are characteristic. The chest is broad, deep antero-posteriorly, but short; it is often called barrel-shaped, from its enlargement, and from the increase of the antero-posterior diameter giving it rather a circular than a transversely oval shape. The shoulders are raised; the upper ribs are closer together, and the lower ribs wider apart than normal; and the epigastric angle is very obtuse, measuring 105° or more. The elevation of the ribs alters the relative positions of the nipple and the heart's impulse; the nipple is often found on the fifth rib, and the heart's impulse in the sixth space. Percussion gives excessive resonance over the parts of the chest which are normally resonant, and an extension of the resonance over areas which are normally dull. Thus the hepatic and cardiac dulnesses are encroached upon, the right lung being resonant down to the sixth space or seventh rib, and the superficial heart dulness often disappears altogether. On auscultation the breath sounds are very much diminished or scarcely audible, but the expiratory murmur may be much prolonged when there is coincident bronchial spasm, and rhonchi may be audible.

The enlargement of the lungs also affects the signs connected with other organs. Since a larger portion of lung than is normal lies between the heart and the chest wall, the impulse of the heart may be imperceptible in the fifth space, the cardiac sounds are faint, and the fact of dilatation or hypertrophy may be concealed.

In small-lunged emphysema the chest is more nearly circular in its outline, but it is not enlarged; the lungs do not cover the heart; and the heart is not hypertrophied, but atrophied. The percussion note is hyper-resonant, and the inspiratory murmur is feeble, but the expiration is not prolonged.

In both forms the rhonchi of bronchitis are frequently present; in extreme cases there are râles at the bases of the lungs, with an impaired note due to œdema.

Complications. Chronic bronchitis is frequently present, with or without bronchiectasis. In elderly people there is commonly myocardial degeneration with hypertrophy and dilatation of the left side, as well as of the right side, of the heart, and there may be general œdema. There is often arterial degeneration associated with senile arteriosclerotic kidneys. This type of case is more fully considered on p. 255.

Diagnosis. Its recognition depends upon the altered quality of resonance,

and especially upon the extension of resonance over the præcordial area, and downwards over the liver. In the small-lunged variety the altered quality of resonance and the dyspnœa are the chief features. The Röntgen rays show a more extensive and lighter area over the lungs than in health, and a lower position and less extensive movements of the diaphragm.

Prognosis. Actual recovery does not occur, only relief of symptoms. The duration of life depends upon the extent of the change, the liability to bronchitis, and the state of the cardiac muscle. In most cases the final result does not come under several years.

Treatment. This must be directed to improving the general health of the patient, to avoiding all risk of bronchitic complications, and to relieving these when they occur. Thus the patient should have nutritious and digestible diet, should be well clothed, live in warm, well-ventilated rooms, and avoid east winds and the night air. Tonics, such as cod-liver oil, iron, strychnia, and quinine, are used. Attempts have been made to compensate for the loss of elastic tissue. Thus Gerhardt advises assisting expiration by mechanical compression of the thorax; this is done by another person with the hands upon the lower part of the thorax for five or ten minutes every day. The accompanying bronchitis should be treated. The treatment by compressed air, as in the steel chamber at the Brompton Hospital, depends on the increase in the concentration of oxygen in the inspired air, and this has been found of value in emphysema, particularly if there is bronchitis. An oxygen tent can also be used.

COLLAPSE OF THE LUNGS

(*Atelectasis Pulmonum*)

A distinction is often made between lungs that have never completely expanded (atelectasis) and those that have after expansion partly returned to the fœtal state (collapse). *Atelectasis* is congenital, and is seen in very weakly children, whose respiratory movements are insufficient to draw in the required amount of air. It occurs the more readily because the lungs after removal from the body at birth are about the same size as the chest cavity, and so there is not the same suction power, compelling the entry of air, as there is in later life, when the lungs are smaller than the chest cavity. *Collapse* is an acquired condition due to failure of air to enter the lungs, and results from (1) obstruction to the entrance of air by the air passages, (2) compression of the lung from without. It is not due to paralysis of the diaphragm, since it never occurs after phrenic avulsion.

(1) *Obstruction* may arise from chronic enlargement of the tonsils, adenoid growths in the naso-pharynx, much more often from the viscid, mucous, or purulent secretion of bronchitis, especially in children, and as a part of broncho-pneumonia, and in older people from constriction of the bronchus by neoplasm or by aneurysm or some other of the causes previously mentioned.

(2) The causes of *compression* are numerous: in the chest itself it is most frequently due to pleural effusion, but also to enlargement of the heart, pericardial effusion, mediastinal tumours, aneurysms of the aorta, and angular curvature of the spine (kypho-scoliosis); in the abdomen, to the pressure of tumours growing from the upper surface of the liver, especially hydatids, abscess and neoplasm, of sub-diaphragmatic abscesses, hydatid of the spleen, ascitic fluid, and ovarian tumours.

(3) In wounds of the chest and sometimes other parts of the body, a *massive* collapse of the whole of one lung may occur. There is no necessity for the wound to penetrate into the chest cavity, and the lung opposite to the side of the wound may be affected. The condition may or may not be associated with hæmothorax. *Massive* collapse occurs not uncommonly after operation for acute abdominal conditions. It is now considered to be due to blocking of the tubes

by inflammatory products, the pneumococcus, Type IV., being mainly responsible (49). Consequently the air is absorbed from the alveoli, and so collapse occurs.

Morbid Anatomy. Lung in a state of collapse or atelectasis has a violet or dark purple-grey colour, and is tough, airless, and dry on section. Isolated patches are seen to be slightly depressed below the general surface. Unless subsequently the seat of inflammation, they may be again expanded by forcible inflation with air.

Symptoms. In congenital atelectasis the child is weakly, more or less livid, with rapid shallow breathing and feeble cry. With each inspiration the lower part of the chest is drawn in, and the intercostal spaces are depressed. Examination may elicit a little loss of resonance at the bases, and occasionally some râles, but feebleness of breath sounds is the chief physical sign. The collapse of bronchitis is rarely extensive enough to reveal itself by auscultation, its distribution being lobular and scattered.

When collapse is more extensive and uniform different stages can be recognised by the physical signs. A very slight degree of collapse may occur at the bases from temporary disuse of the lung as a result of early pleurisy, or from prolonged dorsal decubitus. When the affected area of lung is auscultated, the breath sound is very feeble; if the patient breathes deeply, there is a louder vesicular murmur, and at the end of it fine crepitations, which are due to the fresh expansion of hitherto collapsed air vesicles.

The physical signs of collapse due to obstruction of a bronchus have just been considered. In the case of compression by fluid, etc., the early signs may be dulness, diminished tactile vibration, and either diminished or faintly bronchial breath sounds. When complete they are absolute dulness, absence of breath sounds and tactile vibration.

In the massive collapse associated with retraction of the chest wall due to wounds, there is dulness, and there may be deficient breath sounds and absent tactile vibration, but in advanced cases there may be instead loud bronchial breathing and increased tactile vibration. The chest wall is retracted, the intercostal spaces depressed, the diaphragm raised and immobile, and the heart drawn over to the affected side. When a hæmothorax is present on the affected side, although the chest wall is retracted, the heart may be pushed over towards the sound side. This occurrence is strongly in favour of the primary cause being paralysis of the chest wall, because in the last case this persists even though the pressure in the chest on the same side is increased by the hæmothorax. Massive collapse after operations is commoner than is generally supposed. Probably the cases are often diagnosed as pneumonia owing to the physical signs.

The symptoms are dyspnœa, which, however, may be slight when the patient is at rest, cyanosis, and sometimes pain.

Treatment. Oxygen, with or without CO_2 as a respiratory stimulant, is the correct treatment for massive collapse and in atelectasis of the new-born good results are obtained, though some method of artificial respiration may also be required (49) Elliott and Dingley recommend that expectorant medicines with potassium iodide should be given, that all abdominal bandages should be loosened as far as possible, and that the patient should be encouraged to make full inspiratory efforts, especially of an abdominal type, for five minutes every hour. Bronchial obstruction may be removed by bronchoscopy.

ŒDEMA OF THE LUNGS

Ætiology. Some degree of œdema of the lungs is found in the majority of post mortems, especially where the patient has been lying for some time in bed before death. For this reason it is most marked at the base and along the

posterior borders of the lungs (hypostatic œdema). Certain diseases are particularly likely to cause it; these are myocardial disease and especially aortic regurgitation, where it may come on acutely owing to rapid failure of the left ventricle, while the right ventricle goes on pumping blood into the lungs; hydræmic nephritis; an inflammatory œdema generally accompanies acute pneumonic processes. Suffocative poison gases produce œdema of the lungs.

Morbid Anatomy. A lung affected with œdema is bulky, heavy, and exudes when incised an immense quantity of serous slightly blood-stained frothy fluid.

Symptoms. The chest may be at first resonant, but later shows some impairment of the note at the bases behind; here the breath sounds are deficient, and there are heard only abundant fine and medium râles. In the acute form (*acute suffocative œdema*) the patient is taken suddenly with expiratory dyspnœa and orthopnœa or rattling respiration, which may be a protective mechanism; the inspirations are made as short as possible as the lowering of pressure would help œdema formation. On the other hand prolonged expiration against resistance from contracted bronchioles (asthmatic breathing) increases the pressure in the lungs; this principle is made use of in treatment. Other symptoms are restlessness, sense of suffocation, more or less cyanosis, small rapid pulse, and expectoration of large quantities of colourless or blood-stained, frothy, watery fluid. This may be quickly fatal, or subside in the course of a few hours. There may, however, be no expectoration until some days have elapsed, and, indeed, none at all, in some quickly fatal cases. In the final œdema of pneumonia, the râles are audible over the whole of the hitherto healthy lung. It has only recently been recognised from experimental evidence that the nocturnal breathless attacks or paroxysmal dyspnœa of elderly subjects (*q.v.*) are sometimes due to acute pulmonary œdema (**49**).

Diagnosis. Acute pulmonary œdema coming on suddenly in a person, who has been carrying on his usual occupation, must be distinguished from coronary thrombosis where the pain is severe, and from pulmonary embolism, in which the expectoration occurs later and contains more blood.

Treatment. When the disease is of circulatory origin the apparatus suggested by Plesch should be used. The principle is to apply a positive pressure to the inside of the lungs so that the over-active right ventricle will be hindered. The air is supplied by a motor fan to a tightly fitting mask and escapes into the outside air through a resistance (**49**). The author now uses an electrolux blower, and a water manometer attached near the mask indicates the pressure, which should be 3 or 4 inches of water. Remarkably good results have also been obtained with the oxygen tent. In very acute cases venesection may be tried.

PNEUMONIA

Inflammation of the substance of the lung, as opposed to the bronchial tubes, is called pneumonia. As an *acute* disease it leads to consolidation by exudation into the air vesicles of inflammatory products, which are usually absorbed in the course of recovery. In a *chronic* form it causes a dense fibrous transformation of the interstitial tissue, which is permanent. Of acute pneumonia two typical forms can be distinguished from one another by the following features: *Lobar pneumonia* occurs at all ages, but more often in adults, affects large portions of the lung at the same time, and has all the characteristics of a specific infectious disease, with a limited duration, a quick recovery, and sometimes epidemic prevalence. *Broncho-pneumonia* affects chiefly infants, children, and elderly persons, invades several small areas of the lung, and is much less definite in its course and modes of onset and termination.

Experimentally, pneumonia has been produced in rabbits by insufflating one

main bronchus with cultures of pneumococci (Types I. and IV.) of varying virulence. When the virulence is low the cocci are taken up or side tracked by those alveolar systems that open directly out of the walls of the larger bronchi, and broncho-pneumonia, with proliferation of the alveolar endothelial cells, results. With higher virulence the cocci increase rapidly and spread out into the lung tissue, producing a lobular pneumonia, and with still higher virulence a lobar pneumonia with polymorphonuclear reaction and occasionally a fatal lymphangitis; while if the dose is too large they may spread through the pleural surface, causing pleurisy with effusion and pericarditis. With the highest virulence of all a rapidly fatal septicæmic invasion takes place and the lungs show only a patchy serous exudate, desquamating alveolar cells and small hæmorrhages, without any polymorphonuclear reaction, similar to the appearances observed in very fatal epidemics in schools. Positive blood cultures are often obtained during the first two or three days, but not later; and it has been found that the cocci are within the leucocytes; only in cases of fatal septicæmia are they free. This suggests that a positive blood culture at the beginning of a specific fever, *e.g.* cerebrospinal fever or typhoid, cannot be taken to prove that the infection is primarily blood born; it may only mean the escape of phagocytes into the blood-stream in the early period when the bacteria are rapidly proliferating in a particular focus, while metastatic foci, such as "rose-spots," are only places where these circulating phagocytes happen to be held up (**9**). These observations suggest that all pneumonia is the result of infection through the air passages, and this is now generally recognised. Evidence has been brought forward that the primary lesion is due to blocking of the larger bronchi by plugs of sputum, which are more viscous in the case of the pneumococcus than the streptococcus; thus the latter causes a broncho-pneumonia. X-ray shadows in lobar pneumonia (Plate 3) are often wedge-shaped like an infarct; the diaphragm on the affected side is raised; the heart is never displaced to the opposite side. The virulent pneumococci spread peripherally into the lung; but if the non-virulent Type IV. is present there is massive collapse instead of pneumonia. Much experimental evidence has been brought forward in favour of this view (**49**).

LOBAR PNEUMONIA (PNEUMOCOCCAL)

(*Croupous Pneumonia*)

Ætiology. The disease occurs in both sexes, but it is twice as common in males as it is in females, the difference between the two sexes being least marked in the very young, and in old people. It is seen also at all periods of life from infancy to old age, but it is more frequent in adults up to middle age. It occurs much more often in the winter and spring than in the summer and autumn, when the temperature is undergoing sudden changes, when the winds are east or north-east, or when the weather is wet or cold. Habits and occupations which involve exposure dispose to pneumonia. Intemperate habits also dispose to it, and greatly increase its mortality. One attack does not exempt from another; indeed, pneumonia is said to have occurred as many as fifteen or twenty times in the same patient, but more than two attacks are not very common.

Cold or chill often seems to be a determining event and there is commonly a history of preceding respiratory catarrh. Cases of direct contagion appear to be undoubted; and many instances are recorded in which pneumonia has spread rapidly through villages, large buildings, or households, precisely like an epidemic fever. Lobar pneumonia also occurs as a complication or sequela of some other diseases, such as mitral disease, acute nephritis, and diabetes; but it is rare as a complication of tuberculosis. Traumatic pneumonia sometimes occurs from a blow on the chest, if the injured lung becomes secondarily infected. In

pneumonia the primary seat of infection is the lung; the *pneumococcus* is found in the lungs and sputum, and in severe cases in the blood, possibly due to escape from the lungs; hence this bacteriæmia hardly constitutes *septicæmia*. The four types of the pneumococcus have already been described (*see* p. 56).

Morbid Anatomy. In pneumococcal pneumonia, the part of the lung affected is converted from a spongy structure into a solid mass. In the earliest, or first, stage of *congestion* or *engorgement*, the lung is heavy, reddish brown in colour, exudes a frothy, reddish serum on pressure, and breaks down more readily than in health. The capillaries are dilated and tortuous from distension with blood, and minute hæmorrhages may be present. In the second stage—called *red hepatisation*, from the resemblance which the consolidated lung bears to the liver—the organ is of a dull red colour, finely granular on section, completely airless, solid, sinking in water, but breaking down readily under the pressure of the finger. The contents of the alveoli, which may be detached in fine granular masses, are seen to consist of fibrin, containing some red blood corpuscles and leucocytes. What has actually happened is that the walls of the alveoli have been so distended with fluid exuded from the capillaries that the endothelial cells have given way, and the air spaces have become flooded with fluid that soon coagulates (**42**). The third stage, *grey hepatisation*, is also characterised by its solidity, but the colour is greyish yellow or simply grey, and the surface is less granular than that of the red stage. Microscopically it differs from the latter in that the air cells and alveolar walls are crowded with leucocytes, while fibrinous exudation and red corpuscles are in very small quantity. The change of colour is attributable to the leucocytes in the alveoli. A fourth stage, that of *purulent infiltration*, is also described; but this is only an extreme condition of grey hepatisation. The lung is softer, yellowish in colour, and yields to scraping or pressure a quantity of yellow purulent fluid, which is provided by the disintegration of the infiltration filling the air cells, the leucocytes becoming fatty and granular. A true *abscess*, however, is exceedingly rare as the result of typical acute pneumonia. It is doubtful whether the stage of purulent infiltration is ever reached in cases that recover; it is true, recovery, or *resolution*, is sometimes accompanied by physical signs (*redux crepitation*) which indicate that the exudation is softening into fluid. But many patients get well without such evidence, and with so little expectoration that the removal of the exudation can only be explained by its absorption directly by the lymphatics; in but few cases the amount of sputum is very considerable.

The inflammation of the substance of the lung is accompanied, in a large proportion of cases, by acute pleurisy, and the double lesion may be spoken of as *pleuro-pneumonia*, but the name is not generally used except for cases in which the pleurisy is clinically a prominent feature.

Localisation. Pneumococcal pneumonia is nearly always partial, affecting the base more often than the apex, and the right lung somewhat more often than the left. X-ray examination usually shows a wedge-shaped shadow of variable size (Plate 3, A, B, C), and this has long been recognised in the case of children (**33**); occasionally the shadow forms a band in the periphery parallel to the chest wall. Infiltration may be present without physical signs. The shadow may imitate epituberculosis, but it disappears much quicker. Sometimes both lungs are affected, but the disease commonly begins in one earlier than the other.

Symptoms and Physical Signs. *First Stage.* A rigor or shivering (*69*) occurs, in a large proportion of adult cases, as the first definite sign of illness; the temperature rises to 102°, 103°, or 104°, and there is well-marked pyrexia, with malaise, loss of appetite, vomiting (*33*), furred tongue, and in some cases an eruption of herpes on the lips (*17*), which is to be regarded as a favourable sign. Children often have convulsions, but rigors uncommonly. The symptoms may

(The *italic* numbers in brackets refer to percentage incidence of symptoms in 558 cases of lobar pneumonia among soldiers at Aldershot, 1915–17 (**25**).)

be at first vague, accompanied perhaps with pain in the head (*35·6*) or pains all over (*9*), or the implication of the lung may be indicated by shortness of breath and severe pain in the side (*60*), attributable to pleurisy. Auscultation at this early period may detect nothing, but sometimes there is heard a fine dry crepitation, which has been compared to the noise produced by rubbing between the finger and thumb a lock of hair near the ear; it is mostly heard towards the end of a deep breath, but sometimes during the whole of inspiration; and it is explained by the separation of the walls of the alveoli, rendered unnaturally adhesive. More often the first deviation from the normal is a marked diminution or loss of the vesicular murmur over the area which subsequently gives the signs of the second stage, or consolidation. The percussion note may be still unaltered, or only slightly less resonant than normal. In other cases a tympanitic note is obtained. This is liable to occur when the pneumonic process is central to begin with, so that there is relaxation of the surrounding lung (as in Skodiac resonance).

Even as early as this there may be slight cough, with the characteristic *rusty sputum*. This is brought up as a mass of transparent, airless, jelly-like mucus, of a yellow, orange, russet-brown, or even bright red colour, and extremely viscid, so that it adheres to the side or bottom of the vessel with little or no tendency to flow. The pneumococcus may be detected in the sputum by Gram's method of staining; but it is not at first abundant, and the sputum consists chiefly of hyaline mucus, sero-albuminous exudation, some red corpuscles, small alveolar cells, large endothelial cells, and a few polymorphonuclear cells. Hæmoptysis (*1·6*) is an occasional feature.

The physical signs of the *second stage*, or stage of consolidation, are often rapidly developed. There is decided dulness over the part of the lung affected. Over the same area there is high-pitched bronchial breathing, at first soft and distant, but in a short time much louder. If the patient speaks, there is bronchophony, the words uttered being often distinctly heard, and apparently shouted up into the stethoscope; whispered words are also distinctly transmitted. The fine crepitation heard as an early sign may still be audible in portions of lung which are being involved by the spreading inflammation; but over areas which give loud bronchial breathing and bronchophony no râles will be heard unless there is associated bronchitis, and then they will be consonating. Tactile vocal fremitus is sometimes increased and sometimes diminished. There is evidence that in nearly all cases the latter is due to a thin layer of fluid in the pleura (**26**). During this development of the physical signs the patient is necessarily confined to his bed, but he often has orthopnœa; his cheeks and forehead are flushed; his eyes are bright, and show a vivid consciousness of his distress; his breathing is quick, and the respiration may rise to 40, 50, 70, or even 80 in the minute. The pulse is quickened, but not in proportion to the respiration; it may be 100 to 120, or somewhat higher; thus the pulse respiration ratio is altered from the normal 3 : 1 or 4 : 1 to 2 : 1 or $1\frac{1}{2}$: 1. The temperature is maintained generally at a high level, 103° to 105°, with little variation; and the skin is dry, and gives a sense of pungent heat to the hand placed on it. The blood pressure is generally a little below the normal. The cough, which is usually, though not always, present, is not very frequent, is hard, dry, and often painful; and the viscid, rusty sputum is brought up with difficulty. The urine is scanty, high-coloured, acid, and deposits urates; the chlorides are much diminished and may be absent, and there is not infrequently a small quantity of albumin. There is generally leucocytosis with increase in the polymorphonuclear cells, which persists for a long time in severe cases. The patient may become delirious (*4*), especially at night. Lividity or cyanosis may be a striking feature. It has been found in such cases that the saturation of the arterial blood with oxygen is diminished, being 80 per cent. instead of 95 per cent., which is the normal (Stadie). This desaturation is due to the arterial blood being a mixture of aerated blood from

the healthy part of the lung and non-aerated blood from the diseased lung. Later cyanosis often wears off, when the circulation through the diseased lung is slowed.

The general condition of the patient continues very much the same for some days, or more often there is an increase in the severity of the symptoms. The pulse and respiration are quicker, the temperature continues high, the tongue becomes drier and browner, and the delirium at night is more decided. The physical signs are generally observed to alter from day to day, indicating the spread of the consolidating process, so that crepitation and bronchial breathing extend higher and higher up to the chest, until the apex is involved, and the physical signs may be apparent in front under the clavicle.

When the illness is apparently at its worst, improvement takes place, in many cases quite suddenly. On the sixth, seventh, or eighth day, in a large proportion of cases, the temperature, the pulse, and respiration fall, in the course of twelve or eighteen hours, nearly to their normal limits; the tongue becomes moist; and the patient feels himself in all respects better. This *crisis* (*56·4*) is accompanied with profuse sweating. In about half the cases the fever ends more gradually (*lysis*), occupying from four to five days while falling from the acme to normal.

The physical signs gradually clear up after the temperature is normal. *Redux crepitations* are heard in this stage. They are rather coarse crackling or bubbling râles, due to the loosening of the exudation and its presence in the tubes. With the change in the lung, the sputum is also altered, losing its characteristic tinge, becoming yellow or green, muco-purulent, and at the same time less viscid.

Type I. pneumonia, which accounts for 30 per cent. of cases, especially in young adults, usually presents the classical symptoms ending by crisis. In Type II. the symptoms are more severe and there is often no crisis. Type III. is particularly liable to attack the elderly. Type IV. occurs at any age. In fatal cases death occurs from failure of the heart, or from œdema of the hitherto unaffected lung, or from both combined. All the symptoms are aggravated—the respirations are increased in frequency; the pulse is quick, small, and feeble; the face becomes livid or cyanosed; the physical signs of dilatation of the right ventricle may be observed; the tongue is dry, brown, and cracked; delirium is more or less continuous, and muttering and coma gradually supervene. On auscultation loud, coarse râles are heard on both sides of the chest. As the patient becomes feebler the temperature falls, the skin becomes cold and is bathed in profuse perspiration. Death commonly takes place during the height of the illness, between the fifth and the tenth days. Occasionally, however, a pneumonia runs a fatal course in two or three days.

Complications and Sequelæ. The former are mostly the result of secondary pneumococcal infections, spreading directly from the lungs to neighbouring structures, or being carried by the blood stream. *Pleurisy*, with formation of lymph or serum, is hardly a complication, as it is present in practically every case. *Empyema* (*20·8*) is not so common, but it should be suspected if fever continues into the third week, with dull percussion note, and disappearance or change of the bronchial breath sounds. Rarely a pneumothorax occurs in the course of pneumonia, from rupture of air vesicles into the pleural cavity. *Pericarditis* (*2*) is frequently associated with empyema on the left side. *Peripheral neuritis*, *nephritis* (*0·5*), *peritonitis*, *suppurative meningitis* (*1*), and *arthritis* (*0·5*), are among the rarer pneumococcal complications. Rarely a true *pneumococcal pyæmia* has occurred with suppurative arthritis and pustules and abscesses under the skin, yielding a thick greenish pus containing pneumococci in pure culture. *Malignant endocarditis* (*0·72*) (especially of the aortic valve) has been seen in association with pneumonia, and as a result of its specific organisms. In a small number of cases there is pronounced *jaundice* (*1·3*); a faint icteric tinge is more common. Acute *dilatation of the stomach* sometimes

occurs in the course of the illness, and *parotitis* may ensue in severe cases. *Chronic pneumonia, gangrene* and *abscess of the lung*, and *bronchiectasis* are rare sequelæ.

Diagnosis. In the early stages of rigor and high fever pneumonia may be indistinguishable from other *acute illnesses*, such as typhoid, scarlatina, or small-pox. Frequently the pain or distress in one side of the chest will indicate acute disease there, and the absence of breath sounds, or the fine crepitations, at one spot, followed by dulness, bronchial breathing, and bronchophony, will show the nature of the illness. But the pain may be very misleading; it frequently extends to the abdomen, or is felt chiefly in the abdomen, so that *appendicitis*, *peritonitis*, or *cholecystitis* may be first thought of. A careful watch on the pulmonary bases is required to guard against error. In other cases a short cough, with expectoration of rusty sputum, will occur before the development of the physical signs. These last may, indeed, be delayed for five or six, or even ten, days, and they may require much looking for and be first found in unlikely places, such as over the scapula, or at the top of the axilla. The absence of rashes characteristic of the exanthemata, the rapidity of respiration out of proportion to the pulse, the flushed face and bright eye, the characteristic sputum, and the presence of herpes about the mouth are useful points in making a diagnosis. An examination of the blood may help, as the presence of leucocytosis excludes typhoid fever, malaria, and influenza. The Röntgen rays are also of value, as already described.

When physical signs appear, it has to be determined whether pneumonia or *pleuritic effusion* is present, or a combination of both. The diagnosis of these two conditions from one another is dealt with under Pleurisy. The diagnosis from broncho-pneumonia is considered later (*see* p. 158).

Prognosis. The average mortality of lobar pneumonia is about 18 per cent. It is very low in young children, but increases with age. The disease is more fatal to the intemperate, and to those who have been insufficiently fed. Early or violent delirium, failing pulse, lividity and cyanosis, are all symptoms of bad augury. Type III. pneumococcus, against which there is no serum available, is responsible for the gravest cases and the mortality is up to 40 per cent. The prognosis in Type I. cases is better than in Type II., the mortality being 10-15 per cent. in the former and 20 per cent. in the latter. The mortality of Type IV. is 10 per cent. The mortality is higher in America.

Treatment. The patient of necessity takes to his bed, and generally in the height of the disease requires to be supported in a semi-recumbent position by means of pillows or bed-rest. Physical rest with freedom from anxiety is one of the most important elements in treatment. Unnecessary medical examination should be avoided. He should have abundance of warm fresh air, in a freely ventilated room, no less than in any other infectious disease. A diet suitable for a febrile illness should be given (*see* p. 21). Milk will naturally form an important element in it; but eggs and cereals, in the form of milk puddings, Horlick's malted milk, fish or minced chicken, etc., may be added. It is important to consult the patient's taste in such a matter. Beef tea or mutton broth, though not foods in themselves, may be appreciated.

In early stages the bowels should be opened, and a free action of the skin should be encouraged by the use of acetate or citrate of ammonium, with small doses of Dover's powder. This last will relieve the pleuritic pain, or opium may be more frequently given in small doses (3 to 5 minims of tincture) with the saline. Local applications such as antiphlogistin, an ice bag or a poultice may also relieve pain. In mild cases this may be all that is required, but in the severer cases delirium and increasing prostration will have to be met. For the former chloral, chloralamide, and potassium bromide may be employed; but when there is much dyspnœa chloral must be given with caution, because of its depressing effect upon the heart and respiration. For the same reason, morphia must be sparingly used in the later stages. The subcutaneous injection of hyoscine hydro-

bromide ($\frac{1}{100}$ grain) is often useful and safer. For the increasing cardiac failure digitalis is often given, and small quantities of brandy or other spirit, up to the extent of 3 or 4 ounces daily. Where there is right-sided failure, venesection may be required; but oxygen is the best treatment for all these complications. Where there is much secretion in the tubes, ammonium carbonate (5 to 7 grains every three or four hours) may be given. Recently artificial pneumothorax has been employed, and has been successful, in averting pleuritic pain (27). When the crisis is past, and the temperature has fallen to the normal, the treatment requires simply to be directed to the strengthening of the patient by the administration of quinine and other tonics.

It is now generally agreed that Felton's concentrated anti-pneumococcal serum can save life and even abort the disease. At present it is expensive and the quantity limited, so that it is reasonable to limit its use to patients over seventeen, when the prognosis is bad, the special indications being, sudden onset with severe prostration, weak rapid pulse, poor temperature and a leucocyte response, and positive blood culture. It is essential to type the pneumococcus; but this is a matter of a few minutes, and it is only of value against Types I. and II. A Type I. and a Type I. and II. mixed serum is available. It should only be given within the first five days of the disease and the dose in Type II. cases should be double that in Type I. In the latter 20,000 units are slowly given intravenously, diluted in saline, which has been freshly prepared to avoid thermal reactions. Second and third doses of the same size are given at eight to twelve-hourly intervals, and a fourth or fifth dose may occasionally be required.

Administration of Oxygen. When there is lividity or cyanosis oxygen should be given. For practical purposes two methods are available: (1) *The Nasal Catheter.* The cylinder furnished with a fine-adjustment regulating valve is connected first with a Woolf's bottle containing water and then with a rubber catheter which is pushed right to the back of the nose. The connecting tubing should be wide—not much less than $\frac{1}{2}$ inch in diameter. The rate of supply of oxygen is regulated by keeping the bubbling in the bottle at a constant rate. It can be measured by filling a pint measure with water and holding it inverted in a basin of water. On placing the catheter beneath the measure the water is displaced by oxygen. It should take about twenty seconds to collect a pint in the case of an adult. The rate for children may be slower. Instead of the nose the catheter may be pushed as far back as possible through the mouth. A double tube with its nozzles just inside each nostril is another plan; the Müller valve, as used by Davies and Gilchrist, which stops the flow of oxygen during expiration and prevents waste (49) is not really necessary. The wasteful and ineffective way of delivering oxygen through a funnel should never be used.

(2) *The Oxygen Tent.* The principle of the tent is that the patient lies in an atmosphere enriched with oxygen (40 to 60 per cent.), while the carbon dioxide, moisture and heat are removed. A number of different tents have been described. In the tent in Plate 4, A, the heat and moisture are removed by ice-containers, which are let in through the roof of the tent, while the CO_2 is removed by ventilating the atmosphere through a canister of soda lime by means of an "injector" screwed into the head of the cylinder, so that this pressure of oxygen in the cylinder provides the motive power (49). Clinical apparatus is provided for determining the percentage of O_2 and CO_2 in the tent. There is experimental evidence from arterial puncture on pneumonia patients, that the tent is more effective than the nasal catheter; lives have been saved with the tent, which would almost certainly have been lost if treatment with the catheter had been persisted in. The writer has saved 20 out of 28 grave cases of pneumonia by means of the tent. The question arises whether CO_2 should be given in addition to oxygen. This can be effected by preventing complete absorption of CO_2 in the circuit, so that the patient partly rebreathes the CO_2 he has himself produced. In the writer's opinion CO_2 may perhaps be given in the early stages of pneumonia, to increase the

depth of breathing and promote a slight cough and to loosen the viscid plug of mucus, which is the primary cause of the condition, as already described. By this means the disease might be aborted. But in the later stages, when the heart is fatigued, oxygen alone should be used. It is a remarkable fact that pleuritic pain often disappears in the tent.

FRIEDLÄNDER PNEUMONIA

From observations on cases in which lobar pneumonia has been due to the *Bacillus pneumoniæ* of Friedländer, it appears that it is generally a severe disease with a bad prognosis, that the lung in a fatal case oftener presents a blackish-grey than a red colour, and that the section is covered with a slimy mucus. The alveoli contain numerous bacilli and desquamating epithelium. Suppuration and gangrene are much more frequent than in the usual form, and the temperature is more variable. The bacillus of Friedländer may be accompanied by the pneumococcus, and it may be the cause of a lobular as well as a lobar pneumonia.

BRONCHO-PNEUMONIA

(*Catarrhal, Lobular or Interstitial Pneumonia*)

Ætiology. (1) *Primary Broncho-pneumonia.* When the pneumococcus in pure culture attacks the lungs in children under five years old, it may produce a typical lobar pneumonia, but it more often attacks the alveoli in patches over the lung. Such cases have been called *primary broncho-pneumonia* (West) or *primary lobular pneumonia.* Except for the patchy distribution in the lungs, these cases resemble the lobar pneumonia just described, and there is no associated bronchitis. There is no necessity to say anything more about them. (2) *Broncho-pneumonia* proper, sometimes called *secondary broncho-pneumonia* or *acute interstitial pneumonia,* always starts from inflammation in the smaller bronchi, which spreads into the surrounding air vesicles. It occurs commonly in children under three years of age. It is a frequent complication of measles and whooping cough, and also follows other infectious diseases (scarlet fever and influenza, etc.). Ill-nourished town-dwelling children are thought to be more liable to broncho-pneumonia, and it is probable that rickets also disposes to it. Broncho-pneumonia occurs in adults from inhalation of foreign particles, especially septic materials from the throat, into the lungs (*inhalation pneumonia*) ; it is a common result of the spread of diphtheria down the bronchial tubes to the bronchioles ; it is often a terminal event in any long-continued wasting disease, especially in elderly people who have been obliged to lie recumbent for weeks ; when it attacks the most dependent parts of the lung it is known as *hypostatic pneumonia.* It may occur after operations under general anæsthesia, and it is a frequent cause of death in those who have been nearly drowned. Carcinoma of the œsophagus may be fatal by invading the lung and setting up pneumonia. But septic particles may reach the lung by the blood vessels, and pyæmia is characterised by its suppurative pneumonic foci. To many of these cases the term *septic pneumonia* is applied.

The bacteriology of broncho-pneumonia is complicated, and a great number of bacteria have been found in various combinations. A specific fever, such as measles or influenza, is to be regarded as exerting a depressing effect on the resistance of the individual, so that the lungs are invaded secondarily by various organisms. In the United States army the hæmolytic streptococcus was found to be the most important agent and the most fatal ; but the pneumococcus, *B. influenzæ* and *Staphylococcus aureus* were also present on occasions. Friedländer's bacillus and in cases of diphtheria the Klebs-Löffler bacillus also occur.

Morbid Anatomy. In broncho-pneumonia the consolidation is scattered throughout the lung in the form of nodules, often separate, but tending to

coalesce, so as to form larger masses (*confluent broncho-pneumonia*), but even then still to be distinguished by the eye from each other. On section the solid lung is seen to consist of a number of small grey foci surrounded by dark red zones of hæmorrhage, œdema and collapse. The lung is soft and friable, and on squeezing a bead of pus exudes from the small tubes. The process is sometimes called *splenisation* of the lung. Microscopically the characteristic lesions are interstitial inflammation affecting the bronchial and alveolar walls, and peribronchial lymphangitis, the infiltrating cells being polymorphs in the severer cases. The lumen of bronchus and alveolus becomes filled with catarrhal contents, *i.e.* chiefly large endothelial cells; while in cases of some duration there is a formation of new fibrous tissue in the bronchiolar and adjacent alveolar walls. Hence the name *interstitial broncho-pneumonia* which is often applied to the condition. The streptococci swarm in the bronchioles and thrombosed lymphatics. When the inflammation reaches the surface there is usually some pleurisy. In very acute and fatal cases there is no fibrous tissue formation, and the streptococci are seen invading the alveoli; abscesses may be formed in the lung.

Symptoms and Physical Signs. The former are cough, dyspnœa, and pyrexia; the latter vary with the extent and position of the separate lesions. If the child has already a cough, with rhonchi and râles over the chest, from a preceding bronchitis, the implication of the alveoli may be indicated by a rise of temperature to 102° or 103°, by the cough becoming short, dry, and painful, and by the râles becoming more abundant and taking on a consonating character. But in many cases there are no rhonchi, and the physical signs consist of one or more areas, more or less extensive, in one or both lungs, in which rather sharp crackling râles are heard, with little, if any, change in the percussion note, or areas, also irregular in distribution, over which there is dulness, with bronchial breathing and bronchophony due to the aggregation of a sufficient number of consolidated lobules. Such areas may enlarge or diminish, and spread or clear up as the disease progresses. The sputum consists of mucus or muco-pus with or without streaks of blood, but young children usually swallow it. Exceptionally there may be free hæmoptysis.

The course of the disease is not so definite as in pneumococcal pneumonia. It may end in a week, but often goes on for three or four weeks, or even more. The temperature is generally remittent or even intermittent, and usually falls by lysis; it may be very irregular. The breathing is rapid, and is *inverted*, which is often valuable in diagnosis. There is a quick inspiration, the breath is held for half a second, expiration then occurs with a grunt, and inspiration again follows without an interval. The lower intercostal spaces are depressed during inspiration. There is much cough; the face is flushed, or in severer cases pale and livid. The pulse is quick and small. Delirium is often present. The physical signs frequently alter in the course of the illness, indicating the clearing up of disease at one part, and fresh outbreaks in others; the disease often attacks both lungs. Recovery is mostly gradual, and not sudden, as in pneumococcal pneumonia. Convulsions may precede death.

Diagnosis. Broncho-pneumonia may be confounded in its early stages with other *acute illnesses* characterised by high fever, such as typhoid fever; and the liability of children to marked cerebral symptoms from any acute illness may lead to a diagnosis of *meningitis*. The preceding bronchitis and the predominance of the chest symptoms may prevent a mistake, but an opinion may have to be suspended for a few days. Long-continued broncho-pneumonia may give rise to a suspicion of *tuberculosis*, in which high fever, universally scattered râles, lividity, and cough are prominent symptoms. In *capillary bronchitis* there are dyspnœa, lividity, and râles, but the râles are often confined to the bases; there is no bronchial breathing. There may be profuse purulent expectoration. The diagnosis of confluent broncho-pneumonia from lobar pneumonia may be difficult. In the latter case the signs over the lungs are more uniform, and there

may be a crisis. In broncho-pneumonia there is bronchiolitis, as indicated by consonating râles of varying coarseness in both lungs, and since the patches do not resemble one another in the state of development of the inflammatory process, the breath sounds will change between puerile and fully developed bronchial breathing of varying pitch. But the main distinction is that in broncho-pneumonia the fever is longer and resolution slower. A typical radiogram is shown in Plate 4, B, p. 156.

Prognosis. Though this form of pneumonia is much more fatal than the pneumococcal variety, the prognosis in any given case must depend upon the general progress of the symptoms. Cases that are apparently desperate often recover, and an unfavourable opinion should be given with some caution. In the broncho-pneumonia of old people, and in that which is due to the inhalation of solid particles, the prognosis is more grave.

Treatment. The treatment may be conducted on the same general principles as in the case of ordinary pneumonia. The room should be well ventilated, with free access of air to the patient; open-air treatment has been tried with success. Oxygen should be given continuously for long periods if there is respiratory distress or lividity; the oxygen tent is especially suitable. Tr. belladonnæ in doses of 3 to 5 minims may be given to quite young children in order to dry up the pulmonary secretion. Injections of atropine are also sometimes given. Expectorants are not generally approved of for young children, as they have no power of coughing up sputum. Severe cases often require stimulants to be administered rather freely—*e.g.* for a child three or four years old 20 minims of brandy every hour; or 1 or 2 minims of liquor strychninæ may be injected two or three times daily at this age, and smaller quantities in infants.

ABSCESS OF THE LUNG

Abscess may be a result of pyæmia, and of acute pneumonia. It may result from the same agents that cause gangrene of the lung, *q.v.*, or from the spread of neighbouring suppuration, such as empyema, or subdiaphragmatic abscess, or hydatid disease, or actinomycosis. The differential diagnosis of abscess from consolidation of the lung is difficult until the abscess has burst and discharged pus. Then the cardinal signs are (1) purulent sputum, which may be foul; (2) cough and explosive expectoration; (3) elastic tissue with alveolar arrangement in the sputum; (4) circumscribed dulness on percussion; (5) X-ray appearance of a cavity with a fluid level. When the fluid contents of the cavity have been coughed up there may be the usual signs of a cavity, such as tympanitic resonance if the cavity is large, cavernous or amphoric breathing, metallic tinkling, and pectoriloquy. The multiple small abscesses of pyæmia are not recognisable as cavities; indeed, their presence is usually masked by the surrounding consolidation, or pleuritic effusion. (Plate 5.)

Prognosis and Treatment. *Bronchoscopy* has revolutionised the outlook; after localising the abscess by observing from which bronchus the pus is coming, the principle is to remove the obstruction, which may be complete, partial, or of a valvular nature; pus is sucked out of the abscess cavity and gomenol oil may be instilled into it. After removing the main mass of pus, cultivation of the bottommost layer may yield the infective agent in pure culture, so that a vaccine can be prepared. Vincent's spirillum and fusiform bacillus are not uncommon. The size and shape of the cavity may be determined by instilling lipiodol through the bronchoscope. A single bronchoscopy may result in healing; otherwise it may be repeated. Other factors leading to suppuration have been found by bronchoscopy to be weakening of the cough reflex, overdosing with morphia and atropine, rarely the presence of a foreign body, or non-malignant neoplasm, such as a polyp and rare infections like blastomycosis and actinomycosis (**64**).

FIBROID LUNG

(*Fibrosis of the Lung, Chronic Pneumonia*)

Ætiology. This form of lung disease is comparatively rare except in children, the great majority of chronic inflammations of the lung tissue in adults being associated with tubercle. The cases in which a chronic inflammation is independent of tubercle, and to which the name fibroid lung is given, arise only rarely from a preceding acute lobar pneumonia; but broncho-pneumonia is a more frequent antecedent. Chronic bronchitis and pleurisy are also causes in other instances.

An important class of fibroid lung is that occurring among workers in various factories and mines, known as *pneumokoniosis*. Here the repeated inhalation of an atmosphere laden with the dust of coal, metal, *e.g.* emery, quartz, cotton fibre, fluff, etc., provides a lifelong source of irritation. The disease has received different names according to the particular irritant concerned—*anthracosis* (coal dust), *silicosis* (silica, described later), *asbestosis* (asbestos).

Morbid Anatomy. The characteristic feature of the lung is fibrosis. When fibroid lung results from pneumonia or bronchitis the strands of fibrous tissue, which traverse the lung, originate from the inflammation in the walls of smaller bronchi and from peri-bronchial lymphangitis (as described in broncho-pneumonia), because the lumen of the tubes becomes entirely obliterated with granulation tissue. This *obliterative bronchiolitis* is thus essentially the same process as that which produces bronchiectasis, except that in the latter case the larger tubes have been affected and cavities formed. Hence bronchiectasis and fibroid lung are commonly associated, but fibroid lung appears alone, if the inflammatory process is confined to the smaller tubes (**10**). With the growth of the fibrous tissue contraction takes place, and the lung may be reduced to two-thirds or half its natural size. The contraction of the lung leads to displacement of organs, and, as usually only one side is affected, the mediastinum is pulled in that direction. In late stages the whole lung may be converted into a dense mass of fibrous tissue, of various shades of grey from the presence of pigment, tough in consistence, and creaking under the knife. In pleurogenous cases the mode of production is probably different, and in these cases the lung is fixed to the chest by a thick fibrous layer.

Symptoms and Course. The disease is generally chronic, and patients in whom it is recognised have usually complained for some months or years. The patients are short of breath, and have cough and expectoration, which vary with the extent of the cavities in the lungs (*see* Bronchiectasis). The patient is often thin, but may be well nourished, and is at any rate for a time free from the fever, night sweating, and general constitutional disturbance observed in phthisis. Hæmoptysis is often present. The disease is commonly unilateral; the corresponding side of the chest is retracted, the shoulder depressed, and the angle of the scapula tilted outwards; the impulse of the heart is shifted towards the affected side, and the healthy side of the chest is hyper-resonant. The affected side expands but little; it is dull on percussion. There is deficient air entry when the small tubes are obliterated, otherwise there is bronchial breathing, bronchophony, pectoriloquy and consonating râles. Tactile vocal fremitus is variable. The lung affected shows some opacity to X-rays, while the ribs show "roof tiling" (*see* p. 168). Thickening or *clubbing* of the finger ends (*see* p. 565) is often pronounced. Eventually there may be right-sided heart failure.

Diagnosis. The condition has to be distinguished from phthisis, from chronic pleurisy with effusion, and from malignant growth in the chest. From *phthisis* the absence of fever and constitutional disturbance is the chief distinguishing feature; the disease is often rigidly unilateral and basal, whereas

phthisis, which is usually apical, rarely reaches an advanced stage in one lung without affecting the other; and tubercle bacilli are not found in the sputum. *Pleuritic effusion* of old standing with retracted chest may closely resemble the fibroid lung, and exploration with a needle may be required to clear up the diagnosis. The history with *intrathoracic carcinoma* is likely to be short. There may be pains and extensive consolidation, and signs of pressure or displacement of the heart. X-ray should always be carried out, and bronchoscopy.

Prognosis is ultimately bad, but the course may be very slow, extending over ten or fifteen years. Children sometimes recover. Death may take place from failure of the right heart, or from the gradually increasing exhaustion which follows profuse discharge, or from metastatic abscesses, in particular cerebral abscess.

Treatment. The patient should be placed under the best possible climatic and hygienic conditions. He should have bracing air in the summer, but a warm climate in the winter; avoid exposure to chills at all times; and have nourishing diet and tonics, such as quinine, iron, and cod-liver oil. Cough, expectoration, and other symptoms should be treated as they arise in the same manner as directed under Phthisis and Bronchitis and Bronchiectasis.

Anthracosis. The coal miner's is a healthy life, which is surprising considering the amount of carbon that is deposited in the lungs, making them black to the naked eye. Carbon seems to protect against tuberculosis. In spite of this, in certain areas, such as S. Wales, silicosis occurs and causes death from chronic pulmonary disease, while the percentage of silica in the lungs is much above normal in miners who have died from other causes (**51**).

Silicosis. This is a widespread industrial disease, for which the workman can claim compensation, and which has been intensively studied in S. Africa, owing to its prevalence in the Rand gold mines (**52**). In the *simple type* the silica causes nodular fibrosis of the lungs and root glands; this forms a characteristic uniform discrete mottling on the X-ray film in the upper half of one or both lung fields, and later becomes generalised; the opacities are usually intenser and better defined than in generalised tubercle, though the resemblance may be close. An early suspicious appearance is a generalised arborisation, like a leafless tree, due to increased density of the bronchial or possibly the vascular tree in the lungs. At first there are no symptoms, but later there is a cough, with recurrent "colds," shortness of breath, moderate expectoration, but no emaciation; there may be pleurisy. In the *infective type* tuberculosis is added, because after inhalation the silica becomes converted by hydration into colloidal silicic acid. Mineral silicates also become decomposed by the CO_2 of the tissues into silicic acid. The latter causes a granulomatous mass to be formed, consisting of a central area of necrosis, surrounded by inflammatory layers. Tubercle bacilli, present in such small numbers that the tissues would ordinarily deal with them, multiply rapidly in the central area, become too many for the local defences and so spread to other parts (**50**). The opaque areas in the X-ray film become more irregular in size and distribution, and hilar shadows become prominent, and the case becomes one of fully developed open pulmonary tuberculosis. Prevention consists in blasting at the end of the day's work to avoid dust, water to lay the dust and good ventilation.

Asbestosis. Asbestos is iron and aluminium silicate. The disease is very insidious, developing after six to twelve years' work. The lower lobes are especially affected, showing a diffuse fibrosis with increased thickening of the pleura. The diaphragm becomes thick and of cartilaginous hardness and invades the base of the lung, giving a very characteristic irregular or woolly appearance of its upper surface in X-ray films. Eventually bronchiectasis supervenes; there is some doubt as to whether there is any particular liability to tuberculosis. The sputum contains characteristic "asbestosis bodies"; otherwise the symptoms resemble those of fibroid lung.

GANGRENE OF THE LUNG

This is a comparatively rare disorder, which may arise, however, in a variety of circumstances. It is one of the terminations of acute lobar pneumonia, especially in cases dependent on Friedländer's bacillus, and it occurs rarely in phthisis; it may result from the invasion of the lung by adjacent diseases like carcinoma of the œsophagus, abscesses, and suppurating hydatid cysts, from the pressure of aneurysm on the root of the lung, and from injuries to the chest setting up pneumonia or empyema; as a result of foreign bodies lodged in the bronchus, and from the presence of secretions retained in dilated tubes; from the passage into the lung of particles from septic diseases in the mouth, throat, larynx, œsophagus, such as carcinoma of the tongue or larynx, sloughing of the tonsils, diphtheria, carcinoma of the œsophagus; from particles of food drawn into the lung by accident, or during vomiting, especially in persons who are drunk, insane, comatose, or suffering from laryngeal paralysis; or from infected water inhaled during immersion. Gangrene of the lung sometimes arises in pyæmia after otitis, bedsores, puerperal disorders, etc. It is determined by the presence of putrefactive organisms, including the *Bacillus Welchii*.

Morbid Anatomy. The affected portion of lung is of a dirty, greenish-brown, or black colour, soft, readily breaking down or even diffluent, and often emitting an offensive odour. It is generally surrounded by consolidated pneumonic tissue, into which it may gradually pass, or from which it may be more or less sharply separated off by a line of demarcation; thus in some cases the lesion is diffuse, in others definitely circumscribed. The gangrenous tissue may break down, and be expectorated, so as to leave a cavity with ragged, shreddy walls; and occasionally such a cavity opens into the pleural sac and causes pyo-pneumothorax.

Symptoms. Gangrene of the lung occurring, as it often does, as a secondary lesion just before death, may be overlooked. On the other hand, its symptoms may stand alone, or overshadow those of the primary lesion. Fœtid expectoration and fœtid odour of the breath are the most prominent. The latter may be very penetrating; it is carried to a great distance, and makes it almost impossible for other persons to live in the same room with the patient. The sputum is dirty grey or greenish-brown, or black, from altered blood; and either fragments of gangrenous lung tissue are found, or the microscope detects the typical elastic fibres (*see* p. 170). Occasionally hæmoptysis takes place. Cough, pain in the side, and irregular, and mostly intermittent, pyrexia are also present. The physical signs are those of consolidation and cavity proportionate to the extent of lung disease—viz. dulness, bronchial or cavernous breathing, bronchophony, and medium or coarse râles; but their value in diagnosis must depend a good deal on the preceding disease, if any. The illness may begin with rigor and pain in the side, or with hæmoptysis, or with recurring attacks of fever and fœtid expectoration; in most cases these are soon followed by prostration, with quick small pulse, dry tongue, and death at no great distance of time. Some cases, however, last for months or years, with much variation in the intensity of the symptoms, but without escaping a fatal termination. And in a few cases, with probably a very small patch of gangrene, recovery actually takes place.

Treatment. This is similar to that of fœtid bronchitis or bronchiectasis. Successes have been obtained with arsenobenzol and novarsenobenzol. A gangrenous cavity is sometimes amenable to the surgical treatment of antiseptic incision and drainage or bronchoscopy might be used; and the operation should be considered when a certain diagnosis can be made, and the associated conditions are in themselves not necessarily fatal.

PULMONARY TUBERCULOSIS

Tuberculosis of the lung occurs in several forms. In one there is a general distribution of minute tubercles throughout the organ, arising acutely, and determined by the carriage of the tubercle bacilli by the blood from some other part, such as a bronchial or cervical gland, or a joint or kidney, or less commonly from a focus of chronic disease in the lung itself. This acute form is often part of a general miliary tuberculosis, in which tuberculous meningitis is usually the most striking feature (*see* p. 88). The other forms of pulmonary tuberculosis have this in common, that the affection of the lung usually makes the chief part of the clinical picture.

Phthisis (*φθίω*, I waste) or *consumption* is a chronic disease of adults or later childhood in which tubercles are formed and multiply in one small part of the lung, usually the apex, and spread with very varying degrees of rapidity to other parts of the lung. It is thus at first entirely local. The later changes are assisted by the action of other organisms, especially the *Pneumococcus*, *Streptococcus*, and *Staphylococcus pyogenes*. Apical phthisis probably starts as a direct infection of the lung due to inhaled tubercle bacilli. Much discussion has taken place as to why the apex is primarily affected. Keith has pointed out that this part of the lung is less ventilated than other parts, because the top of the thorax is relatively immobile, the greatest movement taking place at the diaphragm and over the lower part of the chest wall. Since the ventilation is least at the apex, it may well be that the circulation is also least, so that the bacilli find a favourable nidus. Another explanation, not a very probable one, is that the infection begins in the tonsils and spreads along the cervical lymphatics direct to the apex of the lung across the pleura.

Hilum phthisis, or *peribronchial phthisis*, is also a chronic disease of the lungs, which occurs rather uncommonly in adults ; but it is the usual form that chronic pulmonary tuberculosis takes in young children. Tuberculous infiltration of the bronchial glands and of the lymphatics draining into them from the surrounding lung is the chief lesion. It has already been explained that the lung provides the primary focus in these cases (*see* p. 85). Tubercle bacilli are taken up by the lymphatics of the lungs, which become gradually choked or obliterated in the process, beginning at the hilum and gradually extending outwards towards the surface of the lungs. Hilum phthisis may give rise to a more acute tuberculous process at any place in the lungs. Usually, however, it heals in course of years, and it has been suggested that the pulmonary scars found so frequently at post-mortem are the results of this disease of childhood, now extinct. In this case the apical phthisis of adults is a reinfection in later life, although whether the patient who has once had hilum phthisis is specially sensitive to a fresh infection or specially resistant is open to doubt.

Epituberculosis is a widespread consolidation of the lung in children round a small tuberculous focus ; the consolidation is not itself composed of tuberculous granulation tissue, but may be either a non-specific infiltration resembling on a large scale the swelling that occurs in a positive Mantoux test—it has appeared immediately after an injection of tuberculin—or a widespread collapse from pressure on a bronchus by a tuberculous gland, as it has quietly cleared up after removal of the obstruction (**57**). There may be dulness and bronchial breathing and the X-ray may show a uniform shadow, usually in the middle of the right lung, spreading out from the hilum with its apex towards the periphery. Puncture of the area has disclosed tubercle bacilli. It is distinguished from pneumonia, as in the latter the apex of the shadow is towards the hilum, and it resolves in a few days. In epituberculosis resolution takes place after some weeks ; the prognosis is good.

Tuberculous broncho-pneumonia is an acute tuberculous process occurring chiefly in children or young adults, in which caseous tuberculous foci, with com-

mencing cavity formation, are scattered through the lungs. In children it commonly results from the ulceration of a caseous gland into a large bronchus, with rapid dissemination by inhalation of the highly infective material throughout the lung. The apex usually is not specially affected. *Acute pneumonic phthisis*, which has been called " galloping consumption " or *Phthisis florida*, is a still more acute process, and is described later.

The ætiology of pulmonary tuberculosis has already been discussed in the section on tuberculosis in general (*see* p. 83).

Morbid Anatomy of Phthisis. Tubercles form and develop in the lungs in the most typical way, with their giant cell systems, and their tendency to caseate and break down (*see* p. 86). In the common apical lesion the process starts in the wall of a small terminal bronchus. Caseation occurs, and the tuberculous mass breaks down; the material is discharged through the bronchus, and a minute cavity is formed connected with it. Meanwhile the process spreads into the neighbouring lung tissues, which become consolidated partly by caseation and partly by cellular inflammatory exudate. The solid areas are dark in colour, with small white caseous tubercles in bunches scattered through them, and usually a fair amount of consolidation takes place before much cavity formation is seen. Cavities or vomicæ are formed by a mixed process of caseation and suppuration. Adjacent cavities run into one another, and ultimately the lung may be extensively hollowed out. In their earlier stages the walls are often formed of caseous deposit, but in old vomicæ they are quite smooth. They are often traversed by bands, or trabeculæ, which contain pulmonary vessels. The vessels resist the destructive process, whereas the bronchi are generally ulcerated in proportion as the cavities enlarge, and into each cavity one or more bronchi open. The contents of vomicæ are caseous matter, *débris* of lung tissue, and pus. The latter predominates in the older cavities; the quantity is very variable, and it may be so small, under certain circumstances, that no expectoration takes place for considerable periods. It is only rarely that decided putrefaction takes place in phthisical cavities.

The first deposit of tubercle takes place one or two inches below the apex of the upper lobe in the subclavicular region; and fresh deposits occur lower and lower down. This invasion of fresh parts of the lung takes place by direct contiguity, by lymphatic channels, and largely through the bronchi; infective particles are inhaled into them, and thus start fresh centres of disease. By the time that tubercle forms at the lower levels the first lesion may have led to considerable consolidation; and later on, when tubercle is being deposited towards the base, the middle part of the lung will have solidified, and the apex may contain a large cavity. Again, the progress of the disease, while unequal in any one lung, is unequal in the organs on the two sides; and so, in an advanced case, it is common to find the most extensive disease at one apex, and the most healthy tissue, or the only healthy tissue, at the opposite base. A primary lesion of the lower lobe (primary basal phthisis) is rare.

In cases where the resistance is low, many separate foci may originate more or less simultaneously throughout the lungs by inhalation through the bronchi of sputum from some primary focus of infection in the lung. Infiltration of the lung surrounding each of these secondary foci may take place before the caseous matter can be discharged. The whole lung becomes completely solid, being filled with partly caseous and partly gelatinous-looking material, the latter representing parts of the lung not quite so completely destroyed (*caseous lobar pneumonia, acute pneumonic phthisis*). In other cases at post-mortem large cavities are in process of formation, their walls being extremely ragged. If the patient dies in a less advanced stage, the lungs will show numerous discrete caseous and gelatinous areas with early cavity formation (*caseous broncho-pneumonia*), since here the areas have not had time to coalesce to produce the diffuse pneumonic condition.

But in the majority of cases this process of destruction does not have full play. The inflammatory changes present varying changes of activity in different cases; and the mischief may be stopped for long periods one or more times in its course, or may even become abortive at an early date, and go no farther. The development of *fibrous* tissue is the important agent here. It is rarely absent in any but the most acute cases, and in the chronic cases it forms a large proportion of the remaining tissue of the diseased lung. In the consolidated lung there are numerous bands running in the course of the interlobular septa, surrounding the bronchi, the blood vessels, and the cavities, and forming a dense layer under the visceral pleura (fibroid phthisis). The fibrous tissue is frequently deeply pigmented, and is mixed here and there with caseous masses. By its contraction it tends to diminish the size of the cavities, and opposes some resistance to destructive processes; and in some favourable cases a small deposit of tubercle may be ultimately converted entirely into a mass of pigmented fibrous tissue, which, indeed, replaces a similar amount of healthy lung, but is otherwise harmless. In these cicatrices it is not uncommon to find calcareous particles, from the deposit of calcium salts in the caseous material; and around such a cicatrix may arise the condition known as *compensatory emphysema* (*see* p. 146). However, it must not be supposed that fibrous tissue formations and calcification is always the final stage in the healing process. Serial X-ray examination has shown that deposits of this nature may eventually be absorbed and disappear altogether when the patient regains perfect health.

Pleurisy may be present at quite an early stage; it may be dry; but a clear, straw-coloured sero-fibrinous effusion is very common, occurring late in the disease or heralding its approach. Such an effusion may be bloodstained; its characters are described later, and it may be gradually absorbed as the process heals or a dry pleurisy is left and the final result may be the formation of a thick layer of fibrous tissue over the affected portion of lung, commonly uniting the organ firmly to the wall of the chest. This adhesion of the lung has an important influence, for, if the process of excavation advances to the surface at a point which is not adherent, the vomica may ulcerate through, and discharge its contents into the pleural cavity, leading, on the one hand, to an acute pleurisy, generally of the purulent variety—*empyema;* and, on the other, to the entrance of air into the pleural sac—*pneumothorax*, and if fluid is present a hydro- or pyo-pneumothorax.

Another important result of the destruction of tissue is *hæmorrhage:* in earlier stages this follows from congestion alone; in later stages the vessel walls are directly invaded by tubercle, and hence may be eroded, or they may be weakened and dilate so as to form aneurysms, which may reach the size of a pea or bean, and ultimately give way at the thinnest part.

During the course of phthisis tubercle may attack other parts of the body. Laryngeal tubercle results from the continued passage of tubercle-laden sputum through the glottis. Tuberculous ulceration of the ileum or cæcum and fistula in ano result from the swallowing of sputum and its gradual passage through the alimentary canal. Tuberculosis of the peritoneum, kidney, epididymis, vesiculæ seminales, uterus, and its appendages, ribs, spine (with resulting abscesses such as psoas abscess), and other bones and joints, may co-exist with pulmonary disease, either resulting from it or in some cases acting as the primary focus. General tuberculosis with meningitis sometimes closes the scene. Addison's disease is rare. Lardaceous disease of the liver, spleen, kidneys and intestines was found in 20 per cent. of fatal hospital cases some years ago. The heart is small. In acute cases, owing to anæmia or lack of pulmonary aeration, the muscle shows fatty degeneration. In chronic fibroid disease the right ventricle is hypertrophical. Fatty liver is common.

Clinical History of Phthisis. Phthisis may run a rapid or a slow course.

The description which follows will mainly apply to a case which lasts from six months to a few years.

The onset is variable. Many cases begin with cough and expectoration of muco-pus or pus for which no cause can be given, or which is referred to some chill or exposure. Other cases begin with hæmoptysis or spitting of blood. The patient may have been apparently in good health, when sometimes after an effort, but quite as often when still, or walking or doing something which involves no strain, a tickling is felt in the throat, the patient coughs, and is surprised and alarmed to find that what he spits is blood. Thereupon he may expectorate a few drachms or an ounce, or even half a pint. This may remain the only symptom, and an examination of the chest may reveal nothing. But after a time, with or without a fresh loss of blood, cough and expectoration supervene, and the case develops like others. In a small number of cases the first apparent departure from health is an acute pneumonic process in one upper lobe, which only partially clears up, while cough and expectoration persist, and the case takes on all the features of phthisis; and in others the first recognisable illness is a pleurisy with serous effusion occasionally bloodstained, which may even appear to recover completely, and yet be followed by the usual pulmonary changes.

The disease is also very variable in its course in different cases. Patients with the earliest symptoms, whether hæmoptysis, or cough, or wasting, placed under favourable conditions of climate and hygiene, may completely regain their health; and it has long been known that in persons killed by accident, or dying of disease unconnected with the lung, cicatricial and pigmented patches, with perhaps calcareous deposits, are found in the apices which can only be regarded as the remains of former tubercles.

If, however, the infection is well established before being submitted to treatment, the result cannot be so satisfactory. Thus the disease may be fatal in three or four months, or it may last twelve or fifteen years before finally killing the patient; and in this time its progress will be very unequal, often quiescent for months or a year or two, and then making great strides, with hæmoptysis or much fever. While the more rapid cases are fatal chiefly by the extent of lung involved, the cases of longer duration threaten life by a number of complications, some of which are lesions of the lung itself, such as hæmoptysis, empyema, and bronchitis; while others involve distant organs, such as tuberculous meningitis, ulceration of the intestines and diarrhœa, nephritis, and lardaceous disease of the viscera.

Local Symptoms. These will now be described somewhat more in detail.

Cough. This is a very common symptom and generally, though not always, present as long as the disease is in any degree active. The cough is easy or dry, depending on the amount of sputum and ease with which it can be expectorated; with extensive cavities, when the sputum sinks to dependent parts of the affected lobe, it occurs in prolonged attacks, painful to the patient, distressing to those about him, and lasting perhaps more than a minute. With laryngeal complication the cough acquires a hoarse or husky quality.

Dyspnœa. Shortness of breath is often early noticed when there is bronchial spasm; the latter may sometimes be due to allergic asthma. Dyspnœa becomes very marked as more and more of the lung is diseased, and so the surface available for interchange of blood gases is diminished.

Expectoration. In the early stages this is not different from the sputum of bronchitis—that is, it is either simply mucous or muco-purulent; and this is accounted for by the bronchitic processes which frequently accompany phthisis. But sometimes comparatively early, and always in later stages, the sputum becomes purulent, of green or greenish-yellow colour, opaque, and quite free from air bubbles. If it is very fluid, the individual sputa may run together and lose their separate form; but the sputa of phthisis often keep separate long after expectoration, and, from the round, flat shape that they assume in the sputum vessel, they are called *nummular*, or coin-shaped. This is no doubt due to the

accumulation of the secretion in cavities in the lungs, and hence it constantly occurs in phthisis, but may also be present in cases where the cavities are produced by dilated bronchi (bronchiectasis). The microscopical examination for tubercle bacilli is described later.

Hæmoptysis. When hæmoptysis occurs as the first sign of phthisis, the blood is generally bright red and frothy; it is expectorated in variable quantities, and, as a rule, for some hours or days the patient continues to spit pellets of blood which have a darker and darker colour, become gradually less frequent, and then cease entirely. There may at this time be no other sputum. In later stages, when the disease is well established, the muco-purulent or purulent sputum is often streaked or stained with blood. A few streaks in the sputum may proceed from small vessels in the bronchial mucous membrane, but more characteristic of phthisis is the intimate mixture of bright blood with the sputum, or the discharge of pellets of coagulated blood frequently during the day. From time to time may occur more abundant hæmorrhages, like those first described, in which the blood comes up apart from the ordinary secretion; and if a large vessel is ulcerated, or, what is more often the case, if a small aneurysm in a cavity ruptures, several ounces or a pint or two of blood may be discharged within a short time, and death may follow rapidly. Hæmoptysis tends to occur rather more frequently at night than in the daytime, possibly owing to the cold (**28**).

Physical Signs. From the clinical point of view three stages of apical phthisis are described (Turban-Gerhardt classification). In Stage I., which represents early cases, the disease is limited to a small area of one or both apices. In Stage II. there is consolidation, the disease affecting the whole or the greater part of one lobe. Stage III. represents still more extensive disease and all cases where there is considerable cavity formation.

The physical signs are best described according to these stages. In the *first* stage they may be very slight, and vary considerably in different cases. The eye or the hand may detect a slight impairment of mobility on the affected side. For this purpose the relative movements should be watched during tranquil and during full respiration. Careful percussion of the apex may give slight impairment of note as compared with the opposite side. There is normally a band of apical resonance, 4·5 to 5 cm. (1¾ to 2 inches) wide, running over the shoulder (*Kronig's isthmus*). This may be narrowed in disease. An impaired note may also be obtained just below the clavicle, on the clavicle, or in the supra-clavicular fossa. The patient should be sitting in a relaxed position. Auscultation often gives a diminution of the vesicular murmur and the presence of fine or medium râles heard best towards the end of the first inspiration after coughing. The expiratory murmur may be loud and prolonged, as in bronchial breathing, and this may be associated with an increase of vocal resonance. It is, however, very important to remember that prolonged loud expiratory murmur with loud vocal resonance is not uncommon upon the right side in healthy individuals, and especially in females. And, as a rule, repeated examinations at short intervals are needed before one can with confidence state that there is evidence of apical phthisis from the physical signs in an early case. Impairment of note and râles are the most trustworthy signs. However, sounds resembling very closely crackling râles are sometimes produced in the sterno-clavicular joint. Irregular, jerky or wavy breathing—the so-called cog-wheel respiration—is of no diagnostic significance.

In the *second* stage (consolidation) the physical signs are in many respects similar to those of the second stage of pneumonia. According to the extent of lung involved, there is more or less impairment of mobility of the affected side; and when the progress has not been unusually rapid, there is obvious depression of the supra-clavicular and infra-clavicular regions, caused by contraction of fibrous tissue, or perhaps by the earliest destruction of tissue, producing cavities as yet too small to be recognised by physical signs. On percussion there is

increasing loss of resonance as the case goes on; but the dulness is rarely so absolute as that which occurs over a pleural effusion. On auscultation bronchial breathing of different qualities and pitch is heard, and the voice and cough are loudly bronchophonic. Consonating râles and short rhonci are commonly heard.

It is in the *third* stage (excavation), when the disease has existed some time, has seriously involved one lung, or has already begun to attack the other, that the modifications in the shape of the chest are most obvious. On the most affected side the chest takes on the type of extreme expiration. It is flat, long, and narrow; the shoulder is depressed and sloping; the lower angle of the scapula is displaced inwards; while the upper ribs in front are wide apart, the lower ribs are crowded together, and the epigastric angle is reduced to its smallest size. The crowding together of the ribs gives an X-ray appearance, called "roof-tiling," generalised mottling is shown in Plate 6, A, (*see* p. 170). In addition to this general change in the chest, there is retraction of the upper part of the chest and a corresponding impairment of movement. On percussion the note is dull, even though cavities are present; but when the cavity is large a hyper-resonant note is obtained. If there is a large cavity in free communication with the bronchial tube, and the patient's mouth is open, percussion will often elicit the *cracked pot sound*, or *bruit de pot fêlé*, which is somewhat like the sound resembling the clink of coins produced by striking the two clasped and hollowed hands upon the knee. There are two elements in its formation: (1) the presence of a cavity filled with air; (2) the rapid passage of the air out through a narrow opening on percussion. On auscultation over cavities one may obtain bronchial, cavernous, or amphoric breathing, according to the varying degree of excavation and fibrosis around. It is only truly amphoric when the cavity is large. Bronchophony and pectoriloquy will also be found. Crackling râles of large size and *metallic tinkling* are heard over cavities. The auscultatory sounds are best brought out on deep inspiration or on coughing, when sometimes the sound of *post-tussive suction* may be heard. A cavity probably does not give distinctive signs as compared with consolidation, unless it has reached at least the size of a walnut. At the same time it must be pointed out that a cavity has been found *post-mortem* when there were no signs of it during life.

Circulatory System. The heart becomes smaller in chronic phthisis, as has been shown by X-ray measurements of its width carried out by means of the ortho-diagraph. The principal factor that causes this is presumably the chronic under-exercise; it is a disuse atrophy.

General Symptoms. *Pyrexia.* From the earliest days of phthisis fever may be present, but it generally bears some relation to the activity of tuberculous processes in the lung, so that, if the mischief becomes inactive from time to time, the fever may for a corresponding time be absent; but it is often present continuously for months. The temperature is commonly higher in the evening than in the morning, and is either remittent or intermittent in type. The higher degrees of fever are accompanied with the discomfort and malaise common in pyrexia. There are, especially in the advanced stages of the disease, profuse sweats as the temperature falls, and occasionally there is slight chill before the sweating. Actual rigors, however, are exceptional, and the most common event is for the patient to sleep more or less quietly in the early part of the night, so far as the cough will let him, and to wake up in the early morning to find himself drenched with perspiration. Some night sweating is not uncommon even in early stages.

Loss of Flesh and Strength. Emaciation is the rule in phthisis; it may be one of the earliest symptoms, and may give a note of warning when the cough has been thought to be a mere bronchial catarrh; towards the end of a chronic case the emaciation is extreme. Exceptionally, nutrition is maintained fairly well even when the physical signs show that there is a considerable and even apparently active lesion. The muscular power is soon enfeebled, and the patients lose

energy, becoming languid and unfit for prolonged exertion, whether of mind or body. The mental condition in many patients, however, is one of great hope and confidence; even when helpless in bed they often fail to realise how ill they are, and look for complete recovery could they but once get rid of the cough.

Anæmia is a frequent symptom, both in the early and late stages, and is intensified if there has been loss of blood from hæmoptysis.

Cyanosis. The face may be livid, especially in acute cases involving a large area of lung, so that the oxygenation of the arterial blood is imperfect. In chronic cases in which the right side of the heart has become somewhat dilated there is more obvious cyanosis, which is due chiefly to retardation of the venous circulation, so that more oxygen is removed from the systemic blood in the capillaries than usual.

Clubbing of the fingers is a common feature of phthisis, though not peculiar to it. The appearance is more pronounced on account of the wasting of the rest of the finger. The same change may be seen in the toes. (*See* Hypertrophic Pulmonary Osteo-arthropathy.)

Dyspeptic Symptoms, such as anorexia, nausea, and vomiting, may occur at any time during the course of the disease. In the last stages sickness or loathing for food is so marked that it is one of the chief difficulties of doctor and nurse to get the patient to take anything at all. *Diarrhœa* is common in late stages; it may be due simply to catarrhal condition, to tuberculous ulceration of the ileum, or to lardaceous disease. The stools are variable, sometimes yellow in colour, undigested, and containing a little mucus or blood. *Peritonitis* is very rarely the result of a tuberculous ulcer. More often it is due to tubercles in the peritoneum, but it is not a common complication.

As well as the symptoms detailed above, symptoms may arise from the deposit of tubercle in other parts of the body, as described in the section on morbid anatomy. Of these, *laryngeal tuberculosis* is the commonest. In addition, there may be various septic complications, such as furuncles, bedsores, etc., in the later stages, and *femoral venous thrombosis*, which is more common on the left side.

Other Forms of Pulmonary Tuberculosis. *Pneumonic Phthisis* (*Scrofulous Pneumonia*). This begins very much like an attack of acute pneumonia, with pain in one side, high fever, chills, and night sweats, cough and expectoration. The physical signs also are those of pneumonia; but they are most marked at the apex, and spread downwards. Dulness, bronchial breathing, and bronchophony are accompanied by coarse mucous râles, consonating râles, and loud clicks. Often the condition is much more marked in one lung than in the other. The mischief extends rapidly: the pyrexia is severe, there are profuse sweats, appetite is entirely lost, and prostration becomes extreme. The indications that the lung is breaking down are more and more marked; the temperature assumes an intermittent type; the sputum is purulent, and contains *débris* of lung tissue. The illness is often fatal in the course of from five to twelve weeks, either by exhaustion or by hæmoptysis, which is always abundant if it occurs at all.

Hilum Phthisis. This is a chronic form of disease. The patient, usually a child, sometimes an adult, complains constantly of a tired feeling. The temperature is often slightly raised, being perhaps 99° F. in the morning and 100° F. in the evening (rectal). There is an impaired note over the root of the lung behind, on one or both sides, between the vertebral borders of the scapulæ, and Krönig's isthmus may be diminished. Râles are seldom heard. In adults there may be no alteration at all in the percussion note. In contrast to these very indefinite physical signs, the X-rays show increase in the normal root shadows, probably due to lymphatic infiltration, and an extensive fine mottling all over the lungs. It is only when the process, which is at first central, reaches the surface, that râles may be heard over the chest in various situations, particularly over the outer surfaces of the lungs.

Fibroid Phthisis. This is a very chronic form of apical phthisis, often affecting one lung only. Clinically the case is distinguished by the evidences of contraction of the diseased lung; the chest is sunken; the heart is displaced to the affected side; the opposite lung may extend its resonant area in the same direction; the spleen and stomach if the left lung is diseased, or the liver if the right, may be drawn far up into the chest. The physical signs of cavities are chiefly at the apex, as in other cases of phthisis; but impaired resonance, bronchial breathing, and bronchophony are perhaps present over the whole of the affected lung. If the other side is involved, it is only at the apex. There is often not much cough or expectoration; there is no sweating, and the temperature is normal. In the later stages there may be failure of the right side of the heart, with shortness of breath, dropsy and cyanosis.

Diagnosis of Phthisis. In advanced cases the symptoms and physical signs make the diagnosis obvious. Except in the earliest stages, and in periods of quiescence or arrest, the sputum will show *tubercle bacilli.* For their detection they require to be stained, and to be submitted to a microscopic power of 350 or 400 diameters. The Ziehl-Neelsen method of staining is now commonly employed. A cover glass is smeared over with a thin layer of sputum, which is dried by gently warming and then fixed by passing the slide three times through the flame of a spirit lamp. A solution of 1 part of fuchsin in 10 parts absolute alcohol is added to 100 parts of a 5 per cent. aqueous solution of phenol. This is heated till the steam rises; and the cover glass is floated on it, film downwards, for three or four minutes, rinsed in water, and immersed in a 20 per cent. solution of sulphuric acid until it is decolorised. It is then washed in water, and counter-stained by means of a nearly saturated watery solution of methylene blue, again washed quickly in water, dried, and mounted in xylol balsam. The sputum may also be injected into a guinea-pig for diagnostic purposes, and the animal is examined for miliary tuberculosis after six weeks.

The fragments of *elastic tissue,* which are present with sputum in the later stages, may be seen with the microscope either by teasing out the little rough nodules which are sometimes found, or by boiling the sputum in liquor sodæ for twenty minutes, and examining the sediment. Elastic tissue is found in any case where there is active destruction of lung tissue.

It is much more difficult to be certain of the presence of phthisis in its early stages. Apart from the more obvious symptoms of cough, expectoration and wasting, which may all be absent, valuable indications are obtained from (1) a feeling of tiredness complained of by the patient; (2) changes in the rectal temperature: in very early cases the rectal temperature in the early morning is lower than that of the average normal subject, *i.e.* below 97° F. Later on, at 7 a.m., it is constantly above 98·4° F., and in the evening above 99·5° F. an hour after exercise. It must be remembered that in women the rectal temperature is normally slightly raised for a week before or occasionally after the beginning of menstruation. (3) There may also be a history of pleurisy.

The first *physical signs* of any value in diagnosis are impaired resonance at one apex with diminished vesicular murmur, or diminished vesicular murmur with râles on inspiration or on coughing. The *Röntgen rays* give valuable help in the diagnosis of phthisis, and there may be typical appearances before there are physical signs (Plate 6, A, 7, pp. 168, 174). There may be early limitation of the movement of one diaphragm.

The various *tuberculides* when recognised on the skin suggest some internal tuberculous lesion (*see* later).

Tuberculin in Diagnosis. The Mantoux test is now universely used. Old tuberculin (Okell, 1930) is concentrated ten times over steam, and is put up fortnightly in strengths of 1 in 10,000, 1,000, 100, 10, using as diluent normal saline containing 0·5 per cent. phenol. 0·1 c.c. of 1 in 10,000 is injected intracutaneously as described on p. 140. A delayed, persistent, inflammatory

response, not reading its maximum until twenty-four or forty-eight hours, indicates tuberculous infection (**53**). Curiously enough, glycerinated veal peptone broth acts just like tuberculin (**54**); this is reminiscent of the fact that the antigen for the Wassermann reaction is made from non-syphilitic material. If no reaction is obtained, the next strength is employed, and so on.

Diagnosis by the Complement Fixation Reaction. The use of the Bordet-Gengou reaction for diagnosing tubercle, like the Wassermann reaction for syphilis, has recently given good results according to some workers. An emulsion of living tubercle bacilli is used as antigen. This, when mixed with serum from a tuberculous patient, fixes complement and so prevents the hæmolysis of red cells by a sensitised hæmolytic serum (**30**).

Before *hæmoptysis* is regarded as indicative of tubercle it must be clearly made out that the blood really comes from the lung, and not from the stomach, nose, or teeth; the descriptions of a patient are often very unsatisfactory or misleading. Blood from the lungs should be coughed up, and should be bright red and frothy; it is often preceded by a tickling in the throat, and not by the sense of nausea, which is more common with hæmatemesis. Further, if the blood has come from the lungs, the patient will usually spit up blood mixed with sputum for twenty-four or forty-eight hours after the free hæmorrhage has taken place. In *purpura*, blood may be expectorated actually from the lung, but the cause will be readily distinguished by the associated symptoms. Hæmoptysis sometimes occurs in mitral stenosis in young people. Although phthisis, alcoholism, and cirrhosis of the liver are often associated, bleeding from the lungs may occur in the course of *cirrhosis* quite independent of tuberculosis, and it is not infrequent, especially in older people, as the result of abnormally *high arterial pressure.*

Phthisis is sometimes masked by an intercurrent *bronchitis* or *pneumonia.* The accentuation of the physical signs at one or other apex is important, as well as the history of the illness, hæmoptysis if present, and the detection of bacilli in the sputum. The possible confusion with *bronchiectasis* has been mentioned (*see* p. 137). *Empyema* is accompanied by fever, sweating and emaciation; and if it bursts through the lung, there will be cough and purulent sputum. The physical signs will usually be at the base.

Prognosis. In scarcely any disease are cases so different as they may be in phthisis. Discovered in its earliest stage, it may be cured so completely that no trace of it can be detected clinically; it may in other cases be fatal in a few months; or it may last ten, twenty, or even fifty years with obvious physical signs and symptoms throughout. The variable elements are the virulence of the infection and the capacity for resistance on the part of the patient, and it is difficult to estimate which will gain the upper hand until the patient has been under observation or treatment for some time. Improvement may occur at once under treatment, or, at any time in the course of the illness, the protective powers of the patient may be so increased as to cause arrest of the process for a long period. And in no case should hasty predictions be made as to when the end will take place. However, certain factors are known to influence the prognosis. Thus the after-histories of phthisis patients who had been discharged from King Edward VII. Sanatorium at Midhurst showed from three to seven years after discharge 15·6 per cent. of deaths in Stage I. (Turban-Gerhardt), 38·0 per cent. in Stage II., and 70·4 per cent. in Stage III. When tuberculous laryngitis was also present the figures were 42·9, 63·3, and 78·3 per cent. respectively. This complication made the prognosis much worse, especially in the early stages (**5**). The presence of other complications is also unfavourable. The prognosis is much better if as the result of treatment either there is no sputum or tubercle bacilli cannot be found in it. The prognosis also depends on the amount of care that the patient can take of himself after discharge. It is in general much worse in the case of the industrial classes than in the well-to-do.

Pregnancy has an unfavourable influence on the disease, a fact which is first noticed after the confinement.

Prevention. Fresh air and good food, as recommended for a patient with phthisis, are advisable for children born of phthisical parents. It is by such means that they can best increase the resistance of their tissues against the bacillus. Phthisical persons about to marry should be informed of the risk that their offspring may develop the disease. There is also a definite risk to the healthy partner from infection. With a phthisical patient living in a house, the danger of infection to the other healthy occupants must be guarded against. The patient should sleep in a room by himself. Underclothes and bed linen should be scalded before being washed. There should be ample ventilation in the house. The sputa should in all cases be ejected into antiseptic fluid (5 per cent. carbolic acid solution), and they should finally be rendered innocuous by exposure to boiling water for ten minutes. Tuberculous mothers should not suckle their infants.

Treatment. The most important treatment for an early case is absolute rest until there is no longer any pyrexia, and for chronic cases one day in bed every week is a golden rule. The other requisites are fresh air (*see* p. 5) and plenty of good food. The patient should as far as possible lead an easy life, free from care. In a woman pregnancy should not be permitted, and should be terminated at an early stage if it has begun.

Treatment with the above objects should be taken *as soon as possible* after the evidence of tuberculous infection is confirmed. The methods available may be divided into two groups: *general*, namely, sanatorium treatment with or without change of climate; *specific*, namely, tuberculin treatment, artificial pneumothorax, and sanocrysin. Symptomatic treatment must also be carried out as required.

Sanatorium Treatment. The first object of sanatorium treatment is to teach patients enough about the disease, so that they may live the rest of their lives under conditions favourable to recovery. The second object is to provide for a minimum period of three months, which however ought to be considerably longer, conditions which favour the beginning of their recovery. Patients should not be kept too warm, since cold stimulates metabolism; they live night and day practically in the open air, either in the open or in shelters screening the patient from the wind and rain. The bedrooms and day rooms are thoroughly ventilated, and the rooms are constructed so as to prevent any accumulation of dust. The patients are well fed, having three meals daily of plain but varied food, while care is taken to see that they eat a sufficient quantity of it by weighing any remains after the meal. Exercise is only permissible when the morning temperature is normal, and the evening temperature not above 99·5° (rectal); the exercise will probably raise the temperature for a time; if it does not fall to a normal value after an hour's rest, the exercise should be stopped. The patient begins by taking a slow walk, and the amount of exercise is gradually increased. In any case, he rests one hour before meals and one hour after; and violent exercise and indulgence in exciting games or recreations are prohibited. The clothing of the patient must be suited to the temperature of the air. Treatment on this system has benefited many patients temporarily, but it must be submitted to for very much longer than the period of three months for which it is sometimes prescribed. In fact, a carefully controlled series of results among poorer class patients showed that three months' sanatorium treatment was not at all beneficial, presumably because in his normal surroundings the patient had become more or less adapted mentally and physically to fight the disease, but after a stay in a sanatorium he lost this adaptation and did not regain it on going back to his ordinary surroundings and work (Ward). At the same time a short stay will be of value to teach the patient the principles of his treatment, in order that he may at his own home carry them out as far as circumstances will

permit. In particular, rest, ventilation, the collection and destruction of sputum and plenty of nourishing food should be insisted upon, and the patients should learn how to take their own temperatures and stay in bed so long as it is raised. In this connection the tuberculosis dispensaries are valuable.

A development of the sanatorium is the tuberculosis *colony*, where patients can live with their families more or less permanently under favourable conditions in the country, following an occupation that partly covers the cost of the treatment (**31**).

Change of Climate. The places usually selected are South Africa, New Zealand, high altitudes in Switzerland or the Tatra, at places such as Davos, Montana, and Maloja, or the English east coast. The physiological effects of a mountain station, with its relatively low oxygen pressure in the atmosphere, are unique (**55**), and the benefit obtained is doubtless attributable to them, in particular the stimulating effect on the blood-forming organs, which causes polycythæmia and increase of hæmoglobin in the blood (*see* p. 5). A prolonged stay is often desirable, and it is safer to spend some time beforehand at an intermediate station, such as Bâle. The patient may in any of these places obtain a dry, cool, and bracing air, which he can enjoy for several hours daily outside the house, without the risk of catching cold; and he may spend the whole of the winter, avoiding the cold, damp, and fog of that season in the greater part of England, and returning to his home in the summer, when the weather is more tolerable. With the advent of winter he must again seek the climate which he has found suitable. A dry climate is especially desirable for phthisis patients who have a secondary bronchitic infection. In more advanced cases milder climates may be beneficial, such as that of the Riviera or the English south coast. "Sun-bathing," or heliotherapy, or treatment with ultra-violet light, such as is carried out in surgical tuberculosis, is not usually advisable, since it may cause hæmoptysis from congestion of the lungs. Such is the Swiss experience; but it may, perhaps, be tolerated better in this country. It should only be very slowly begun by gradually increasing the surface exposed, beginning with the extremities. Sunburn must be avoided. The aim should be to produce an erythema, which is followed by pigmentation. Where the disease is active, with slight fever on exertion, hæmoptyses, etc., heliotherapy should not be used (**32**).

Tuberculin Treatment. This aims at immunising the body against tuberculous infection by the production of anti-bodies. Koch's new tuberculin, or "T.R." (tuberculin Ruckstand)—an emulsion of triturated human bacilli—is perhaps the tuberculin most generally employed. The present practice with regard to the dosage is to keep it just below the point at which a *reaction* is obtained. It should only be employed for afebrile cases, and the temperature should be carefully observed all through the treatment as a test of the reaction. It is safer to give a very small dose at first, such as ·001 c.mm. of whatever preparation is used, double this quantity, ·002 c.mm., in three or four days, double this again, or ·004 c.mm., after a similar period, and so at similar intervals, or twice a week, until a slight reaction, either local or general, is observed, namely, some thickening at the site of injection, or fever, headache, malaise, etc. These symptoms generally occur within twenty-four hours and subside in about the same time. After three or four days again the last dose may be repeated, when the reaction, if it occurs, will be less, and soon the same dose fails to produce any reaction at all; that is, tolerance to that quantity is established. The dose should now be increased by much smaller additions every half-week until a reaction again occurs, and so on. The duration of the treatment is from six months to eighteen months or two years. A tuberculin made by Beraneck is injected intracutaneously. Some results have been published of the use of a vaccine made from tubercle bacilli after removal of their fatty envelope (**34**).

Artificial Pneumothorax. This treatment was described in 1821 by Carson, of Liverpool; but it is only within the last few years that it has been widely adopted.

One reason that may prevent tuberculosis of the lungs from healing is that the tissue is kept expanded by the negative pressure in the thorax, and any cavities that form cannot close up. If air is injected into the thoracic cavity, the lung will collapse; it is also congested, which may help the healing process (**65**).

The operation is especially suitable in cases in which one lung is extensively diseased and the other is relatively sound. In the past it has been used chiefly for advanced cases, but the tendency at present is to use it more widely; in fact, for any case of one-sided disease where the process is extending. There is statistical evidence that the treatment is beneficial (Saugman). Hæmoptysis is a special indication for immediate induction of a pneumothorax on the side of the hæmorrhage. The treatment is illustrated in Plate 6.

The apparatus consists essentially of a trocar and cannula connected on the one hand with a water manometer, and on the other with a receiver filled with air, so that a measured quantity can be passed into the chest. The skin and deeper tissues are anæsthetised with 0·5 per cent. novocaine. The puncture is made either directly or after a slight incision through the skin; and the fact that the needle is in the pleural cavity is recognised by the oscillations of the manometer fluid, which, of course, shows a negative pressure. These oscillations should be from 4 to 6 cms. of water; and if the oscillations are no more than 1 or 2 cms., the needle is probably not in the pleura. When it is certain that the needle is in the pleural cavity, the air is driven in to the extent of 300 c.c. to 500 c.c., or until the manometer oscillates about the zero point. After a week more air may be injected.

Refills should be given according to the absorption of the gas, in amounts from 500 to 800 c.c. and at weekly or fortnightly intervals to begin with, though later on the intervals may be longer, as absorption will be less. They should be continued for three years or longer. The final pressure should never be greater than + 10 cms. of water. The chief accident in the past has been due to air embolism; but this cannot occur if the needle is really in the pleura, and that is the object of having the manometer. Quite rarely unpleasant effects are noticed which are ascribed to the pleural reflex, viz. dyspnœa and palpitations, pallor, and sometimes even loss of consciousness. Sometimes the mediastinum is weak and readily displaced to the opposite side. There may be discomfort and dyspnœa. The condition can easily be diagnosed by X-rays, and here emphasis should be laid on the necessity for screening every case before and throughout the treatment. "Ballooning" of the pleura towards the healthy side sometimes occurs; but if without symptoms, it does not matter. About half the cases develop a clear effusion during treatment. When this begins, treatment should be less active, as the pleura is inflamed. The fluid need not be removed unless the temperature rises, and if removed, it should be replaced by gas. An extension of the pneumothorax treatment suitable for quite early cases consists in admitting into the pleural cavity quite a small volume of air, which is found to collect round the infiltrated part of the lung and cause a partial collapse, while the healthy part remains expanded. A partial pneumothorax can be induced on both sides. Refills must, however, be carried out frequently (**35**). When a pneumothorax tends to close up in spite of repeated refills, or a tuberculous empyema forms, these are indications for performing oleo-thorax (*see* p. 137).

Where a complete one-sided pneumothorax has been successfully induced, 70 per cent. of the patients have succeeded in getting back to work, but the main difficulty in the treatment is the existence of adhesions, which hinder collapse, and in this case there are only 33 per cent. of successes. It is impossible to diagnose adhesions until the attempt at injection is made. Sometimes they will break down of themselves after repeated refills; but when this is not the case, attempts have been made to divide them. They are localised by introducing a thoracoscope, and they are then cauterised. Unfortunately this kind of operative procedure is apt to lead to tuberculous empyema unless the band is divided right

at the periphery. Various new types of apparatus have recently been described (**56, 57**).

Two other operations—thoracoplasty and phrenic evulsion—have lately been carried out with success. In *thoracoplasty* the hinder portions of the ribs are removed extra-pleurally from just in front of the angles to as near the transverse processes of the vertebræ as possible. In complete thoracoplasty parts of all ribs are removed from the first to the tenth ; but in cases where the disease is limited to the lower lobe a few of the upper ribs may be left intact. Light ether anæsthesia is to be preferred. Forty-five per cent. of cases have become subsequently fit for work after this operation (**36**). In *phrenic evulsion* the nerve is pulled up from its attachment to the diaphragm on one side through an incision in the neck, so that the diaphragm on that side is raised and paralysed. The operation may be carried out in conjunction with artificial pneumothorax or thoracoplasty, or in basal phthisis, or to prevent cough when due to adhesion of the lung to the diaphragm (**37**).

Sanocrysin, a thiosulphate of gold and sodium, may be used in the case of patients who have not responded well to other forms of treatment. It is claimed to have in the body a direct destructive effect on tubercle bacilli. It is distributed in sterile ampoules containing weighed quantities from 0·1 to 1·0 gm. The crystals are dissolved in sterile distilled water immediately before use to form a 10 per cent. solution. The solution is injected intravenously, care being taken to avoid leakage into the subcutaneous tissue where it acts as an irritant. The dose must be adjusted to the body weight of the patient and to the nature of the inflammatory change in the lungs. In cases where the disease has become chronic, and the lesions are surrounded by fibrous tissue, a large dose may be given ; while in acute cases with recent extension of the disease, a very much smaller dosage is indicated. The urine must be tested for albumen before commencing treatment, and daily throughout the course, and a dose must not be given unless the urine has been free from albumen for forty-eight hours. The initial dose will be from 0·1 to 0·5 gm., according to the weight of the patient and the character of the lesions. There may be a reaction in the form of increased pyrexia, vomiting, diarrhœa or exanthematous rashes on the skin. As soon as the reaction has subsided, or if there be none, after forty-eight hours, the second dose is given, it being 50 per cent. larger than the first. After this a further dose is administered every seventh day, the amount being increased up to 1 gm. if the patient can stand it. The total quantity for the course is 8 to 10 gm. for a patient of 10 stone, and proportionately less for those who are lighter.

Symptomatic Treatment. During treatment in a sanatorium drugs are avoided as much as possible, and it is generally found that the symptoms disappear with the improvement of the patient. It is in all cases essential that the digestion should not be upset by the medicines administered.

Cough. The rapid diminution of cough has been constantly observed in the open-air treatment. The patient should resist coughing as far as possible. If it is preceded by a tickle in the throat, painting the lingual tonsil with iodine may be effective. Otherwise it may be treated as described under Bronchitis.

Night Sweating. This can be generally checked by 1 minim of liq. atropinæ sulph. given in a little water at night, or 2 or 3 grains of oxide of zinc in a pill, with $\frac{1}{6}$ grain of extract of belladonna. Arseniate of iron ($\frac{1}{5}$ grain), or picrotoxine ($\frac{1}{50}$ grain), or tincture of nux vomica may also be used. Night sweating usually means too warm clothing at night or excessive auto-inoculation by the patient with his own toxins—too much exercise, for instance—and reflects on the management of the case by the physician.

Hæmoptysis. The patient should be kept in bed in the semi-recumbent posture ; but he should be allowed to change his position when he likes. The most effective hæmostatic is the slow intravenous injection of 20 c.c. of a 15 per cent. solution of calcium chloride. A simple plan is to give 5 to 15 grammes of sodium

chloride by mouth. Sodium bromide may be substituted if the patient is nervous. Bleeding often ceases after inhalation of a few drops of amyl nitrite. In some dangerous cases of hæmoptysis, the induction of pneumothorax has been successful. Hypodermic emetine injections have been successful when the bleeding is slight and continuous (Flandin). The traditional method of treatment is to place an ice-bag on the chest and inject morphia ; but this has the disadvantage that the blood is kept stagnating in the lungs and so helps to cause an acute spread of the tuberculous process. It has been found that hæmoptysis is largely independent of the patient's movements (**38**).

Diarrhœa. For this one must carefully regulate the diet, and use the vegetable astringents, mineral acids, opium, sulphate of copper in ¼-grain doses, or carbonate of bismuth.

Pleuritic Pains are frequent, and are often relieved by antiphlogistine or thermogene wool or by painting the surface of the chest with tincture of iodine. Anodynes internally may be necessary. Many believe that pleuritic effusion delays the progress of the disease in the corresponding lung, and postpone tapping until pressure is extreme. An empyema requiring evacuation may be aspirated.

Excessive Expectoration. This condition may be treated by antiseptic inhalation and expectorants as described under Bronchitis. Drainage with the head down and feet raised may be useful (*see* p. 137).

SYPHILIS OF THE LUNG

Apart from the ulcerations of the bronchi, with resulting stenosis, which have been shown to be due to syphilis and may be diagnosed by bronchoscopy (**64**), the lung tissue itself may exhibit the effects of the disease in various forms. One is that of the ordinary *gumma*, which is extremely rare in adults, though more common in infants, and gives rise to no recognisable clinical symptoms. Another is the so-called *white pneumonia* of syphilitic infants. The lungs are enlarged, white, dense, and firm ; their section is smooth and opaque ; they are sometimes resistant, at others easily broken down. The microscope shows a diffuse cellular inflammation of the lung, with thickening of the alveolar walls, and desquamation and fatty degeneration of the pulmonary epithelium. This condition may affect the whole lung, or one part may be uniformly altered, while the other contains only isolated areas. In another variety the alveoli are lined by cubical epithelium, and the connective tissue is replaced by a fibrous stroma infiltrated with cells from the cubical alveolar epithelium. Spirochætes have been found in these cases. As these lesions are found chiefly in still-born children, they have but little clinical importance.

POISONING BY IRRITANT GASES

Poisonous gases used first of all by the Germans in 1915 during the war were (1) *suffocative*, such as chlorine, phosgene, and chloropicrin. These act chiefly on the lung alveoli, causing acute œdema, thrombosis of the capillaries, and disruptive emphysema. In patients who recovered, the œdema fluid disappeared in a few days ; but bronchitis and broncho-pneumonia often came on, and emphysema persisted ; (2) *lachrymatory* gases—also used in shells, *e.g.* xylyl bromide and chloropicrin ; (3) "*mustard*" gas—really an oily liquid which is scattered on the ground or on to the clothes and slowly evaporates. Nothing was usually noticed for some hours except a faint smell of mustard. There then developed severe conjunctivitis, vomiting with epigastric pain, widespread erythema of the skin with vesication leading to severe burns and inflammation of the mucous membrane of the respiratory tract, which caused the most dangerous symptoms. The whole surface became ulcerated and covered with a fibrinous

membrane, it was secondarily infected, and if death did not come on at once broncho-pneumonia supervened.

Later Effects. Many patients who have been gassed develop the " effort syndrome " (*see* later). The following symptoms have been observed, shortness of breath on exertion (*70*), persistent cough with sputum (*54*), pain or tightness across the chest (*25*), palpitation and occasional giddiness (*14*), morning vomiting or nausea (*12*), headache (*9*), neurasthenic symptoms (*7*), soreness of eyes (*5*). The blood may show polycythæmia. In this connection Haldane, Meakins and Priestley have observed that these patients sometimes lose the power of breathing deeply, and can only take rapid *shallow* respirations after exercise. They believe that these patients suffer from want of oxygen because the ventilation of the deeper alveoli is defective, so that the blood from these parts is imperfectly aerated. Treatment in an oxygen chamber relieves the symptoms more or less permanently, and the polycythæmia diminishes (Hunt and Dufton).

Various pulmonary sequels to mustard gas poisoning have been described, many of them being of a relapsing character, *i.e.* bronchitis, emphysema, asthma, œdema, pulmonary abscesses, and " pseudo-tuberculosis " with wasting, fever, bronchitis and apical râles, but with no tubercle bacilli in the sputum. There is fibrosis of the lung. These conditions are due to secondary infection after the injury due to the gas. Finally, true tuberculosis of the lungs may be found, probably in those cases where the disease has been previously arrested.

PULMONARY EMBOLISM AND THROMBOSIS

The nature of embolism and thrombosis is dealt with in the section on Diseases of the Blood Vessels, but the special liabilities of the pulmonary circulation to this accident may here be described.

The pulmonary artery and its branches are in direct communication with the systemic venous trunks through the right ventricle and auricle ; and accordingly micro-organisms, particles of coagulated blood, or of any other kind, which become loose in the veins of the body or limbs, must be carried into the right cardiac cavities, and thence into the pulmonary artery, where they will be impacted in a larger or smaller branch according to their size. A large old laminated clot may block one of the main branches. In some cases the embolism is a long thrombus from a medium-sized systemic vein which is folded up in a ball.

Pulmonary thrombosis is commoner than pulmonary embolism, occurring in 85 per cent. of thirty-five consecutive autopsies where these lesions were present. Blood clots are found in the branches of the pulmonary artery in all parts of the lungs and there is evidence of their ante-mortem formation in the commencing organisation of the clot or deposition of pigment. The diagnosis of " pulmonary embolism " or " pulmonary thrombosis " usually implies that there is a serious lesion producing widespread effects in the lungs with urgent symptoms, and placing the patient's life in immediate danger.

Pulmonary embolism and thrombosis may result from thrombosis of the femoral vein, such as occurs in typhoid fever, or phthisis, or fracture of the femur in older persons. They may result from acute infections, such as pneumonia, and from surgical operations which involve an incision of the anterior abdominal wall, especially in older people (**39**). Micro-organisms have in many cases been found in the clots. The effects of the emboli vary with their size. If one of the main branches of the pulmonary artery is blocked, rapid death is a necessary consequence. When the embolus is smaller there is time for changes to take

(The *italic* numbers in brackets refer to percentage incidence of symptoms in 83 cases in the Oxford area.)

place in the lung, and hyperæmia, petechial hæmorrhages, œdema, and collapse with emphysema around it, are found.

In auricular fibrillation which is particularly associated with mitral stenosis small thrombi may form in the auricles owing to their failure to contract, and those from the right side may pass into the lungs and block the smaller arterioles and give rise to local hæmorrhages in the lungs, which are known as *pulmonary infarcts*. Thus a conical portion of the lung wedge-shaped in longitudinal section, its base to the surface of the lung and its apex internally, becomes solid, firm, dark red in colour, and airless; and under the microscope the air vesicles are seen to be filled with red blood corpuscles. The base of the cone bulges on the surface of the lung beyond the surrounding vesicular tissue, and in a short time the surface may present early pleuritic changes. These infarcts are most common in the lower lobes and often involve the lower edge to a considerable extent, when the description of them as conical or wedge-shaped hardly applies. They are commonly about 1 inch in diameter, but sometimes reach a much larger size.

Other bodies may act as emboli besides these venous and cardiac thrombi, namely, particles of growth, and rarely a small hydatid cyst, but quite commonly also pyogenic micro-organisms. When the latter are carried, either alone or with particles of thrombus, into the lung, the conical infarcts soon become abscesses, and are often accompanied by broncho-pneumonia of the adjacent tissue, or by serous, sero-purulent, or purulent pleurisy.

Fat embolism of the pulmonary capillaries is a result of injury, which allows the passage of fat into the vessels. Globules of fat are very commonly seen microscopically in the lung capillaries after death from surgical injuries.

Symptoms. The symptoms of embolism of the pulmonary artery and its main branches vary with the size of the vessel obstructed and the degree of obstruction. When a large thrombus from the femoral vein is impacted in the pulmonary artery or one of its main branches, death may be absolutely sudden; the patient may start up from bed in alarm and fall back dead, or there may be a few minutes' dyspnœa with cyanosis, or, on the other hand, syncope or convulsion. If the obstruction is less complete, the condition may be one of syncope, or syncope with asphyxia, or with rigors, pain in the chest of varying severity, a sense of suffocation, dyspnœa, developing perhaps into Cheyne-Stokes' respiration, and finally slowing down and ceasing. The face may be pale and livid, the jugular veins distended, and the hands cold and clammy. On auscultation the breath sounds are harsh and exaggerated. The onset of symptoms is sudden. In pulmonary thrombosis the symptoms are similar in character, but the onset, rapid as it may be, is gradual.

The symptoms of the occurrence of an infarct will also vary with the size of the vessel obstructed, and the nature of the thrombus or particle impacted. If it is a relatively large vessel, the symptoms may resemble those above described, but will be of less severity. With a sufficiently large infarct there may be breathlessness, palpitation, and even rigor. The extravasation of blood into the lung tissue often reveals itself by the expectoration of blood, or hæmoptysis; and the blood may be in moderate quantity, or in small separate blood sputa or may only render the mucous sputa blood-coloured or rusty. Pain in the side will result from the concomitant pleurisy, and after the event there may be some febrile reaction with or without rigors. Only if the infarct is very large will it give rise to an area of dulness, and suppression of breath sounds; but some crepitation is possible. If an extensive area of dulness is found in a cardiac case in which infarcts are suspected, it must be remembered that the mixed condition of congestion and œdema, known as *red induration* and *brown induration*, is a common result of valvular disease, and often co-exists with infarcts.

Septic infarcts are frequent in pyæmia, and indeed are the characteristic post-mortem lesion of that disease in its acute form. The foci are commonly quite small, and incapable of giving rise to definite physical signs other than some

crepitation. But the pleurisy and effusion which so often accompany them will give the usual signs, and febrile reaction of septic type with rigors and increasing prostration will be present.

Fat embolism, when present in sufficient amount, may be one of the causes of surgical shock, owing to obstruction of the pulmonary circulation. The symptoms are dyspnœa, prostration, red frothy sputum, quick pulse, cyanosis, and râles over the lungs.

Diagnosis. The diagnosis of pulmonary embolism or thrombosis depends very much upon the antecedent data, such as the known existence of venous thrombosis or sepsis, associated possibly with some abdominal operation. The existence of heart disease may suggest pulmonary infarction. Of all the causes of hæmoptysis, heart disease is the next most frequent to pulmonary tuberculosis; the knowledge of this fact goes a long way to a safe diagnosis.

Prevention. It is suggested that after abdominal operations, if there is no peritonitis, and after labour, early movement of the legs and pelvis and massage should be permitted, so as to prevent stagnation, which predisposes to thrombosis. This must be stopped if it is believed that a thrombus has formed. Deep breathing should be carried out systematically to prevent stagnation in the lungs which leads to thrombosis, and to facilitate the venous return from the abdomen. If the patient is blanched blood transfusion should be carried out before operation. The patient should be allowed to drink plenty of water to avoid concentration of the blood.

Treatment. An emergency operation has now been perfected for removing an embolism from the pulmonary artery.

INTRA-THORACIC NEOPLASMS

The commonest causes of intra-thoracic neoplasm are primary carcinoma of the lung and carcinomatous or sarcomatous metastases in the lungs, pleura or bronchial glands, arising from primary growths elsewhere in the body. These are dealt with below. Other pathological conditions that may rarely simulate clinically primary carcinoma of the lung are in the *mediastinum*, growths of the thymus and thyroid (including intra-thoracic goitre), dermoids, teratomas, Hodgkin's disease, mediastinal sarcoma, lympho-sarcoma, primary carcinoma of the œsophagus extending into the lung, *in the pleura* a number of benign tumours, such as fibroma, etc., and endothelioma and sarcoma. *In the lung* benign tumours are very rare; but hydatids, gumma and inflammations may lead to confusion (**60**).

PRIMARY CARCINOMA OF THE LUNG

Ætiology. Primary carcinoma of the lung occurs at all ages, but most frequently (77) * between forty and seventy. It is four times as common in males as females. Undoubtedly there has been an increase of recent years in its incidence. Since chronic irritation is an established ætiological factor of carcinoma, causes of irritation have been looked for, such as influenza, and following the great epidemic in 1918–19 an increase of carcinoma has certainly been noted; irritation from dust, as in the mines of Saxony, is a possibility; but if inhalation is a cause the right lung should be affected more readily than the left, because the right bronchus is larger and more directly placed; but both lungs are affected about equally. Inhalation of exhaust gases from motor cars, poison war gas, tobacco smoking, road dust, are possible factors (**61**).

Morbid Anatomy. Primary growths of the lung are classified in three groups according to their origin: (1) from the bronchial epithelium, (2) from the bron-

* The numbers in brackets are percentages taken from an analysis of 139 autopsies at the London Hospital (**41**).

chial mucous glands, (3) from the lung substance. In the first group the tumour is chiefly localised in one of the larger bronchi, which becomes obstructed; the growth does not spread diffusely but tends to break down and form bronchiectatic cavities. It is columnar-celled. With the second group, which also tends to be localised round the bronchi, there is abundant mucous secretion. However, the cells are so variable in these tumours that this classification is not of much use. More than half of all tumours belong to the "oat cell" type; the cells and nuclei, which stain deeply, are oval and the cytoplasm scanty. Metastases are commonest in the lymph glands, but they occur variously in other organs. Other complications are as follows: pleural effusion (28), viz., purulent (6·5), sanguinous (7), clear (14·5); partial or complete occlusion of a bronchus (56); bronchitis, bronchiectasis, broncho-pneumonia, collapse gangrene, abscess (11·5), emphysema, fibrosis, thrombosis and invasion of pulmonary vessels; pericardial invasion (44·5); invasion of or pressure on œsophagus (16·5); invasion and obstruction of superior vena cava (11·5); thrombosis of large systemic veins (17), which occurred almost as frequently in the lower as in the upper limbs.

Symptoms. *Cough* (66) may be dry to begin with; it may occur in severe paroxysms, or be "brassy" from pressure on trachea or bronchi; it may cause temporary congestion of the veins of the neck. *Sputum* is present in over half the cases, and in most of these there is some *hæmoptysis* (36). *Pain* (64) is variable in intensity; it may be gnawing, stabbing, dragging, or it may be a feeling of pressure or suffocation; it is usually in the chest, but may be felt in neck, abdomen, loins and limbs; it often results from metastases in vertebra or from pressure on nerves. *Wasting* (52) may be associated with malaise, weakness and pallor, but patients are usually not anæmic. *Dyspnœa* (50), apart from breathlessness on exertion, is often a late symptom, unless there is a pleural effusion; it may occur in paroxysms and there may be inspiratory stridor. In one case the CO_2 pressure in the arterial blood was increased and the oxygen saturation diminished, showing that there was obstruction to the interchange of gases in the lung (7). *Pyrexia* (39) often resembles the hectic temperature of phthisis, and it may be associated with chills and *night sweats* (17). Tachycardia may be present without temperature (19). *Secondary deposits* are sometimes found clinically (24); and other symptoms are *cyanosis* (21), which is often associated with *dilated veins* (19·5), and which may be seen in head and neck, upper limbs, thorax and abdomen, and are important because they show that there is obstruction in the mediastinum, with the result that the blood finds its way to the heart, by anastomoses under the skin between branches of the intercostal and the abdominal veins. Even with this compensation, the venous current may be much obstructed, and, on stooping down or making any exertion, the face becomes still more congested and cyanosed. In obstruction of the superior vena cava the flow of blood on the surface is entirely downwards, and in obstruction of the inferior cava it is upwards. This last, however, rarely results from intra-thoracic tumour, although it is possible for the malignant growth to reach the inferior cava, just above the diaphragm. *Œdema* (18) is often a late sign and associated with cyanosis and dilated veins; œdema of the head and neck and either arm is very characteristic; it may be transitory, being brought on by exertion or stooping or by cough, and may be associated with a sense of suffocation. There are *laryngeal paralysis* (17); *dysphagia* (11); *vomiting* (11); *clubbing of the fingers* (6·5), but this figure is probably too low; *headache* and *vertigo*, inequality of the pupils and other signs of excitation or paralysis of the sympathetic (*q.v.*). *Arteries* often maintain their course through a tumour unmolested. They are sometimes compressed, with the effect of weakening or obliterating the peripheral pulse.

The *physical signs* are very variable, depending on the position and size of growth, and on the presence of complications. At first they may be only those of obstruction of a bronchus, already described, often accompanied by stridor.

As the size of the tumour increases, with deposits not only in the bronchial glands but spreading out into the lung, there is impairment on percussion chiefly in front of the chest in the upper part, but not reaching up to the apex; there may be bronchial breathing over this area, increased T.V.F. and bronchophony, or either breath sounds, T.V.F. and voice sounds may be absent. The same physical signs may be present at one base behind if the growth extends downwards. The physical signs of the various complications may be present.

Diagnosis. Some cases may run their course without any thoracic symptoms at all. There is a small *cerebral* group of cases due to metastases which resemble cerebral tumour, meningitis, encephalitis, etc., and a *spinal* group which may be diagnosed as myelitis, spinal caries or lumbago, and a group with acute abdominal symptoms. The stridor produced by compression of a bronchus may be mistaken for the rhonchus of *bronchitis*. The former is constant in time and position; the latter is variable, and changes from place to place within a few hours, or disappears at intervals. Where the growth produces intra-thoracic complications, such as mediastinal pleurisy, effusion, empysema, bronchitis, bronchiectasis, broncho-pneumonia, these may be diagnosed without realising that growth is the primary cause if the characteristic symptoms such as congestion of veins and local œdema are absent. Phthisis and pneumothorax must also be differentiated. A rapidly recurring sterile pleural effusion after paracentesis will suggest carcinoma, especially if it is bloodstained, though it must be reiterated that tubercle is the commonest cause of a bloodstained effusion. Cytological examination is usually of no help. On the other hand, growth may be suspected in a middle-aged patient, when the signs are those of fluid, but no fluid is obtained on exploring the chest. Carcinoma of the lung is readily confounded with an *aortic aneurysm*, and, apart from the well-known physical signs of aneurysm, X-ray examination provides the most certain means of differential diagnosis in most cases. An aneurysm has a clearly defined edge, which shows expansile pulsation; but pulsation may be seen with a growth adherent to the aorta. The shadow of an irregularly infiltrating neoplasm gradually merges itself into the surrounding lung, and no true edge can be seen at all. Examination after lipiodol administration may show obstruction of a bronchus. Bronchoscopy is of great value; a piece of growth is removed for diagnosis histologically. Temporary relief may be obtained by dilating a stricture and allowing pent-up secretions to escape. X-ray examination after pneumothorax with removal of an effusion when present will be of special value in diagnosing pleural growths. Thoracoscopy is also used (Plate 2, B, p. 137).

Treatment. When the growth is accessible to bronchoscopy the treatment has been revolutionised, since it is possible to implant radon seeds at periodical intervals. The operation of lobectomy is also used

SECONDARY DEPOSITS IN THE LUNGS

Symptoms. When the lung is the seat of numerous nodules of growth, scattered indiscriminately through it, the patient suffers at first, at any rate, but little discomfort, and there are no physical signs unless pressure is exerted on a bronchus. In the later stages there will be dyspnœa, rapid breathing, lividity, frequent cough, and mucous expectoration; and on auscultation numerous rhonchi and râles are heard over the whole chest. The condition bears some resemblance to miliary tuberculosis, but the temperature may be normal. When the pleura is involved there is commonly an effusion which may contain blood and malignant cells.

Diagnosis. When growth is known to exist in other organs, or when a carcinoma of the breast or of the jaw has been removed by operation, the presence of unaccountable dyspnœa should make one think of its occurrence in the lung; and in cases where the pulmonary symptoms are most prominent the presence

of large hard glands in the neck, or a tumour of the testis, or a rigid spine from implication of the vertebræ, may sometimes give the required clue. X-rays may show in early cases characteristically rounded opacities in the lungs.

The **prognosis** is bad and the duration of the case is not likely to be longer than a year. The **treatment** must be directed to relieving pain and cough and procuring sleep. Deep X-ray therapy may cause temporary recession of the growth and re-expansion of the lungs (**62**), or radium may be employed in massive doses. A liquid effusion accompanying the growth may be aspirated, but it will probably return quickly.

PLEURISY AND EMPYEMA

The chief features of pleurisy, or inflammation of the pleural membrane, are either the formation of "lymph" on the pleural surface (dry pleurisy), or the exudation of serous fluid (pleurisy with effusion), or the production of pus (empyema).

Ætiology. In a large number of cases the onset of a dry pleurisy, or pleurisy with effusion, occurs insidiously in apparently healthy persons, and is often attributed to exposure to cold. Among such cases a large proportion, perhaps 50 per cent., are undoubtedly tuberculous in origin. Many have a history of tubercle, or they afterwards die of phthisis or other tuberculous lesions. In many cases also the fluid inoculated into animals produces tuberculosis. Such cases of pleurisy are chronic in their course.

The pleura is subject to what is usually a more acute form of inflammation often leading to empyema as the result of many other infections, especially pneumococcal infections, and those of scarlatina, measles, rheumatic fever, septicæmia, and influenza; pleurisy is also a frequent complication of Bright's disease. In other cases the infection is more directly local, as, for instance, when the pleura is injured by fractured ribs, or when there is an extension to the pleural surface of (1) lesions in the lung, like those of pneumonia, pyæmic abscesses, growth, tubercle, or hæmorrhagic infarcts; (2) lesions of the parietes, such as abscesses, in the axilla, breast, neck, or abdominal cavity.

Pleurisy, pericarditis, and peritonitis may occur together from the same infection, which is in acute cases rheumatic, septic, or pneumococcal, in chronic cases often tuberculous; this is known as *polyorrhomenitis*, or *polyserositis*.

The micro-organisms found in different forms of pleurisy are the following: pneumococcus, streptococcus, staphylococcus, *Bacillus tuberculosis* and *B. typhosus;* more rarely Friedländer's bacillus, *B. coli communis*, *B. diphtheriæ*, *B. influenzæ*, and *Micrococcus tetragenus*. They may be combined, as, for instance, pneumococcus or tubercle bacillus with streptococci or staphylococci; the last are not commonly found alone. In the sterile sero-fibrinous effusions of tuberculosis, tubercle bacilli are absent; tuberculous purulent effusions are also usually sterile on routine cultivation, and tubercle bacilli are rarely found except after inoculation into a guinea-pig. In purulent effusions of children, pneumococci are mostly found (80 per cent.), and in those of adults streptococci are more common (75 per cent.).

Pathology. *Dry Pleurisy.* The first stage consists of dilatation of the vessels of the pleura, quickly followed by exudation of fluid and migration of some leucocytes. The fluid coagulates and the resulting fibrin mixed with the leucocytes, often called loosely "lymph," is deposited on the free surface. The membrane is at first minutely injected, and very soon the naturally shining surface is rendered dull by the fibrin, which can be detached as an extremely delicate membrane. If the exuded material is more abundant, it forms thick layers, firm or pasty, generally rough on the surface, or villous, or reticular.

Pleurisy with Effusion. In this case an exudation of serous or sero-fibrinous fluid soon follows the production of "lymph" in a dry pleurisy, or if the process is more chronic an exudation of serous fluid occurs without the previous formation of "lymph." The fluid may accumulate to the extent of 2 or 3 pints or more in the pleural cavity. It has a yellow or greenish-yellow colour, a specific gravity of 1,005 to 1,030, often 1,015 to 1,018, and it becomes almost solid on boiling from the albumin it contains. Not infrequently there are a few flakes of fibrin, or a quantity is deposited from the liquid a short time after its removal. The liquid is quite clear, or it is opalescent or turbid from the presence of corpuscles. In acute cases eosinophil or polymorphonuclear cells predominate, in the more chronic cases the cells are relatively few and they are lymphocytes. In acute cases the cells may be in sufficient quantity to form a thick layer at the bottom of the fluid after its removal, and there is every gradation between this and the formation of thick pus. Sometimes the liquid is more or less tinged with blood, proceeding from new-formed vessels in the organising "lymph."

This effusion of fluid is one of the most important results of pleurisy. Confined within the cavity of the pleura, it must displace the lung from its relations to the diaphragm and the wall of the chest, and in proportion as more fluid is effused, the lung becomes collapsed. This is not due to the pressure of the fluid, but to the elasticity of the lung, which naturally favours its retraction; and, indeed, it may be found that even with a considerable quantity of fluid in the chest the pressure is still negative. But, even though this is the case, it may yet be higher than the pressure in the opposite pleura, so that the heart is displaced towards the healthy side. However, in some cases the pressure in the fluid may be greater than atmospheric, especially if it is purulent, and then, besides displacing the heart and mediastinum, it bulges the wall of the thorax outwards, distends the intercostal spaces, and forces downwards the diaphragm with the subjacent liver or spleen. In extreme cases the great vessels may be pressed upon and narrowed (Elliot Smith).

Pleurisy heals, like other inflammatory processes, by organisation of the fibrin covering the two surfaces, *i.e.* the new formation of blood vessels and of fibrous tissue. The effusion, if present, is absorbed in the course of days or weeks, and the lung and the chest wall finally come into contact either by expansion of the former, or by a gradual sinking in of the latter, or by a combination of these processes. In mild cases there may be no evidence in later years that any inflammation has ever occurred. On the other hand, the pleura over the lung may show a patch of thickening and be white in colour, while the surface is smooth and shiny. More often the parietal and visceral pleura have been in contact during organisation, so that they become united by fibrous tissue, which is known as an *adhesion*. Adhesions commonly occur between the lobes of the lungs. The vast majority of elderly people who die show evidence of some previous pleural inflammation. In severe cases the pleura may be greatly thickened, and fibrous tissue may invade the lung, producing fibroid lung.

Empyema. The micro-organisms responsible for empyema or purulent pleurisy have already been enumerated. An empyema may be primary in the sense that it is the first or only inflammation caused by an organism that has entered the body through some portal of entry. Again, it may be associated with disease in the neighbourhood—pneumonia, fractured rib, pulmonary abscess—and, lastly, it may be metastatic from disease elsewhere in the body, as in pyæmia. An empyema, like an abscess elsewhere, always begins with an exudation of clear fluid or of a fluid slightly turbid from leucocytes and flakes of fibrin. The length of this stage is variable; it is sometimes prolonged, as when a tuberculous pleurisy becomes purulent—quite a rare occurrence. In pneumococcal empyema there is less delay before suppuration occurs; when, as is usually the case, the empyema is associated pneumonia, suppuration usually takes place during or after resolution forming a *meta-pneumonic* empyema. In this case

the pneumonia is primary and the invasion of the pleura secondary. In empyema due to the hæmolytic streptococcus suppuration may be delayed or take place quite rapidly, so that when a streptococcal pneumonia is present, the empyema is present simultaneously—it is *syn-pneumonic*. In other cases pus is found on the first occasion that a pleural effusion is suspected.

Sometimes an empyema finds its way through the pleural sac, either perforating the lung, so that the pus is expectorated, or "pointing" in one of the intercostal spaces, often the fifth, and bursting spontaneously. In either case, air may find its way into the pleural cavity, and give rise to *pyo-pneumothorax*. Rarely an empyema opens through or behind the diaphragm into the abdomen. But, if unrecognised or untreated, it may remain a long time without perforating, with incomplete absorption, rendering the patient cachectic, and preparing the way for lardaceous degeneration of the viscera.

Both in serous and purulent effusions, the cavity is occasionally divided into separate spaces by adhesions between the lungs and the parietes. The fluid is then said to be *loculated*, and the condition is of importance when the case is treated surgically.

Symptoms and Physical Signs. *Dry Pleurisy.* The onset of pleurisy is characterised by severe pain, caused or aggravated by the act of breathing. The pain is commonly situated low down at the side of the chest; but it may be anywhere, depending on the position of the inflammation. It is cutting or tearing, and is intensified not only by breathing, but by coughing, sneezing, and every kind of exertion. The patient generally lies on his back or on the healthy side. Acute pleurisy may begin with a chill, and there is mostly some pyrexia, in which the temperature may reach 103°, but is more often 101° or 102°. With it are the usual accompaniments: furred tongue, loss of appetite, and malaise.

On examining the chest some impairment of movement on the affected side and deficiency of vesicular murmur at the painful spot are observed; but the characteristic physical sign is the *pleuritic rub*, or friction sound, which arises by the movement upon one another of the two pleural surfaces, roughened by exudation. The sound varies with the degree of friction. In acute cases the rub may be strictly localised and easily missed; it may even be absent, if the patient is prevented by the severe pain from making the inspiratory movement necessary to produce it. In chronic cases the friction may be so great that it can be felt by the hand placed on the chest, as well as heard with the stethoscope, and is quite painless.

Pleurisy with Effusion and Empyema. When liquid is effused, the two pleural surfaces become separated, the friction sound disappears, the pain diminishes, and symptoms and physical signs occur which are the direct result of the presence of liquid and the compression or displacement of the various organs which it affects. The chief symptom is shortness of breath, especially on exertion, and this dyspnœa is in proportion to the amount of liquid effused. He lies on his back, or on the affected side, to allow the greatest freedom to the healthy side. He may be entirely free from cough, or may have slight cough without expectoration. The pupils are occasionally unequal in pleuritic effusion, that on the affected side being larger.

As in other inflammatory conditions, the temperature is variable. In tuberculous pleurisy, for example, it may be very high, suggesting active disease in the glands of the hilum, perhaps; but usually the rectal temperature may only rise to 100° or 100·5°. In empyema, streptococcal or staphylococcal, it is also variable, but is usually high and intermittent or remittent, often with rigors, and the patient is and feels very ill, as in other acute fevers.

As the fluid usually gravitates to the most dependent part of the chest, there is absolute dulness at the base behind, while vesicular murmur, vocal resonance, and tactile vocal fremitus are much enfeebled, or entirely absent. With a

considerable quantity of fluid the following physical signs are observed: On *inspection* the affected side of the chest is motionless. The heart is displaced: with effusion on the right side, its impulse may be perceived beneath or outside the left nipple; with effusion on the left side, an impulse is often felt in the intercostal spaces to the right of the sternum, generally the third, fourth, and fifth, even as far as the right nipple, and in rare instances beyond it. In cases of clear effusion the circumference of the chest on the affected side is not increased; it may be diminished. In empyema it may be increased and the intercostal spaces, instead of being slightly depressed below the level of the ribs, are filled up (or "obliterated"); there may be slight œdema of the chest wall. The spleen or liver may be displaced downwards. On *percussion* dulness is observed in front, in the axilla, and behind, and is continuous with dulness on the opposite side corresponding to the displaced heart. At the same time on the opposite side of the chest the resonance is not unaffected, for a triangular area of dulness is found of which the apex is close to the spine at about the level of the angle of the scapula, and the base extends from the spine along the lower border of the lung for from 2 to 3 inches (*Grocco's paravertebral triangle*). The explanation is as follows: Normally the expansion of the central part of the lung is only possible because the tension of the posterior mediastinum is increased, which prevents it from being sucked over. This increased tension is due to action of the opposite diaphragm. When this is deficient, as in pleural effusion, the mediastinum gives at each inspiration, so that the central part of the lung on the unaffected side receives less air and the percussion note is impaired. When the liquid is sufficient only to reach above two-thirds the height of the chest, there may be heard the peculiar modification of the percussion note under the clavicle and above the level of dulness, which is known as *Skodaic resonance*, which is due to relaxation of the lung (*see* p. 123). On *auscultation* there is diminution or absence of breath sounds, of vocal resonance, and of tactile vibration over the dull area. At the upper level of the fluid where the lung is relaxed bronchial breathing or compensatory breathing may be heard: bronchophony or *ægophony* may be present. On the opposite side the breath sounds are exaggerated, but over Grocco's triangle they are diminished. In extreme cases where the lung is compressed solid, there may be loud bronchial breathing instead of absent breath sounds. Where there is great displacement of the viscera, the disturbance of the respiratory functions may at length be fatal. The patient becomes more and more livid, rhonchi and mucous râles are heard in the hitherto healthy lung, and asphyxia ensues. Sometimes there is sudden syncope, which may reasonably be explained by pressure on the heart and great vessels.

In the case of young children the dulness on percussion is not absolute, and bronchial breathing may be heard all over the dull area, and this may lead to the belief that the lung is solid. The displacement of the heart may help in such a case.

Very rarely the pulsation of the heart (or perhaps the aorta) is communicated to a pleural effusion, either as a shock or wave transmitted to a large serous collection or as a more localised, perhaps visible, pulsation in an empyema, pointing through the chest wall. This is described as *pulsating pleurisy* or *pulsating empyema.*

In the early stage of *interlobar pleurisy* there may be pain, cough, and oppression of breathing, but no distinctive sign. When liquid has collected to the extent of 6 or 7 ounces or more, percussion may give a dull note in the middle zone of the chest, with resonance above and below; and this may be accompanied by râles. Hæmoptysis is a frequent symptom in *interlobar pleurisy* (Dieulafoy), and if the fluid is purulent, as it often is, it may open into a bronchus, be coughed up and so heal itself, though occasionally a discharging cavity may remain for months or years.

In *diaphragmatic pleurisy* the effusion is located between the lung and the diaphragm; it is not generally abundant; it is often preceded by severe pain with tenderness on pressing over the insertion of the diaphragm into the tenth rib in front, or on compression of the phrenic nerve in the neck. Dulness, friction sound, and ægophony are absent unless the trouble reaches the main pleural cavity, and thus a small collection of liquid, encysted here, may easily be overlooked.

Similarly a *mediastinal pleurisy* may show few distinctive signs until the collection of liquid is sufficient to press upon the important structures in the middle line of the chest. These signs are dyspnœa, attacks of oppression, wheezing and stridor, dysphagia, a brassy cough, hoarseness of voice, and distension of the veins on the surface of the chest. At the same time there may be tenderness on pressure of the dorsal vertebræ, and there may be paravertebral dulness with weak breath sounds, ægophony and râles. Over the pericardium pleurisy gives rise to so-called *pleuro-pericardial friction* (*see* p. 127). Mediastinal empyemas are liable to be discharged through the bronchial tubes. The diagnosis will be helped by X-rays, which will show whether the obstructing mass is pulsatile or not.

Diagnosis. In dry pleurisy the pain has to be distinguished from other pains in the chest, the most common of which is *pleurodynia*, or fibrositis. This is increased by movement, but is unaccompanied by fever or by rub. Intercostal *neuralgia* is distinguished by its relation to the nerves, and by the tender points characteristic of neuralgia. Perihepatitis and perisplenitis may give rise to pains aggravated by breathing, for these structures are compressed by the descent of the diaphragm during inspiration.

In the stage of effusion we have to consider, first, whether there is liquid in the pleural cavity, and, secondly, what is the nature of the liquid, whether serum or pus. In acute cases, pleurisy and *pneumonia* are most likely to be confounded together, because in the early stages of pneumonia the breath sounds are often absent. Pleurisy is generally characterised by the absence of tactile vibration and the more absolute percussion dulness; and the larger effusions cause displacement of the heart, which is conclusive. With the X-rays a very dark shadow, whose upper concave margin rises sharply from the spine towards the axilla, is produced by pleural effusion; and the line of the diaphragm is not seen (*see* Plate 7, B, page 168). The lung above shows a faint darkening from condensation, and there is occasionally a line of demarcation (*see* Plate 8).

In chronic cases, fluid may be simulated by most *consolidations* of the lung tissue, whether from deposit in its substance or from compression; such are some cases of tuberculous consolidation, fibroid lung, the induration which results from heart disease, growth in the lung, compression from the front by pericardial effusion, and from below by subphrenic abscess and by growth or hydatid of the liver. The physical signs common to these conditions are dulness, loss of breath sounds, of vocal resonance, and of tactile vibration—that is, absence of all evidence of healthy lung—simply because these growths or collections of liquids compress or push up the lung in the same way as a pleural effusion does. Another cause of dulness at the base, frequently mistaken for pleural effusion, is obstruction of one bronchus; but in this case the dulness is not usually so absolute as with pleural effusion. X-ray examination is of particular value in distinguishing subdiaphragmatic tumours, abscesses or cysts from a pleural effusion, because the diaphragm constitutes the upper surface of the former, and is convex, though it may be raised and immobile with respiration. The upper surface of a pleural effusion is concave.

With empyema the patient often has a sallow appearance or even marked anæmia; the temperature has often a hectic type, ranging from 98° or 99° in the morning to 102°, 103°, or 104° in the evening, and with this rigors or profuse sweatings may occur. But the chest may be full of pus when the temperature is quite normal. There is pronounced leucocytosis in empyema. The sudden

occurrence of purulent expectoration in the course of pleurisy is an important indication of an empyema which has ruptured into a bronchus; and in cases of long duration the ends of the fingers become thickened, or "clubbed." Œdema of the chest wall occurs more frequently in empyema than in serous effusions, but in neither case is it an early sign. The chest wall overlying an empyema may be tender on pressure. In young children, a combination of cough, dyspnœa, vomiting and wasting suggests empyema.

Serum may be present in the pleural cavity from other causes than pleurisy—namely, local and general dropsy. The physical signs are the same, but *hydrothorax*, as the condition is called, generally follows upon disease of the heart, or Bright's disease, or pressure upon vessels by growth in the chest; and there is an absence of the febrile accompaniments of pleurisy.

In all but acute cases the pitfalls are so numerous in diagnosis that an early appeal should be made to exploration with a suitable needle and syringe. This has the additional advantage of determining, as it alone can, the nature of the fluid, and of affording material for microscopic and bacteriological examination. In passive effusions (hydrothorax) large endothelial cells predominate, but lymphocytes may be present; in infective forms of pleurisy due to streptococcus or pneumococcus the polymorphonuclear and large mononuclear leucocytes are found in excess; while in tuberculous pleurisies lymphocytes often predominate, but polymorphonuclear cells are often present as well. Tuberculosis is the commonest cause of a bloodstained effusion, but the latter also occurs with growth.

If organisms cannot be directly cultivated from the pleuritic serum, and tubercle bacilli cannot be found, its tuberculous origin may be demonstrated by the *inoculation* of a guinea-pig.

As indicated in the description of the symptoms of the localised pleurisies, their diagnosis may be very difficult. A mediastinal pleurisy is liable to be confounded with mediastinal growths, whether malignant or lymph-adenomatous; but the history of the former is usually short, and the onset rapid. Help may in all cases be obtained from the X-rays.

Prognosis. Most cases of pleurisy without effusion, or with a sero-fibrinous effusion, get well either under medicinal treatment or after removing the liquid; but their subsequent history may be often unfavourable. Empyema is very fatal in children under two years old; only 25 per cent. recover (**40**). This is because it is usually only one manifestation of a general pneumococcal infection, which simultaneously causes pneumonia, pericarditis, etc. In older children empyema usually follows pneumonia and there are no other complications, and so the prognosis is good, better even than in adults, and more promising the earlier the pus is evacuated. This is probably because in children the majority of cases are pneumococcal, while in adults more are streptococcal. If a pneumococcal empyema is complicated by pericarditis, which is not infrequently the case, the prognosis is bad; but cases have recovered.

Treatment. If the pleurisy is tuberculous, the general treatment described under pulmonary tuberculosis should be instituted.

Pain may be alleviated by the application of linseed meal poultices, antiphlogistin or thermogen wool, and the administration of opium or morphia internally, or morphia subcutaneously. The use of blisters, of leeches, or of cupping over the painful spot, also generally gives relief. The affected side may be strapped, and by this means the respiratory movements are restrained, the pain is allayed, and inflammatory action is probably in some measure checked. An excellent alternative method, devised by Sir Charlton Briscoe, is to fasten a belt* tightly round the chest; a brass spring is let into the belt on the sound side, so that expansion with inspiration is possible here. The strapping should

* The belt is made by Brice & Evelyn, Wigmore Street, W.1.

be applied in broad strips from the spine to the sternum, alternate strips passing obliquely upwards and obliquely downwards, till the whole side is covered. The patient should be kept at rest. If effusion takes place, anodynes will be less needful, and salines, such as the acetate and citrate of potassium, or of ammonium, may be given for their effect upon the excretions of the skin and kidney, the increase of which will favour absorption of the effused fluid. After a time iodide of potassium, squill, or other diuretics may be added, and it is possible that absorption is increased by counter-irritation, such as may be obtained by painting the tincture or solution of iodine over the affected side.

The most usual practice at present in cases of tuberculous effusions is to remove the fluid only when it is present in excessive amounts. It is believed that moderate quantities may be actually beneficial by compressing the lung and diminishing movement, on the same principle that artificial pneumothorax is beneficial. If the heart is pushed over, or there is absolute dulness over most of one side of the chest, some of the liquid should be removed by a trocar and cannula. The best rule is to allow it to escape until it is under atmospheric pressure, *i.e.* until it no longer runs out of the cannula of its own accord. To save time an aspirator is often used, or the liquid is drained away by syphonage through a flexible tube into a vessel placed on the floor; but it must be remembered that it is easy by such means to remove more liquid than is desirable. A recent method is to replace the fluid by air. Great help in expanding the lung may be obtained by simple breathing exercises. The patient should take deep breaths at frequent intervals, and should also blow out against resistance.

If an exploration by the needle shows that the liquid is purulent (empyema), the surgeon should make a free incision under an anæsthetic, local or general, and resect a piece of rib, and allow the pus to drain away. Children under two do not stand rib resection very well. A cannula may be introduced between the ribs by means of a trocar, and tied in position by tapes round the body. A rubber tube which just fits the cannula is introduced into the empyema cavity and the contents evacuated into a thick-walled conical flask, permanent suction being kept up by means of a filter-pump or other contrivance (**41**). In cases of neglected empyema of long duration, in spite of free drainage, the cavity continues to secrete pus, and the wound does not close. If this goes on too long, the supervention of lardaceous disease is to be feared. There are three possible methods of procedure: (1) The cavity may be washed out with eusol until the contents are practically sterile as tested bacteriologically. Carrel's method of continuous drainage may be used. The wound may then be allowed to close, so that the patient has permanently a sterile pneumothorax. It is best not to wash out an ordinary acute empyema cavity, as deaths have been reported from *pleural reflex syncope*. This is probably due to vagal inhibition produced by irritation of the inflamed pleura. This danger is not apparently present in chronic cases. (2) A fairly extensive surgical operation may be carried out involving the resection of enough ribs to allow the hand to enter the chest. The thick visceral pleura is peeled off (decortication), and the lung rapidly expands and fills up the cavity. (3) Thoracoplasty (*see* p. 175).

The problem often arises as to whether an operation should be carried out in cases of acute pleural effusion due to the streptococcus, for instance where the fluid is somewhat turbid and contains large numbers of polymorphonuclear cells when examined microscopically. The answer is that rib resection should only be used when actual pus is present, but the turbid fluid may be removed by aspiration if present in large amount. American observations at Camp Lee, Va., showed the advantage of this procedure in empyemas due to the hæmolytic streptococcus. In early cases pneumonia is often present with the pleurisy; further, if resection of a rib is carried out at too early a stage, the operation wound may become infected leading to a septicæmia. The effusion, even though turbid, often clears up without operation. On the other hand, pus may develop

in two or three weeks, and then rib resection should be carried out. During the surgical treatment of an empyema the patient should be supported in every way by good food, fresh, bracing air, and by tonic medicines, such as quinine, iron, and cod-liver oil.

HYDROTHORAX

The term is applied to the collection of fluid in the pleural cavity, not as a result of inflammation, but in consequence of heart disease or Bright's disease, cirrhosis of the liver, or interference with the circulation in the chest by growth. It is, indeed, dropsy of the pleural cavity; and the liquid contains less albumin and less fibrinogen than are found in pleurisy. Its physical signs are similar to those of pleuritic effusion, but the rub is, of course, absent. Arising, as it often does, from a general or central cause, it is much more often bilateral than pleurisy is; but occasionally a very large one-sided effusion may be merely dropsy. The recognition of hydrothorax, however, generally depends on the history and the previous existence of the diseases which cause it. When the liquid has been removed, the kind of cellular elements it contains may help the diagnosis, as described under Pleurisy. If acetic acid is added to an inflammatory effusion, a white turbidity is produced. This does not occur with a passive effusion.

Its **Treatment** is mostly of secondary importance, being involved in that of the lesion which causes it. As the liquid is almost certain to recur if removed, paracentesis or aspiration should only be performed when a very large effusion, whether on one side alone or divided between the two, is seriously impeding respiration.

HÆMOTHORAX

By this term is meant the effusion of blood in quantity into the pleural cavity; it is not used for the merely bloodstained serous effusions so common in pleurisy. Hæmothorax commonly results from wounds, injuries or from rupture of a thoracic aneurysm. In the case of wounds the greatest danger to life is from the blood becoming infected from the outside. It occurs sometimes in tuberculosis of the pleura, or from rupture of a pulmonary vessel into a phthisical cavity and later extravasation into the pleura. Exceptionally it occurs from bursting of an emphysematous bulla (Newton Pitt); or from degenerated vessels in association with cirrhosis of the liver, granular kidney, or dilated heart; or from malignant disease. And sometimes it appears to be primary, and the origin is never explained.

The **Physical Signs** are those of liquid in the pleural cavity. In hæmothorax following wounds the diaphragm on the same side is high and immobile; the lung is much compressed, and above the fluid it is greatly relaxed, so that Skodaic resonance is especially marked.

The **Diagnosis** will depend, in the case of aneurysm, on the previous history, and on syncope and pallor indicating rapid loss of blood. A hæmothorax may only be discovered on exploration.

Treatment. If the liquid be aspirated, it is very likely to return; and probably it is better to leave the blood to be absorbed, unless it is causing distress by direct pressure. In the case of wounds a moderate hæmothorax may be aspirated a week after the wound, and it is often an advantage to replace it by oxygen. A septic hæmothorax requires free drainage.

CHYLOTHORAX

Rarely an effusion into the pleural cavity is found to be white and milky, like the fluids sometimes present in the peritoneal cavity. In some cases it is a true *chylothorax*, in others a *chyliform effusion*, in which the milky appearance is not

due to the fatty elements of chyle, but to granules of a lecithin compound (*see* Chylous Ascites). The causes are the same as in the case of the peritoneum. Cases of chylo-hæmothorax have been recorded as a result of injury to the thoracic duct in the chest.

PNEUMOTHORAX

Pathology. The presence of air in the pleural cavity constitutes a *pneumothorax.* If serum is present at the same time, it is a *hydro-pneumothorax;* if pus accompanies the air, a *pyo-pneumothorax;* if blood, a *hæmo-pneumothorax.*

Air may gain an entrance to the pleural cavity—(*a*) through an opening in the chest wall, (*b*) through a breach in the surface of the lung, or (*c*) occasionally from the rupture of some other air-containing viscus in the neighbourhood. (*a*) A pneumothorax may be brought about by any wound in the side which passes through the whole thickness of the chest wall; it is commonly produced artificially when a piece of rib is resected for empyema (pyo-pneumothorax), or in the treatment of phthisis by inducing artificial pneumothorax. (*b*) It is produced by a fractured rib puncturing both layers of the pleura, so as to let out air from the lung into the pleural cavity, while the skin remains intact. In nine out of ten cases of pneumothorax occurring spontaneously from rupture of the surface of the lung, the result is due to phthisis when a vomica ulcerates through into the pleural cavity; and less commonly an empyema makes its way through the pleura into the lung, and air passes into the pleural sac, so as to form a pyo-pneumothorax. In acute pneumonia the pleura has been known to rupture, so that air has escaped and a pneumothorax has been formed; and a pyæmic abscess or gangrene of the lung may lead to a similar result, or an emphysematous bulla may burst. Very occasionally a pneumothorax occurs spontaneously from rupture of the lung in quite a healthy person, possibly as the result of some sudden strain. (*c*) Air may also enter the pleura in consequence of a spinal or mediastinal abscess burrowing into the pleura; and ulcer or carcinoma of the stomach, or carcinoma of the œsophagus, may let in air from the alimentary canal.

A pneumothorax may be described as open, closed, or valvular, according to the condition of the opening which created it.

Open Pneumothorax. When air enters the chest from an external wound, and the wound remains patent, the lung collapses by its own elasticity; and not only the lung of the wounded side, but also the opposite lung, may contract somewhat and draw with it the mediastinum, so that slight lateral displacement of the viscera takes place, just as it does in liquid effusion. The same thing may happen if the pneumothorax results from rupture of a cavity in phthisis, supposing the aperture to remain patent, so as to keep the pleural sac in communication with the bronchial tubes. In both these cases the mean pressure of the air in the pneumothorax is equal to that of the atmosphere.

Closed Pneumothorax. When the aperture is small it may be quickly closed by lymph; further extravasation is prevented, and the air may then be completely absorbed. This happens in cases of laceration of the pleura by fractured rib, and sometimes in pneumothorax from disease of the lung. In closed pneumothorax there is a slowly progressive absorption of the enclosed air; the pressure is negative, and the displacement of organs is, *cæteris paribus*, less than in open pneumothorax.

Valvular Pneumothorax. A third possibility is that a shred of pleural membrane or lymph hangs over the aperture, so as to form a valve. The air is then drawn into the pleural sac by inspiration, but is unable to escape during expiration; the mean pressure becomes positive—that is, it exceeds the pressure of the atmosphere, and the displacement of viscera and distension of

the chest may be extreme; thus the heart may be pushed far over to the opposite side, and the liver or spleen may be driven down by the flattening or inversion of the diaphragm. A valvular opening may, like others, become closed by adhesions.

The amount of collapse of the lung, and displacement of the viscera, is influenced in different cases by the previous condition of the lung. If the lung is extensively diseased in phthisis, or in great part adherent, the collapse will be less than if the lung is for the most part healthy.

Physical Signs. Resonance depends on the presence of a cavity and of elastic walls capable of vibrating in unison with the air waves (*see* p. 122). The elasticity of the walls depends largely on the pressure of the air inside the cavity. If the pressure is very high, as in a valvular pneumothorax, the note is dull. It may also be dull if the pressure inside is the same as the atmospheric pressure, as occurs after the resection of a rib for empyema. Under favourable conditions of pressure, whether the latter is greater or less than the atmosphere, a tympanitic note is obtained on percussion, and this is accompanied by the *bruit d'airain*, or *bell sound* (*see* pp. 123, 127), and in very favourable circumstances by *metallic tinkling* (*see* p. 126). The dependence of the *bruit d'airain* on the elasticity of the walls of the cavity, which itself is determined by the pressure of the contained air, can be demonstrated by the student to himself as follows: He closes his mouth, blows out his cheeks, lays one coin on the cheek and strikes it with another. A musical sound is obtained if the pressure exerted by the cheeks on the enclosed air is correctly adjusted. Another characteristic sound is due to the dropping of fluid from the upper part of the chest into the liquid below, the noise being reverberated with almost musical quality. The respiratory murmur is often entirely inaudible, or faint amphoric breathing is present. Amphoric breathing may be due to compression of the lung or possibly to an opening leading from a bronchus into the pneumothorax; but a fainter sound may occur even when adhesions have shut off the lung from the pleural cavity. Vocal resonance and tactile vibration are generally much diminished, but bronchophony or pectoriloquy may be present when there is amphoric breathing.

If there is also liquid effusion, it gravitates to the lowest part of the chest under all circumstances. If the patient is recumbent, the posterior part of the chest is dull, and the anterior part is tympanitic; if the patient now sits up, the lower part of the chest, back and front, becomes dull, while the upper part, back and front, is resonant. If *Hippocratic succussion* be employed, a splashing sound will be obtained (*see* p. 126).

The **Symptoms** of pneumothorax are very variable, depending largely upon the amount of antecedent disease. If it supervenes upon a lung extensively diseased, it may add but little to the distress already present; if it occurs in a lung for the most part, or entirely, sound, the symptoms will be pronounced; lastly, if in a case of phthisis with extensive disease on one side pneumothorax occurs on the other side, the result may be quickly fatal. The symptoms in the severe cases are sudden pain with a sense of something giving way internally, then distress of breathing, with more or less collapse, small pulse, lividity, and sweating. The breathing is rapid; the chest is distended on the affected side, and the intercostal spaces are depressed on inspiration.

These troubles may be aggravated until death takes place within a few hours or two or three days, or the first severe symptoms may subside, and comparative ease may follow, but generally with rapid breathing and orthopnœa.

Diagnosis. A resonant note associated with deficient breath sounds or distant bronchial breathing suggests the diagnosis, but without X-rays mistakes are common. X-rays show the transparency due to air in the pleural cavity, the collapsed lung, the depressed diaphragm on the same side, and the displaced heart (*see* Plate 7 B, p. 174). The presence of fluid in a pneumothorax produces a very characteristic X-ray appearance when the patient is examined

in the vertical position, because it is opaque and its upper surface is a horizontal line, while above it there is transparency owing to the air (*see* Plate 9, A). Further, on inclining the body the surface of the fluid still remains horizontal. A *diaphragmatic hernia*, that is, the escape of the stomach or the colon into the thorax through an aperture in the diaphragm, may closely resemble pneumothorax in its physical signs, and it may arise in the same way, from a contusion of the chest. Pneumothorax may also be simulated by an unusually high position of the stomach in the chest in consequence of contraction of the left lung, and by abscess beneath the diaphragm containing air (*subphrenic pneumothorax*, Plate 32, A, p. 407).

Prognosis. The occurrence of spontaneous pneumothorax in phthisis is on the whole, a favourable event, and cases have improved subsequently (*see* Artificial Pneumothorax). In other cases the prognosis is, on the whole, good with suitable treatment, though it depends on the attendant circumstances.

Treatment. This is, in the main, palliative. For the intense pain and distress accompanying the rupture opium or a subcutaneous injection of morphia ($\frac{1}{3}$ to $\frac{1}{2}$ grain) should be administered, and hot poultices and fomentations should be frequently applied. Stimulants, as wine, brandy, or ether, may also be required. In cases of extreme distension it may be desirable to perform paracentesis, a trocar and cannula being inserted between the ribs over the resonant area and the air allowed to escape till atmospheric pressure is reached; the relief is, as a rule, only temporary, and the paracentesis may have to be repeated. Alternatively, in the case of valvular pneumothorax, a steady negative pressure can be applied, using a Sprengel's filter pump (**63**). If the communication with the lung becomes closed, the air will probably be absorbed; but to facilitate its absorption it may be replaced by oxygen. A simpler plan is to use a high percentage of the oxygen in a tent; the nitrogen diffuses out and the pneumothorax then rapidly disappears. In hydro-pneumothorax the serum may be left alone, or, if present in large amounts, it may be removed by paracentesis. If a pyopneumothorax is producing constitutional symptoms, *i.e.* temperature, rapid pulse, etc., it should be treated like an empyema with rib resection and drainage. Otherwise the liquid may be dealt with like serum.

DIAPHRAGMATIC HERNIA

This condition, which is of rare occurrence, may be mentioned here, because the contents of the thorax are necessarily modified by the invading viscus, and physical signs are produced which may closely resemble those of pneumothorax. In diaphragmatic hernia one or more of the abdominal contents, generally a portion of the stomach, or of the omentum, or of the colon, passes upwards into the thorax through an aperture in the diaphragm. Mostly the aperture is the result of injury, such as a forcible sudden compression of the chest, or it is a congenital defect, or the enlargement of a natural opening. The lesion is more frequent on the left side, and the stomach is commonly the viscus, which passes into the thorax and is drawn upwards in the process (Plate 9, B).

Symptoms. When the diaphragm is ruptured by injury, the early symptoms, such as pain, dyspnœa and collapse, are partly due to the direct effects, and partly to the sudden disturbance of the contents of the thorax with compression of the lung on the same side. Pleurisy and peritonitis may also supervene with the symptoms referable to them. But in many cases the first effect of the injury passes off, and the symptoms are partly pulmonary and partly gastric or gastro-intestinal. The pulmonary symptom is mainly shortness of breath, but it is remarkable how little disturbance may be felt on the side of the chest in some cases. On the side of the abdomen are generally observed indigestion, pains,

flatulence, and perhaps vomiting. These symptoms may come on periodically, being due to distension or kinking of the viscera in their abnormal situation. In a recent case severe symptoms were noticed at periodic intervals, when for some reason the stomach was forced up through the diaphragm compressing the lung.

The physical signs noted in the chest are hyper-resonance in the lower part occupied by the herniated viscus, with loss of breath sounds, gurgling sounds heard on succussion or spontaneously, metallic echo and the *bruit d'airain*. The heart may be displaced if the visceral transfer is considerable.

Subphrenic pneumothorax may also present somewhat similar physical signs. It is more common on the right side, and the liver is depressed by it into the abdomen. The hyper-resonance resulting from it is not likely to rise so high in the chest as in either of the other two cases, and the history will probably assist in the diagnosis (*see* Plate 32, A, *facing* p. 407).

Diagnosis. The diagnosis of diaphragmatic hernia can only be made with any certainty by X-ray examination after an opaque meal (*see* Plate 8, B).

Treatment. Some patients are not very seriously inconvenienced after the first troubles have passed. Surgical treatment involves opening the chest, removing portions of ribs, returning the viscus to the abdomen, and sewing up the diaphragm.

MEDIASTINITIS

Inflammation of the mediastinum may be suppurative or non-suppurative. The former, or *mediastinal abscess*, arises from numerous causes, of which injuries by bullet, stab, or blow, and tuberculosis of the lymphatic glands are the most frequent, while occasionally it follows upon pneumonia, pleurisy, erysipelas, or enteric fever. The abscess may be in the anterior or in the posterior mediastinum, more often in the former. The chief symptoms are sternal pain and pyrexia. Physical signs will only be apparent if the abscess reaches a sufficient size, when there may be dulness, localised tenderness, œdema over the sternum, and ultimately fluctuation at the border of that bone. The pus must be evacuated as soon as possible, and, if necessary, the sternum must be trephined or a portion resected.

Adhesive or non-suppurative mediastinitis may also arise from traumatism and general infectious disease, but its most common associations are pleurisy and rheumatic pericarditis, especially the latter, forming then *mediastinitis fibrosa* This has been described under Adherent Pericardium.

REFERENCES

1	M. Brown and C. G. Imrie ..	1932	*Quart. Journ. Med.*, N.S., **i.**, p. 319.
2	Ff. Roberts	1922	*Journ. Physiol.*, **56**, p. 101.
3	Sir W. Hale-White ..	1924	*Lancet*, **i.**, p. 263.
7	Campbell, Hunt and Poulton ..	1923	*Journ. Path. & Bact.*, **26**, p. 234.
8	P. H.-S. Hartley and I. J. Davies	1923	*Brit. Med. Journ.*, **i.**, p. 1052.
9	J. F. Gaskell	1927	*Lancet*, **ii.**, p. 951.
10	C. McNeil and A. R. MacGregor..	1927	*Brit. Med. Journ.*, **ii.**, p. 582.
11	C. Wall and J. C. Hoyle	1933	*Brit. Med. Journ.*, **i.**, p. 597.
12	W. Burton Wood	1930	*Lancet*, **i.**, p. 1339.
13	S. Van Leeuwen	1922	*Neurotherapie, No.* **6.**
14	H. W. Barber and G. H. Oriel ..	1928	*Lancet*, **ii.**, pp. 1009, 1064.
15	S. Van Leeuwen	1924	*Klin. Woch.*, **3**, p. 520.
16	A. Francis	1917	*Practitioner*, August.
17	S. Van Leeuwen	1923	*Klin. Woch.*, **2**, *No.* **27.**
18	J. Freeman	1920	*Lancet*, **ii.**, p. 229.
19	S. Van Leeuwen and Varekamp..	1921	*Lancet*, **ii.**, p. 1366.

20	A. G. Auld	1921	*Lancet*, **i.**, p. 698.
21	S. Gilbert Scott	1926	*Brit. Med. Journ.*, **i.**, p. 939.
22	S. van Leeuwen	1927	*Brit. Med. Journ.*, **ii.**, p. 344.
23	McCrae (Lumleian Lectures on Foreign Bodies in the Bronchi) ..	1924	*Lancet*, **i.**, pp. 735, 787, 838.
24	Review on Respiratory Diseases ..	1920	*Med. Sci.*, **i.**, p. 462.
25	A. Abrahams	1920	*Lancet*, **ii.**, p. 543.
26	Zadek	1921	*Med. Sci.*, **5**, p. 103.
27	Review on Pneumonia	1921	*Med. Sci.*, **5**, p. 110.
28	W. Smith	1924	*Lancet*, **i.**, p. 257.
29	S. L. Cummins	1924	*Brit. Med. Journ.*, **i.**, p. 186.
30	B. Alcock, M. Douglas, and H. C. Lucey	1925	*Lancet*, **i.**, p. 1332.
31	Sir C. Allbut and Varrier-Jones	1922	*Lancet*, **i.**, p. 105.
32	B. Hudson and Leonard Hill ..	1924	*Lancet*, **i.**, p. 1147.
33	Weill and Dufont	1922	*Journ. de radiol. et d'electrol.*, **6**, p. 1.
34	W. C. Bosanquet	1928	*Lancet*, **i.**, p. 24.
35	R. C. Wingfield	1924	*Lancet*, **ii.**, p. 354.
36	Gravesen	1923	*Brit. Med. Journ.*, **ii.**, p. 506.
37	H. Morriston Davies	1926	*Brit. Med. Journ.*, **i.**, p. 315.
38	C. Lillingston	1923	*Lancet*, **i.**, p. 96.
39	W. A. Lister	1927	*Lancet*, **i.**, p. 112.
40	H. C. Cameron and A. A. Osman ..	1923	*Lancet*, **i.**, p. 1097.
41	F. J. Poynton and Reynolds ..	1921	*Lancet*, **ii.**, p. 1100.
42	W. S. Miller	1923	*Journ. Exp. Med.*, **38**, p. 707.
43	W. S. Miller	1913	*Journ. Morphol.*, **24**, p. 459.
44	S. C. Simpson	1929	*Quart. Journ. Med.*, **22**, p. 413.
45	G. H. Oriel	1929	*Guy's Hosp. Reps.*, **79**, p. 376.
46	G. H. Oriel	1929	*Personal Communication.*
47	R. S. Bruce Pearson	1933	*Guy's Hosp. Reps.*, **83**, p. 86.
48	F. A. Knott and J. W. Thornton	1933	*Guy's Hosp. Reps.*, **83**, p. 63.
49	Argyll Campbell and E. P. Poulton	1935	"Oxygen and Carbon Dioxide Therapy." *Oxford Med. Pub.*, 1935,
50	W. E. Gye and E. H. Kettle ..	1922	*Lancet*, **ii.**, p. 855.
51	S. L. Cummins and A. F. Sladden	1934	*Brit. Med. Journ.*, **i.**, p. 554.
52	L. G. Irvine	1932	*Brit. Med. Journ.*, **i.**, p. 693.
53	P. d'Arcy Hart	1932	*Med. Res. Counc. Spec. Rep. Ser.* 164.
54	P. d'Arcy Hart	1932	*Quart. Journ. Med.*, N.S., **i.**, p. 49.
55	A. Loewy	1934	*Arch. Med. Hydrol*, p, 261.
56	G. Maurer	1930	*Lancet*, **ii.**, p. 72.
57	F. G. Chandler	1930	*Lancet*, **ii.**, p. 74.
58	A. J. S. Pinchin and H. V. Morlock	1933	*Lancet*, **i.**, p. 1114.
59	H. C. Cameron	1932	*Guy's Hosp. Reps.*, **82**, p. 290.
60	A. Tudor Edwards	1932	*Brit. Med. Journ.*, **i.**, p. 827.
61	W. Brockbank	1932	*Quart. Journ. Med.*, N.S., **i.**, p. 31.
62	Ff. Roberts	1933	*Brit. Med. Journ.*, **i.**, p. 142.
63	E. R. Boland	1934	*Lancet*, **i.**, p. 231.
64	Chevalier Jackson	1930	*Proc. Roy. Soc. Med.*, **24**, p. 1.
65	R. V. Christie	1936	*Oral Communication.*

DISEASES OF THE NOSE, THROAT, AND EAR

(From the Medical Aspect)

THE NOSE

CORYZA

This disease, familiarly known as a " cold in the head," is a catarrhal inflammation of the mucous membrane of the nose (acute rhinitis), which often involves the pharynx (catarrhal sore throat) and also the conjunctivæ, frontal and other sinuses, and Eustachian tubes, and may spread to the larynx, trachea, and bronchi. It is primarily an infection, which is spread by the inhalation of a spray of saliva from an infected person, emitted during coughing, sneezing, and talking. Sometimes at the end of a period of immunity acquired from the last attack patients may reinfect themselves. The cause of a common cold is a minute " filter-passing " coccoid body, 0·2 to 0·3 micron in diameter, arranged singly, in pairs and in groups, and resembling the virus of poliomyelitis (**1**). If the normal nose and throat are examined bacteriologically there appear commonly to be zones of living bacteria ; *Staphylococcus albus* is present in the anterior nares ; the *B. septus*. which is a diphtheroid, grows at the back of the nose. *Micrococcus catarrhalis* predominates in the nasopharynx, and the *Streptococcus viridans* on the tonsils. When the cold begins the *Streptococcus viridans* is commonly the first organism to multiply vigorously—particularly the more haemolytic strains, and tends to overgrow the more normal inhabitants ; a little later culture may show activity among one or more secondary invaders, such as Freidlander's bacillus, the pneumococcus Type 4 and the *Staphylococcus aureus*, any of which may be found located in the sinuses, when there is local suppuration. There tends to be a predominance of one type of organism according to the epidemic and in some epidemics Pfeiffer's *Bacillus infiluenzæ* is found to the exclusion of all the rest. The chief predisposing cause is congestion and swelling of the nasal mucous membrane. In general this is brought about by a moist atmosphere with the temperature variable, but on the whole cool. It is this latter fact that has given rise to the phrase " catching cold." It is under such conditions that epidemics occur. Again, the conditions indoors may be responsible ; people often sit in a warm stuffy room where the air is stagnant, but where the floor is made cold by draughts. The head is warm, and the feet are chilled. Physiologically the head and nasal mucous membrane should be cool and in fresh moving air, and the feet should be warm (L. Hill).

Symptoms. An attack of sneezing or a raw or rough feeling in the throat and pain on swallowing may be one of the first symptoms ; but these may be preceded by a feeling of indisposition, with chilliness, headache, and loss of appetite. The sneezing is soon followed by the discharge of clear mucus from the nose ; and there is a feeling of stuffiness in the nose, due to swelling of the mucous membrane and loss of the sense of smell. The soft palate, uvula, pharynx, and tonsils are redder than natural ; in more severe cases (*ulcerated sore throat*) superficial abrasions occur on the tonsils, palate, and pharynx, the tongue is furred, and

there is marked constitutional disturbance. At the same time, the eyes are suffused and water freely, there is pain over the eyebrow from implication of the frontal sinus, and there may be deafness from closure of the Eustachian tube. Some febrile reaction is present at the same time. If the catarrh extends to the larynx, the voice is hoarse, and there is constant irritating cough ; and its further spread to the lungs will cause the symptoms described below under Bronchitis. Often after one or two days the acute stage subsides, and recovery is complete. On the other hand, the discharge may continue, becoming thicker and more opaque from the presence of pus with the mucus. It may continue thus for a variable period, from two or three days to two or three weeks. During this time the patient is liable to fresh exacerbations of the inflammation.

Such is the typical picture of a coryza ; but in other cases the infection may begin as an acute laryngitis or bronchitis and subsequently spread upwards to the throat and nose. The clinical picture in different people is variable ; but in the individual person the course of the infection tends to be pretty constant. Thus, in one person a coryza always begins as a pharyngitis, in another as a laryngitis, in another as a bronchitis, and so on. People are thus very prone to suffer from repeated infections which chiefly attack one particular part of the respiratory tract. In those from whom the tonsils have been removed a coryza is more apt to begin as a pharyngitis or laryngitis. After a time recovery may be longer and longer delayed, and a chronic infection may result, taking the form of chronic nasal catarrh, chronic catarrhal laryngitis, chronic bronchitis, etc., depending on the part attacked in the first place.

It must be remembered that acute rhinitis occurs as a specific lesion in some of the infective diseases, such as influenza, measles, diphtheria, congenital syphilis, glanders, and others.

Prevention. A hygienic method of life with plenty of outdoor exercise and a daily cold bath for robust persons, the avoidance of stuffy rooms, and especially of infected persons, are important measures. Personal experience has shown that a treatment devised by W. Glegg for chronic nasal catarrh is of the greatest value. While the patient lies on his back one or two teaspoonfuls of a mixture of paraffinum molle and paraffinum liquidum (1 in 3 or 4) is run down each nostril in turn from a pipette supplied with a rubber bulb. When the mixture is felt in the throat it may be swallowed, or expectorated if it causes looseness of the bowels. This treatment can be carried out once or twice a day, or more often if a cold is threatening. The mixture is also supplied in a collapsible tube and menthol gr. ½ per. oz. may be added, or it may be flavoured with rosettol.

In many cases nasal and bronchial catarrh have been prevented by means of vaccines prepared from bacilli and cocci present in the respiratory passages during epidemics. Autogenous vaccines prepared from cultures of the patient's own organisms in the sputum or obtained by means of sterile swabs from the back of the nose and throat may be injected or added to the stock vaccines. In preparing the vaccines it is important to remember that cultivation and incubation should be carried out *immediately* the material has been obtained. It seems at first sight surprising that vaccines prepared from bacteria should be useful, when the infection is due to a filter-passing organism. It is possible that the causal organism only acts in symbiosis with the secondary invaders, as is the case with hog influenza ; so that it is enough to autogonise them.

Treatment. Personal experience has shown that Glegg's treatment may abort the nasal coryza, and in the later stages, when the secretion has become mucopurulent and discharge is frequent, much relief may often be obtained ; but it will have no effect on infection which has spread to the larynx and trachea. If the cough be troublesome, a few drops of ipecacuanha wine, with spirits of nitrous ether or compound tincture of camphor will relieve. Steam may be inhaled, impregnated with eucalyptus oil by placing five or six drops of the oil in boiling water in a suitable inhaler.

Follicular Tonsillitis. Apart from the infections just mentioned, inflammation of the lymphoid and follicular substance of the tonsils arises apparently spontaneously and in some persons occurs repeatedly at intervals of months or years.

It is probably due to infection, or to increase of virulence of organisms latent in the crypts, combined with depression of the resisting powers of the individual or his tissues.

Symptoms. The tonsil is red and swollen, and presents several yellow or white prominent spots, which are masses of purulent exudate, exfoliated epithelium, polymorphonuclear leucocytes, lymphocytes and bacteria at the mouths of the crypts ; and the surface is covered with more or less mucus. The swelling can be felt externally behind the angle of the jaw. In severer forms the secretion of the crypts is more abundant, and they are distended with large bright white plugs, which may present a close resemblance to the white material of diphtheria. The " follicles " may coalesce to form a patch closely resembling the membrane of diphtheria. Both tonsils are frequently affected. There is moderate constitutional disturbance, furred tongue, feeling of malaise, local discomfort, and pain on swallowing. There is often a considerable rise of temperature. As a rule, the tonsillar cervical glands are enlarged.

Morbid Anatomy. The cells of the parenchyma of the tonsils and of the follicles are increased in number, and very small abscesses may form in the follicles, and burst into the crypts.

Diagnosis. The occasional resemblance to *diphtheria* is most important. Generally the obvious formation of the plug of secretion within a crypt of the tonsil, or the existence of several on each side, serves to distinguish them. A single white patch of some extent, apparently only on the surface, and an extension of this to the soft palate are in favour of diphtheria or Vincent's angina. Bacteriological cultivation should be employed in doubtful cases (*see* p. 66).

Treatment for pyrexia should be instituted (see p. 20). The tonsils may be painted with astringent or antiseptic solutions, such as Tr. iodi B.P., glycerine of tannic acid, and tincture of perchloride of iron in glycerine (5 drops to ℥j). Lozenges of potassium chlorate or rhatany and formalin tablets may also be sucked. Tincture of guaiacum, or tablets of guaiacum, and sodium salicylate are also useful. In severe cases injections of anti-streptococcal serum may be given : anti-scarlatiniform 10 c.c., polyvalent 25 c.c., repeated in two days.

Keratosis Pharyngis is a condition in which small white projections occur at the mouths of the tonsillar crypts and give rise to an appearance similar to that of follicular tonsillitis. It is as a rule symptomless though sometimes a slight sore throat is complained of. It resists all treatment, but disappears spontaneously after persisting for many months.

Peritonsillar Abscess (***Quinsy***). In this condition suppuration occurs between the capsule of the tonsil and the muscular wall of the tonsillar bed. The exact position of the abscess varies, but it generally occupies the upper two-thirds of that space, pushes the tonsil downwards and inwards, and encroaches on the palatal tissues.

Ætiology. This is most common between the ages of fifteen and twenty-five ; some persons are very liable to it, and have it repeatedly. It is due to the spread of tonsil infection beyond the capsule of the tonsil—a peritonsillitis—and suppuration follows.

Symptoms. It may affect one or both tonsils. The tonsil becomes red and swollen to twice its natural size, projecting to the middle line, and pushing the uvula aside ; if both tonsils are affected, they may meet in the middle line, driving the uvula forwards ; the swelling and redness involve the soft palate, which becomes œdematous for a variable distance forwards. The surface is generally smooth, shining, and deep red or purple in colour. Externally there

is obvious swelling behind the angle of the jaw. The illness often commences with a rigor and sickness, and the constitutional disturbance is considerable. The tongue is thickly furred, appetite is lost, and the temperature rises to 103° or 104°. Swallowing and talking are excessively painful, and saliva and mucous secretion collect in the mouth, and require to be constantly expectorated. In from two to four days suppuration occurs; the tumour, which was at first hard, is now softer, and yields to the finger; or the presence of pus may be detected by placing one finger on the tonsil and another outside behind the angle of the jaw. If left alone, the abscess bursts into the throat, the temperature falls, and recovery quickly takes place in from four to seven days, though convalescence may be protracted for some time longer. Rarely the abscess has burrowed into the neck or chest, or eroded the carotid artery, or caused suffocation by discharging its pus into the larynx.

Diagnosis. Quinsy may resemble *follicular tonsillitis;* it is more often unilateral, the fever is more severe, the redness extends to adjacent parts, secretion does not accumulate in the crypts, and pus may be eventually detected. Sometimes the two occur together.

Treatment. The general treatment for pyrexia is used. Ice often relieves the pain; it should be sucked as well as applied to the throat externally. Salicylate of sodium in 10- to 15-grain doses every three or four hours may be given internally to diminish the acute symptoms. Gargling with hot carbolic acid lotion, 1 per cent., relieves pain. If suppuration has commenced, hot fomentations and poultices probably hasten it. When pus is detected, an incision should be made into the prominent part of the abscess with a bistoury, covered up to the last half-inch with plaster, so as to protect the other parts of the mouth. Injection of anti-streptococcal serum is useful in the early stages.

Chronic Sepsis of the Tonsils. This is of common occurrence in children, and often results in enlargement of the tonsils, which may subside as the patient advances in age. But chronic septic tonsils may be small and buried between the pillars of the fauces. Chronic sepsis may result from previous acute tonsillitis.

Pathology. Enlarged tonsils show hypertrophy of the parenchyma and follicular tissues with more or less accumulation of secretion in the crypts, which are also large.

Chronic infection of the tonsils is of importance, as it may provide a focus from which other parts of the body may be infected through the blood stream. Much of what has been said concerning apical abscesses of the teeth also applies here. Dental sepsis is usually more important in adults, while the tonsils are more important as sources of infection in children. In both cases secondary infection is the more likely to occur because the primary focus is deep-seated. In fact, Gardiner regularly obtained cultivations from the deep aspect of tonsils removed at operation. Acute rheumatism and nephritis may often be secondary to septic tonsils, and they may provide an entrance through which tubercle invades the body: in fact, some enlargements of the tonsil are due to tubercle, and actinomycosis of the tonsil has also been observed.

Symptoms. The tonsils are pale pink, lobulated on the surface, and firm in consistence, and pus or caseous material can be squeezed out on pressing with a spatula. When only of moderate size, they may cause no local symptoms. When the tonsils are large adenoids are as a rule enlarged too, and then nasal respiration may be obstructed. The child breathes with the mouth open, and, the nasal passages being little used, the anterior nares are small and the alæ compressed. Swallowing is laborious and clumsy, and speech is suggestive of something being in the mouth. Hearing is also deficient, from catarrh of the Eustachian tube. Cough, nasal catarrh, restlessness, and headache are other symptoms observed in such cases.

Treatment. Tonsillectomy is the standard treatment, and the relative

rarity nowadays of tuberculous glands in the neck may be due to the frequency with which this operation is carried out. Unless there is a very clear indication, operation is best not carried out much under 10 years, as the loss of the protective function of the tonsils may be serious. Bradley observed at a public school that epidemic catarrhal infection was most severe in boys who had had tonsillectomy. If operation is inadvisable, the secretions or caseous masses may be squeezed, syringed or sucked out of the crypts, and antiseptic lozenges be given.

VINCENT'S ANGINA

This inflammatory condition is found in two forms: (1) ulcerative; the ulcers are oval in shape and occur typically upon one tonsil, rarely on both, in children on the tongue and cheeks; ulcerations of the gums round septic teeth are often found to contain Vincent's *Bacillus fusiformis*. (2) pseudo-membranous, resembling diphtheria. It may spread from the tonsil on to the surrounding mucous membrane. Sometimes it does not affect the tonsil, but instead the soft palate or pillars of the fauces. The cervical glands are swollen, and there are difficulty of swallowing and some fever, and the breath is fœtid. Usually in eight or ten days the membrane disappears. The fever is but slight, the glands never suppurate and the prognosis is good.

Two organisms are found in these cases: (1) the *Bacillus fusiformis*, which measures from 6μ to 12μ in length, looks like a long thin triangle, occurs in pairs, with the bases contiguous, and is readily seen by dark ground illumination. (2) *Vincent's spirochæte.*

Treatment. The ulcers should be painted daily with a 10 per cent. solution of silver nitrate; aspirin may be given to relieve pain. Infection of the gums may yield to injections of novarsenobenzol.

PHARYNGEAL TONSILS

This is a mass of lymphoid tissue situated in the naso-pharynx, together with scattered nodules in the mucous membrane of the fossæ of Rosenmüller and of the posterior wall of the pharynx. The mass may be sessile or pedunculated, consisting of finger-like processes, separated by fissures or clefts, analogous to the crypts of the faucial tonsil. It is covered with a layer of columnar ciliated epithelium. Enlargement is common between the third and tenth years of life; it may follow the infectious diseases of children, and is often associated with attacks of catarrhal rhinitis.

The pathological results of hypertrophy of the pharyngeal tonsil, often called *adenoid growth* or *adenoids*, are important. Chronic catarrh may spread up the Eustachian tube, and cause otitis media, and later chronic inflammation of the mucosa. In the course of the growth of the child occur some of the changes referred to under the head of the faucial tonsils. The face is lengthened; the alæ nasi are collapsed; the upper lip is short and retracted; the mouth is often kept open, and a vacant expression is thus acquired: these constitute the *adenoid facies*. Pigeon-breast and a high palatal arch are often present also.

Symptoms. These, of course, vary with the amount of enlargement and consequent obstruction to the naso-laryngeal passage. They are deafness, habitual mouth-breathing worse at night, snoring and "night terrors," and liability to catarrhal rhinitis, with occasional blood in the secretion. In articulation the consonants M and N are badly pronounced, because these sounds cannot be resonated in the nasal meatus. Laryngismus stridulus, nocturnal enuresis, stammering, epilepsy and infantile convulsions are said by some to be excited by adenoids.

Treatment. If the symptoms are pronounced, the growths should be removed surgically. Slighter cases may be improved by breathing exercises, aiming at teaching the child to breathe through the nose.

LINGUAL TONSILS

The lingual tonsils are two or three nodules of lymphoid tissue, situate at the base of the tongue on either side of the middle line. They have the same structure as the faucial tonsil with two or three crypts. They may be inflamed like the faucial tonsils, less commonly have retention of secretion in the crypts, but occasionally hypertrophy, and this more frequently in children than in adults. It is probable that the sensation of "sore throat," which is felt in the middle line and somewhere at the back of the throat, is really in many cases due to inflamed lingual tonsils. The latter are also responsible for the common "tickling in the throat" that gives rise to a "throat" cough, and for the cough in whooping cough. Cough may be allayed by applying to the tonsils a saturated solution of 240 grains of ferric chloride made up to 1 oz. with glycerine, using a wool holder bent at the end. The tongue must be protruded as far as possible during the application (2).

CHRONIC PHARYNGITIS

Ætiology. Chronic inflammation of the pharynx may arise from repeated acute attacks. Infection passing down from the posterior nares is a frequent cause, and in all cases the condition of the nose and of the paranasal sinuses should be investigated. It also results from certain injurious influences, such as the abuse of alcohol, excessive smoking of tobacco, and the continual use of the voice; and when a public speaker inclines the head downwards in addressing an audience on a lower level, and consequently compresses the parts engaged in vocal utterance, he undoubtedly favours its occurrence. It is constantly associated with a similar change in the soft palate, tonsils, or posterior part of the nose.

Symptoms. The mucous membrane may be reddened, with dilated veins; in some cases there are numerous small grey elevations scattered over the pharynx (*granular pharyngitis*); in others small abrasions or ulcerations occur. The grey projections in granular pharyngitis are the enlarged follicles or mucous glands. In some cases the mucous membrane is covered with increased secretion, and the patient is constantly hawking and spitting; in others the surface is dry, and a certain amount of discomfort and difficulty in swallowing, with pricking pain and desire to cough, is the result.

Granular pharyngitis is often spoken of as a distinct affection. It may spread beyond the fauces proper to the top of the pharynx and to the larynx; the mucous membrane is in most cases dry, but sometimes the follicles are covered with viscid mucus. It may cause little or no discomfort; but there may be stiffness and dryness of the throat, constant desire to hawk and spit, and distress and difficulty in swallowing. The effort to talk is also painful, and the patient may be obliged to stop to clear the throat. This condition of things is not uncommon in clergymen, public speakers, and others of like vocation, and has consequently been called "clergymen's sore throat." The symptoms are aggravated by exposure to cold, and an inherited disposition has been observed by some writers.

Treatment. Local treatment is necessary in granular pharyngitis, and, more important, treatment of the paranasal sinus infection. Gargles are of little use, as they do not reach beyond the soft palate; but sprays of alum or tannin (4 to 10 grains of each to the ounce of water) may be employed, or the throat may be painted with astringent solutions, such as nitrate of silver (10 per cent. solution) or Mandl's pigment of iodised glycerine (iodine, 6 grains; pot. iod., 20 grains; ol. menth. pip., 5 min.; glycerine to an ounce).

RETROPHARYNGEAL ABSCESS

This, though chiefly a surgical complaint, requires short notice here, since it is apt to complicate the diagnosis of some throat complaints, especially laryngeal

obstruction. It arises from caries of the spine, but more often from inflammation of the retropharyngeal lymphoid tissue; and it forms a swelling at the back of the pharynx, which may press upon the larynx so as to cause dysphagia, dyspnœa, and asphyxia. Thus it may be mistaken for croup or laryngeal diphtheria, but the cough and voice are not husky and hoarse, as in the latter, but rather "gurgling." In a suspected case the finger should be passed to the back of the throat, when a fluctuating swelling will be felt. It should be opened by the surgeon.

LARYNGITIS

Laryngitis, or inflammation of the larynx, may be acute or chronic, and arises from a number of causes. Amongst these are—the ordinary conditions of catarrhal inflammation, considered under Acute Rhinitis; contact with irritating vapours and air charged with dust; the impaction of foreign bodies or direct injury in other ways; extension of inflammation from surrounding parts, the pharynx, the bronchi and trachea, or the tissues outside; acute specific fevers, such as those of diphtheria and measles; and finally Bright's disease. Chronic laryngitis is either due to infection from the upper respiratory tract or to infection from the lungs by tubercle; syphilis also attacks the larynx. The results differ somewhat according to the cause, and one can readily distinguish a catarrhal laryngitis, an œdematous laryngitis, the membranous laryngitis which is characteristic of diphtheria, and the laryngitis of phthisis and of syphilis.

Acute Catarrhal Laryngitis. This is mostly due to the same conditions as may cause an acute rhinitis, but it also arises from irritating vapours, dusty air, the entrance of foreign bodies, and inflammation spreading from the posterior nares, pharynx or bronchi. It occurs in measles, and less frequently in other infections.

Symptoms. The voice becomes hoarse or is entirely lost; there is a tickling sensation in the throat, leading to a husky cough, with expectoration from time to time of small plugs of mucus. Respiration is generally but little affected, but there may, in exceptional cases, be some stridor; and in children dyspnœa is much more often a marked symptom. Fever may be slight or none. On examination with the laryngoscope the mucous membrane over the arytenoids is swollen and red. The vocal cords are usually inflamed, but sometimes show little change: some mucus may be seen lying on and between them. The ventricular bands may be affected.

Children are liable to a form of acute laryngitis (*laryngitis stridulosa*), which is characterised by the sudden development of suffocative symptoms, frequently in the middle of the night. During the day there is only slight cough and huskiness, but some time in the night the child wakes up suddenly in terror, with severe dyspnœa and a barking or husky cough, followed by loud and prolonged crowing inspiration. The voice is husky and feeble and the features are congested; if the condition continues, the face may become pale and livid, and suffocation seems imminent. Usually, however, in a short time the symptoms become less severe and the child falls asleep. Either on the same night, after a few hours' sleep or on subsequent nights, the same attacks of threatening suffocation with croupy inspiration may take place. In association with these attacks there is more fever (white tongue, flushed face, hot skin, etc.) than commonly occurs in catarrhal laryngitis of adults. The attacks are probably due to laryngeal spasm set up by the presence of tenacious mucus in the glottis. The symptoms are apt to recur in the same child whenever it "catches cold"; they are, however, rarely fatal.

The **Prognosis** of acute laryngitis is mostly favourable; it generally subsides in the course of a few days.

The **Diagnosis** is generally simple, especially in adults: diphtheria is more severe, and may be accompanied by membrane on the fauces, by the expectoration of membrane, or by albuminuria.

Treatment. The patient must not speak. He should be placed in a uniformly warm atmosphere, and should inhale steam from a suitable apparatus frequently. This may be charged with tr. benzoin co. (℥ss to a pint of water). Sprays of menthol (gr. ii or iii in liquid paraffin ℥j), oil of eucalyptus, and creosote are also useful. Demulcent liquids should be drunk freely, or small pieces of ice may be sucked. The irritation of cough should be allayed by opiates. The diet or regimen usual in febrile affections will of course be followed.

For laryngitis stridulosa an emetic is often useful, such as sulphate of zinc (5 to 10 grains) or ipecacuanha (2 to 5 grains of powder, or a drachm of the wine every ten minutes, till vomiting is produced). In addition, hot flannels or a hot sponge should be applied to the throat. In the intervals the laryngitis is to be treated by a warm moist atmosphere (steam kettle) and small doses of bromides and chloral, internally.

Œdematous Laryngitis. This may be a result of laryngitis arising in various ways. It sometimes occurs in catarrhal cases, and in the course of Bright's disease. The usual cause is acute streptococcal infection of the larynx; it is accompanied by severe constitutional symptoms and requires early and vigorous treatment.

The localised œdema described as angeio-neurotic frequently occurs in the laryngeal tissues, and is often fatal (*see* Angeio-neurotic Œdema).

Morbid Anatomy. It consists of an effusion of inflammatory serum into the submucous tissue, and the serum contains many leucocytes, so that it may be sero-purulent, or actual pus is diffused through the tissue.

Symptoms often develop rapidly, a sore throat and some pain on swallowing are soon followed by dyspnœa, which may increase rapidly and demand tracheotomy. Laryngeal examination early reveals œdema of the epiglottis and arytenoids.

The **Prognosis** in cases of extensive œdema is a serious one.

Treatment. Early injections of anti-streptococcal serum are required. Inhalations as for acute laryngitis are comforting, as are cold applications to the neck. Low tracheotomy may become urgently necessary.

Membranous Laryngitis. The most common cause of membranous laryngitis is diphtheria, which either begins in the fauces and spreads to the larynx (*see* p. 65) or attacks the larynx at first, without either then, or later, involving the fauces. It is of interest to note that these primary laryngeal cases are more common in children than in adults, and that they are less often accompanied by albuminuria, or followed by paralysis, than those in which the throat first suffers.

A membranous laryngitis may certainly be produced by traumatic causes or local irritants, such as chemical vapours, boiling water, or impacted foreign bodies. A membranous laryngitis in measles means a superadded diphtheritic infection.

Symptoms. The local symptoms will be like those already described under Diphtheria, but the toxic symptoms of an infectious disease will be absent or little pronounced when the cause is traumatic.

Diagnosis. Generally speaking, children affected with dyspnœa, ringing or "croupy" cough, and inspiratory retraction of the chest wall, without apparent cause, and threatened with suffocation all within four days are suffering from membranous laryngitis; and in the majority of these cases diphtheria is the cause: but it is generally impossible to examine with the laryngoscope, and the first proof of the presence of membrane may be provided at or after the operation of tracheotomy. It is distinguished from laryngitis stridulosa (*see* p. 203) by the more gradual development and more uniform progress of the dyspnœa.

The alternative diagnosis is the presence of a foreign body.

Treatment. Membranous laryngitis may be treated as shown under Diphtheria both when it is due to this disease and when it is associated with

scarlet fever, measles, or other infectious illness. The antitoxin of diphtheria should be used in the first case.

Chronic Catarrhal Laryngitis. This often follows upon acute laryngitis, especially when the latter is not properly treated with complete rest of voice; from infections in the upper respiratory tract; from sinusitis or atrophic rhinitis or chronic nasal obstruction; also from misuse of the voice.

The **Symptoms** are hoarseness and irritation of throat leading to dry cough. Laryngeal examination reveals thickenings on the true cords or in the posterior commissure.

Diagnosis is often difficult between chronic catarrhal laryngitis, tuberculous and syphilitic laryngitis and early neoplasm. For further information the student should apply to the special text-books on laryngology.

LARYNGEAL TUBERCULOSIS

Of patients suffering from phthisis, or pulmonary tuberculosis, a considerable number have a laryngeal affection, which was formerly described as laryngeal phthisis. This is due to the actual invasion of the laryngeal tissues by tubercle, and it is secondary to the formation of tubercle in the lungs. It is usually known as "laryngeal tuberculosis," and was present in 4·8 per cent. of phthisical patients admitted to King Edward VII.'s Sanatorium, Midhurst, in the first stage of the disease, in 18·3 per cent. in the second stage, and in 31·5 per cent. in the third stage. Men and women have an equal tendency to the disease (3). A second form of tubercle affecting the larynx is lupus, which spreads from the pharynx or nose.

Morbid Anatomy. The tubercles occur as minute collections of cells in the mucous or submucous tissues, forming, perhaps, slight prominences on the surface, leading in time to more or less, often considerable, œdema of the surrounding parts, and later to ulceration. In late cases the ulceration is widespread on arytenoids, ventricular bands, cords and epiglottis. Extending more deeply in severe cases, with the assistance of pyogenic organisms, the inflammatory process leads to deep ulceration, to perichondritis and to necrosis of the cartilages. The most frequent seats of the deposit are in the neighbourhood of the posterior commissure, *i.e.* the interarytenoid area, the anterior surface of the arytenoid body and the vocal processes. Next in frequency come the vocal cords.

The **Symptoms** are those of a chronic laryngitis, and in cases of ordinary severity consist of hoarseness of voice, frequent husky cough. Sometimes in early stages the voice may be lost entirely from functional failure. In later stages the voice is lost as a result of ulceration of the cords, and when ulceration attacks the posterior part of the arytenoids swallowing may be not only painful, but difficult on account of swelling of the tissues, or from their destruction preventing perfect closure of the larynx. The cough is occasionally severe and paroxysmal, and expectoration is variable, depending rather on the condition of the lungs than on that of the larynx. In a small number of cases, considerable obstruction to respiration arises. In 12 per cent. of cases the larynx was found to be tuberculous without producing any local symptoms at all.

In early stages the laryngoscope shows pallor of the mucous membrane, and a decided anæmia of the larynx occurs quite early in many cases of phthisis. Asymmetrical patches of congestion on the cords, ventricular bands and in the posterior commissure are characteristic of a mild degree: or in more severe cases a shallow ulcer may be seen on a ventricular band or on the epiglottis. When infiltration takes place the parts often assume a characteristic appearance, the ary-epiglottic folds on one or both sides being swollen up into a pale globular or pyriform tumour, the base backwards, the point forwards; and when both are affected the swellings coalesce in the middle line. The epiglottis may form a

turban-shaped swelling; and the same thickening may effect the ventricular bands, which are, however, often concealed. Subsequently ulcers form upon the swollen tissues as well as upon the vocal cords, especially in the posterior halves.

Diagnosis. This must be made partly from the laryngoscopic appearances, and partly from the condition of the lungs, which are in many cases obviously tuberculous. The pyriform swellings of the ary-epiglottic fold are characteristic of the condition, but when they are absent there may be difficulty in distinguishing it from *chronic catarrhal laryngitis* and from *syphilitic* disease. In the former there are less swelling and more congestion than in tuberculous laryngitis; in syphilis the ulcers are generally larger and deeper, situated upon a more inflamed base, and solitary; the thickening is more irregular, and the disease often unilateral. The ulceration of carcinoma is sometimes difficult to distinguish from that of tubercle; carcinoma is always unilateral in early cases and occurs in older patients.

Prognosis. The presence of laryngeal tuberculosis makes the prognosis of the co-existing phthisis more gloomy (*see* p. 171). Recovery from laryngitis occurred in 25 per cent. of 477 cases at Midhurst. Very often the laryngeal condition progresses or retrogresses as the phthisis progresses or retrogresses; but this is not always the case. The larynx may recover, even though the phthisis gets worse; but with proper treatment the larynx never gets worse if the phthisis is improving.

Treatment. It is essential to treat the disease in the lungs of which the laryngeal tuberculosis is really a part. Intensive irradiation of the body with Finsen light is advocated as in Copenhagen. The most important element in local treatment of the larynx is complete silence on the part of the patient; not even whispering should be allowed. This may cause great mental strain in some patients. In such cases occasional whispering may be allowed. Where there is much infiltration galvano-caustic puncture with a fine platinum point introduced deeply into the tissue has been successful, but this should be employed only when there is no evidence of *active* disease in the lungs. Three or four punctures may be made at a time, after the production of anæsthesia by instillation of 5 drops of a 20 per cent. solution of cocaine. The puncture may be repeated at not less than two weeks' interval. For the pain in advanced cases insufflations of the larynx with orthoform and anæsthetics is helpful, and even an injection into the superior laryngeal nerves. In advanced cases tracheotomy may be considered in order to rest the larynx.

SYPHILIS OF THE LARYNX

Syphilis affects the larynx in many ways: in the hereditary form in infancy and childhood; in the acquired form in secondary and tertiary and intermediate stages. The secondary lesions of acquired syphilis are rare and consist of chronic hyperæmia, superficial ulcerations, and condylomas or mucous patches, of which the last are very rare. In the later stages of the disease a diffuse infiltration of the larynx is the most common. Small gummas varying in size from a pin's head to a pea and deep ulcerations are occasionally seen. Laryngeal œdema and perichondritis with laryngeal necrosis occasionally result, and the cicatrisation of ulcers may lead to scarring, so that serious distortions of the larynx or contractions of the glottis ensue.

Symptoms. These are not distinctive, and vary much according to the severity of the lesion. They are hoarseness or loss of voice, occasionally cough in earlier stages, and more or less dyspnœa in later stages. Dysphagia is rare unless the epiglottis is the site of gummatous ulceration. Dyspnœa may come on rapidly and demand tracheotomy.

Diagnosis. Secondary laryngitis is diagnosed by the presence of other signs of syphilis, *e.g.* skin rash. Tertiary syphilis, apart from a typical gummatous

ulcer, may resemble tuberculous or chronic catarrhal laryngitis. A positive Wassermann test decides the diagnosis.

Treatment. Vigorous antisyphilitic treatment should be carried out. There is a belief, hardly justified, that potassium iodide may cause œdema of the glottis. Tracheotomy should be carried out in order to rest the larynx in the early stages and before cicatricial contraction makes it imperative. In the latter event a tube has to be worn for life; but attempts may be made to dilate the glottis mechanically, or to divide a web by the cutting forceps or dilator, or by the electric cautery.

TUMOURS OF THE LARYNX

Papilloma and *fibroma* are common on the vocal cords, all other benign tumours are rare. *Cysts* adjacent to the epiglottis often projecting into the vallecula are seen but are as a rule symptomless.

The **Symptoms** are hoarseness, and if papillomas are multiple or of large size, dyspnœa, which may be of such a degree as to demand tracheotomy.

The **Treatment** is removal by surgical operations, for the details of which the reader is referred to surgical works, or special treatises.

Malignant Tumours. These are mostly carcinoma, but sarcoma also occurs. They are more frequent in men than in women, and appear commonly after the age of 50. *Intrinsic carcinoma* of the larynx originates (1) on the vocal cords, more commonly on the anterior and central than the posterior regions; (2) in the subglottic region, more commonly in the anterior part of the larynx. A carcinoma of the cord may remain limited for a long time to the cord and the adjoining side of the larynx, but may spread eventually (*a*) across the anterior commissure; (*b*) to the subglottic region; (*c*) to the arytenoids. Eventually the whole larynx may be involved. In the later stages it ulcerates, vegetations spring up about the margins, and these ulcerate in their turn. The surface is often covered with pus, or sanguineous muco-pus, and occasionally free hæmorrhage takes place. Œdematous laryngitis and perichondritis occur as complications. The larynx is, of course, affected sometimes by carcinoma spreading from the pharynx (*extrinsic carcinoma* of the larynx).

Symptoms. The earliest symptom is huskiness or hoarseness of the voice. Laryngoscopic examination discloses a tumour. The cord is often freely movable during the earliest stages, but becomes fixed when the growth spreads. In the later stages there may be severe pain and dyspnœa. As ulceration proceeds the breath becomes fœtid, and hæmorrhage may occur. Gland involvement is very rare until a late stage of the disease.

The **Diagnosis** rests finally on biopsy.

The **Prognosis** is relatively favourable if the condition has been diagnosed in the earliest stage. From a series of fifty-one cases in which the growth was removed after laryngo-fissure there was no recurrence in 80 per cent. from one to thirteen years later, but a quarter of these had died from other causes. There was local recurrence in 16 per cent. The immediate operative mortality was very small (4).

The **Treatment** consists in removing the growth after laryngo-fissure; or by insertion of radium needles to the outer aspect of the growth through a window resection of the thyroid ala.

FOREIGN BODIES IN THE LARYNX

A large number of foreign bodies have at different times found their way into the larynx. Among these are peas, beans, buttons, coins, fragments of bone, shells, pebbles, artificial teeth, portions of solid food, and pieces of children's toys.

The **Symptoms** are divisible into three stages:—(1) The *initial spasm*, which takes the form of a violent fit of coughing, which usually dislodges the object. If this does not occur, the obstruction may be rapidly fatal; but if not, there

follows (2) the *quiescent period*, which may last any time from a few hours to many years. The symptoms may be so slight that it is not always known to the patient or to his friends that a foreign body has been introduced. (3) The stage of *inflammation*, due to infection, produces secondary symptoms, hoarseness, pain, coughing, etc.

At any stage a change in the position of the foreign body may cause sudden death.

Treatment. During stage (1) it may be useful to hold the head down, to help dislodge the body. If the symptoms appear dangerous, a tracheotomy should be performed. During stage (2) the body should be located and removed by means of an endoscope. If opaque to the X-rays, these may also be useful in locating the body.

PARALYSIS OF THE LARYNGEAL MUSCLES

From the peculiar course of the recurrent laryngeal nerve—the chief motor nerve of the larynx—paralysis of these muscles has often a diagnostic importance beyond that of the trouble arising locally. But it may be caused by lesions not only of the laryngeal nerves, but also of the vagus above their origin, and of the medulla oblongata where the nuclei are situated. Thus laryngeal paralysis is a part of bulbar paralysis, results from syphilis and tumours affecting the medulla oblongata and dura mater in the posterior fossa of the skull, and occurs occasionally in association with tabes dorsalis, general paralysis, syringomyelia, and disseminated sclerosis. The vagus in the neck may be compressed by tumours and enlarged glands, or may be injured by bullet wounds or cuts, whether accidental or in the course of surgical operation. The recurrent laryngeal nerves are in danger in two situations: the thorax and the neck; and the left is the more liable to lesion from its curving round the arch of the aorta, whereas the right goes no lower than the subclavian artery. Either of them may be involved in the fibrous thickening at the apex of the lung in chronic phthisis, but the left is especially liable to be compressed by aneurysm of the arch of the aorta, by mediastinal tumours, by enlarged bronchial glands, and by the dilated left auricle in mitral stenosis. In the neck the two nerves ascending to the larynx lie between the trachea and the œsophagus, and may be involved together in carcinoma of the latter, or compressed by an enlarged thyroid body. Paralysis also occurs as a result of diphtheria, influenza, polio-encephalitis and other infectious diseases, chronic alcoholism, and poisoning by lead and arsenic.

In all these cases the paralysis affects the abductor muscles of the vocal cords in the first place, and only later are the adductor muscles involved. When the adductor muscles only fail to act the affection is functional or hysterical (see later).

Complete Paralysis of the Vocal Cords. When all the muscles moving the vocal cord are paralysed the cord takes up a position between *ad*duction and *ab*duction which is known as the *cadaveric* position.

The voice is then weak and may become higher in pitch when an attempt is made to speak loudly. It may be reduced to a whisper, coughing is impossible, during sleep there is noisy stridor, and indeed the danger of suffocation on account of sucking together of the flabby cords calls for tracheotomy. This condition is seen typically in tabes dorsalis.

Paralysis of the Abductors. Although the recurrent laryngeal nerves, supplying as they do all the muscles of the larynx except the crico-thyroid, must contain fibres for both *ad*ductors and *ab*ductors, it is a remarkable fact that coarse progressive lesions of these nerves (compression by tumours or aneurysms) result at first in paralysis of the *abductors* (*crico-arytænoidei posteriores*) alone; it is only later that the internal tensors (*thyro-arytænoidei*) are affected, and last of all the chief adductors (*crico-arytænoidei laterales*). The abductor fibres form

a separate bundle lying internal to the adductor fibres in the recurrent laryngeal nerve of the dog (Risien Russell); but their greater liability to suffer from lesions affecting the whole nerve is apparently due, as shown experimentally, to less powers of resistance to external influences. Abductor paralysis also results from lesions of the medulla where it may be supposed it sometimes depends on a separate affection of the nucleus of the abductor fibres, though adductor paralysis alone never arises under such circumstances. Syphilis and tabes are the most common associates of abductor paralysis arising in this way. It is to be noted that there are no supranuclear lesions of the abductors. Abductor paralysis is probably sometimes the result of a change primarily in the muscle.

The effect of the lesion is that the cord during respiration, not being fully abducted, remains in the cadaveric position, and at first allows ample space for the passage of air; after a time, however, the antagonistic muscle, or adductor, contracts, and the cord is drawn into a position of adduction. Thus in bilateral paralysis of the abductors the cords are seen to be permanently approximated in the middle line to within one-tenth of an inch of each other; on attempted phonation they meet completely in the middle line; on inspiration they do not separate, but are even drawn a little closer together; on expiration they scarcely move, or only in the reverse sense to their slight movement in inspiration. The important symptom is *dyspnœa*, which results from the permanent narrowing of the glottis; this is generally accompanied by *stridor* on inspiration, which is worse on exertion, and often extremely loud during sleep. The voice is clear, or it may be a little hoarse. Coughing can be perfectly effected.

When only one cord is paralysed, dyspnœa only occurs on exertion, and the stridor is absent. On phonation the healthy cord meets the paralysed cord beyond the middle line, and the patient can speak.

Diagnosis. Abductor paralysis may be confounded with spasm of the adductors, with ankylosis of the arytenoids in the position of adduction, and with perverted action of the cords in which they move inwards instead of outwards during inspiration. When the arytenoid is ankylosed the cord is absolutely fixed, and there is generally some thickening about the joint.

It is important to remember that the lesion which causes unilateral or bilateral abductor paralysis may at the same time cause narrowing of the trachea by pressure (aneurysm, tumour) or by cicatrix (syphilis), and the dyspnœa and stridor due to the latter may be wrongly attributed to the former. Tracheal stenosis usually causes expiratory as well as inspiratory stridor; nevertheless the certain recognition of a tracheal obstruction in the presence of laryngeal stenosis is by no means easy (*see also* p. 129). The diagnosis of the remote cause of the paralysis has next to be made by a consideration of other symptoms, such as those in favour of tabes and central nervous lesions, or of thoracic aneurysm and new growths in the neck or chest. Aneurysm is a very frequent cause of paralysis of the left vocal cord. Wassermann's test and the Röntgen rays may have to be used.

The **Prognosis** is generally serious. Except when syphilis is the cause, there is little hope of recovery; when there is double abductor paralysis a constant liability to death from suffocation is present. If the adductors are subsequently paralysed, the obstruction to breathing is diminished, but aphonia ensues. Death may arise from the primary lesion, such as œsophageal cancer or double aneurysm. In long-standing cases the posterior crico-arytenoid muscles become completely atrophied.

Treatment. If the cause of double paralysis is central, or if syphilis is the cause, a vigorous antisyphilitic treatment should be instituted. But if no improvement takes place in a few weeks, and if dyspnœa is constant, or night attacks take place, tracheotomy should be performed and the tube should be worn constantly.

In unilateral paralysis the risk of asphyxia is much less, and the treatment may be directed mainly to the cause.

Paralysis of the Adductors. This is a functional disorder, and rarely occurs alone from structural lesions. The adductors are the lateral adductors, or *crico-arytænoidei laterales*, and the central adductor, or *arytænoideus proprius;* the inner fibres of the *thyro-arytænoidei*, or internal tensors, also act as adductors of the anterior portions of the vocal cords. In the most common form of adductor paralysis these are all affected. When examined with the laryngoscope, the glottis is seen to be widely open; on attempts to speak the cords scarcely move, but remain still at the sides of the larynx. As the cords cannot be approximated, the patient speaks only in a whisper, no laryngeal voice being produced, though sometimes, with an effort, a momentary contact of the cords may be effected. Coughing, in which the cords are brought together by involuntary reflex action, is generally perfect; and from the open condition of the glottis there is no dyspnœa. This constitutes *functional* or *hysterical aphonia*, which is, however, often started by slight catarrh of the larynx, *e.g.* in the earliest stage of phthisis, or by sore throat, or by other local trouble, both in definitely hysterical persons and in others suffering from anæmia or general weakness. In civil practice it occurs in young women and boys as the result of an emotional shock, the individual being struck dumb with terror. The same explanation must be given for most of the numerous cases of aphonia in soldiers invalided from the War, especially when they were exposed to shell fire, or buried after explosions, or otherwise directly injured. Some of the cases, in which a child fails to speak after the removal of a tracheotomy tube worn for some weeks, are also due to functional adductor paresis.

Sometimes the adductor paralysis is less extensive; the internal tensors may be alone affected, so as to produce want of contact of the cords on attempted phonation, each cord presenting in its anterior half a concave margin towards the middle line. And sometimes the central adductor is paralysed, in which case the anterior portions of the cords come into contact, and a triangular space is left open behind, between the arytenoid cartilages. These last two forms are not uncommon in the course of catarrhal laryngitis. They may occur together, producing defective closure in front and behind, while the processus vocales are in contact. In these cases the loss of voice is not so complete as in that first described.

The **Diagnosis** of these conditions is easily made with the laryngoscope. Even without this, the voicelessness of the patient, the absence of dyspnœa, cough, and expectoration, and the power to cough at will, are sufficiently distinctive. Should there be, however, any visible evidence of catarrh, or recurring attacks of aphonia, the possibility of a tuberculous lesion underlying it should not be forgotten.

The **Prognosis** is favourable, and cases of many years' duration may be at length cured.

Treatment. Functional aphonia is to be considered as a symptom of hysteria, and to be treated as such. In most cases it may be removed by means of the methods of suggestion and re-education. In some instances it is sufficient after a preliminary explanation of the fact that the weakness is not due to any organic disease, but is rather of the nature of a forgotten habit, to induce the patient to cough, and to prolong the noise in the form of an "a-a-h." From this he is led on to the letter "A," and so through the alphabet, beginning with the vowels, when it may be demonstrated to his own satisfaction that he can now phonate properly in the formation of words and sentences. This method must not be used if there is any suspicion of tuberculosis. In other cases the application of a faradic current externally in the neighbourhood of the larynx or to the back of the throat may be useful as a method of crude suggestive treatment. If the symptom is not amenable to such methods or recurs, or if it is associated

with other evidences of hysteria, further treatment should be undertaken on the lines recommended under that heading (*see* p. 791).

SPASM OF THE GLOTTIS

In this affection the adductors are spasmodically contracted, and complete closure of the glottis takes place, preventing the entrance of air, and producing asphyxia, or even death. It may occur at all ages, but is especially frequent in infants, in the form now to be described.

Laryngismus Stridulus (*Spasmodic Croup, Child-crowing*) This occurs between the ages of three months and two years, and is more common in boys than in girls. It is promoted by imperfect hygienic conditions, and is more frequent among the poor, and in children who are hand-fed, or nursed by sickly and half-starved mothers. In the majority of cases (75 per cent.) there is evidence of rickets, and the disease often occurs in children who have symptoms of tetany. Laryngismus stridulus is also apt to follow whooping cough. Attacks occur by night and day; but a number of causes may excite a spasm, such as crying, sucking, quick movements, milk getting down the larynx, indigestible food in the stomach, the irritation of dentition, and fits of anger; but the attacks often occur without any such obvious antecedent. The child may be in fairly good health when it is noticed to make a slight crowing sound occasionally. This may be repeated at intervals without giving rise to any alarm, but it gradually becomes more frequent. After a while the interruption to respiration, at first only indicated by the crowing, becomes more marked. Breathing ceases, the chest is fixed, the face becomes pale and livid, the head is thrown back, and the facial muscles are slightly twitched. In a short time the spasm yields, and the air enters with a loud crowing noise through the still imperfectly opened glottis; and the child in a few minutes more may return to its playthings. In the severest cases the glottic spasm is accompanied by the *carpopedal contractions* of tetany; the fingers are bent into the hand, the thumb within the fingers, and the hand is flexed on the wrist; the legs are extended, the feet bent on the legs, the soles turned inwards, and the great toe widely separated from the others. General convulsions may be added to these. Occasionally death takes place during a fit, from complete stoppage of the respiration; and as the crowing is really the signal that the spasm is relaxing, it will be seen that in the fatal cases death may occur quite silently.

Diagnosis. The symptoms are very characteristic, and not easily confounded with those of any other disease. The absence of fever, the shortness of the attack, and the completely healthy condition between the attacks, distinguish it from laryngitis. It may be simulated by the presence of a foreign body (*see* p. 207).

Prognosis. Most patients recover completely, but occasionally deaths are reported.

Treatment. This has to be considered in relation to the general health of the patient, and the occurrence of the attacks. The child must be put immediately under the best possible hygienic conditions: fresh air, well-ventilated rooms, and improvements in its food where this is insufficient or unsuitable (*see* Rickets), and attention to the bowels should be secured. Medicinally cod-liver oil, or cod-liver oil with malt extract, is of great value, and potassium bromide may be given three times daily, in doses of 2 to 5 grains, according to the age of the child, and small doses of chloral. If the attacks are slight, sponging the child from head to feet two or three times daily with cold or tepid water, according to the season, often quickly stops them. In the more severe fits, the head should be raised, the surface of the body and face slapped with a towel dipped in cold water, and ammonia or acetic acid held to the nostrils, or the body may be immersed in warm water, and cold water poured over the head and face. The finger should be inserted and the epiglottis pulled forward.

Spasm of the Glottis in Adults. This occurs more frequently in connection with laryngitis, œdema of the larynx, paralytic conditions, or the presence of foreign bodies; it may also be a danger in epilepsy, chorea, tetanus, hydrophobia, and tabes dorsalis. In the last it constitutes the severer form of laryngeal crisis (*see* p. 679); and this may occur in the healthy larynx, or in one already affected by a paralysis, which is generally of the abductor variety. The entrance of saliva or small particles of food or drink into the larynx may cause most dangerous spasm, and a certain amount is often induced by the application of medicated solutions to the mucous membrane of the larynx. Spasm of the glottis is often the result of hysteria. Allied to this is a functional spasm (*phonic spasm* or *mogiphonia*), brought on in some neurotic persons by the effort of speaking, and relaxing when the attempt to speak is abandoned; it may be confined only to the use of the voice in public, as in singers and teachers.

Treatment. In the first class of cases inhalation of chloroform, amyl nitrite, vapor coninæ, or burning stramonium should be employed, if they can be obtained in time; otherwise tracheotomy may be necessary. The bromides may be given for recurrent attacks.

Hysterical cases require the general treatment of hysteria; and the other functional conditions must also be treated with reference to the general condition of the patient, as well as by breathing exercises, and exercises in voice production.

CONGENITAL LARYNGEAL STRIDOR

Infants are occasionally the subjects of a laryngeal disorder, in which the breathing is accompanied by a peculiar croaking sound. This is generally first heard soon after birth, is continuous for long periods, perhaps all day and night, but may be absent for a few hours at a time. The croaking takes place with inspiration, and is either a rough sound, or more clear and musical; expiration is silent; the cough and cry are, as a rule, normal. There may be a little sucking in of intercostal spaces, but there is rarely any lividity. In some cases the noise is constant during sleep; in others it is absent. It is generally worse when the child is lively or excited. It subsides as the child grows older, but Sir Frederick Taylor found it still present at two and a half years. The child appears to be in other respects quite healthy.

Both during life and after death the glottic aperture is seen to be extremely narrow, the epiglottis being folded on itself, and the ary-epiglottic folds almost in contact. This, however, is only an exaggeration of the normal condition of the infant's larynx, and Dr. Paterson has shown, by direct observation in five cases, that the stridor was due to the drawing into the larynx at each inspiration, and the vibration in this position, of the arytenoids and lax mucous membrane on the upper edge of the cricoid.

The obstruction caused by the deformity diminishes as the parts develop. No direct treatment is of any avail. Tracheotomy might be necessary in the rare event of life being threatened by asphyxia.

ANÆSTHESIA OF THE LARYNX

This occurs in diphtheria, in bulbar paralysis, in tabes dorsalis and general paralysis, and from injury to the vagus or superior laryngeal nerve. It is recognised by the insensibility of the laryngeal mucous membrane when touched with a probe, introduced with the help of the laryngoscope. It is often accompanied by dysphagia from particles of food entering the larynx, the result, according to M. Mackenzie, of paralysis of muscles supplied by the superior laryngeal nerve, *i.e.* those which depress the epiglottis and close the upper aperture of the glottis during swallowing. Anæsthesia from diphtheria usually recovers; the prognosis is generally bad in progressive bulbar paralysis and allied conditions, as food is apt to get into the lungs and set up pneumonia.

The Treatment should be by means of galvanic and faradic applications. Strychnine may be given internally, and dysphagia may necessitate feeding with the œsophageal tube.

THE EAR

The ear consists essentially of three parts :

(1) The conducting apparatus by which sounds are conveyed to

(2) The perceptive apparatus or cochlea, which lies in the dense bone of the internal ear ; from this

(3) The auditory nerve (cochlear division) carries the impulses to the brain.

The conducting apparatus includes the pinna, the external auditory meatus, the tympanic membrane which is the outer wall of the middle ear, containing the ossicles, malleus, incus and stapes : this last fits by a water-tight joint into the oval window, and this is one of the two bony openings into the internal ear ; the other opening is the round window which is closed by a membrane. The internal ear is filled with fluid. Opening into the middle ear is the Eustachian tube from the naso-pharynx ; on swallowing this tube is momentarily opened so that pressure in the middle ear is kept equal to that outside ; the movable tympanic membrane thus maintains its normal position. Auditory impulses as sound waves enter the external auditory meatus and arrive at the tympanic membrane. The vibrations of the membrane in turn are transmitted to the malleus, incus and stapes and thus arrive at the oval window ; an alternative wave can arrive at the round window through the air of the tympanum. These waves are then transmitted through the fluid of the internal ear to the very specialised organ of Corti in the cochlea ; the impulses are thence passed *viâ* the spiral ganglion to the cochlea nerve and so to the brain. Any interference with this mechanism produces deafness.

Deafness. Three classes of deafness are distinguished :

(A) Conduction Deafness ; this includes all causes up to the oval and round windows. Examples are : *wax* or foreign bodies lodged in the meatus ; all forms of middle ear catarrh ; acute and chronic inflammations of the middle ear.

(B) Perception Deafness ; those causes that involve the cochlea, spiral ganglion and auditory nerve ; it is also called Internal Ear Deafness. It may result from senile causes, syphilis, scarlet fever and typhoid ; from certain trades, *e.g.* boiler-makers and caisson workers, from exposure to the firing of revolvers, rifles and guns ; from taking of certain drugs, notably quinine and salicylates and excessive smoking.

(C) Nerve Deafness ; lesions of the auditory nerve itself and of its central nervous connections. This is always complete deafness ; it may be (1) *unilateral :* from mumps, acute labyrinthitis, the involvement of the auditory nerve in tumours ; (2) *bilateral :* from cerebrospinal meningitis, congenital syphilis—in this case it is almost always accompanied by interstitial keratitis and bilateral acoustic nerve tumours.

For tinnitus and vertigo and Ménière's disease, *see* Diseases of the Nervous Systems.

Earache. Pain in or about the ear is due to local inflammation in about 95 per cent. of cases ; in the remaining 5 per cent. of cases, no local cause is found and the pain is a referred one ; these are spoken of as cases of *otalgia.*

Examination of the pinna, external meatus and tympanic membrane will reveal a local cause, generally inflammatory, erysipelas, boils in the meatus or a red and bulging tympanic membrane and appropriate treatment will relieve the pain. Occasionally ulcerations in the meatus or carcinoma of the middle ear occur. When no local cause is found a wide search is needed to find the source of otalgia.

Pain may be referred to the ear from other parts supplied by the same nerves as also supply the ear. (1) Trigeminal ; this may be a true neuralgia. Otalgia

is also frequently referred from carious lower teeth and from unerupted wisdom teeth almost invariably in the lower jaw ; from disease of the tongue, growths and ulcerations ; from inflammations of the parotid gland and arthritis of the temporo-mandibular joint. (2) Glosso-pharyngeal ; this may be a true neuralgia, but pain is also referred from inflammatory or ulcerative lesions of the Eustachian tube and naso-pharynx (carcinoma) of the tonsil, epiglottis, back of the tongue, ary-epiglottic fold and pyriform fossa ; pain in the ear may be the first symptom of carcinoma of the pyriform fossa. (3) Spinal cervical 2nd and 3rd nerves inflammation of the posterior roots with herpes on the scalp and pinna is a source of severe otalgia, as also are lesions involving the cervical plexus. (4) Auricular branch of the vagus, which is doubtless intimately connected with the geniculate ganglion of the facial nerve. Inflammation of this ganglion occurs with a resulting herpes over the area supplied by this auricular branch ; this may be accompanied by facial paralysis and deafness and vertigo.

SUB-ACUTE OTITIS MEDIA

This denotes a mild infection of the middle ear, accompanied by catarrh of the Eustachian tube. The latter tends to be blocked so that the air becomes absorbed and there may be serous exudation, with drawing inwards of the tympanic membrane.

Symptoms. There is discomfort, or slight pain in the ear, deafness, which is apt to be overlooked in children. The patient hears the middle tones of the tuning-fork ; but loses perception of the lowest and highest notes. **Treatment** consists in removing septic foci if present in the nasal sinuses and naso-pharynx, and dealing with the Eustachian obstruction and sometimes removing fluid.

ACUTE SUPPURATIVE OTITIS MEDIA

Ætiology. This infection of the middle ear is nearly always due to a streptococcus, and very often follows the common cold, tonsillitis, scarlet fever, measles, influenza, or is part of a septicæmia. The whole of the middle ear tract may be involved. There is hyperæmia followed by exudation into the tympanum of blood-stained serum which usually becomes purulent in forty-eight hours.

Symptoms. Earache is usually the first symptom, but in children it may be so slight as to be overlooked, while in adults there may be severe headache. There is always deafness and frequently tinnitis. There is the malaise that accompanies any fever ; vertigo is infrequent. Infants may roll their heads from side to side and may develop meningismus. On examining the ear there is at first redness in a line behind the handle of the malleus ; then radiating vessels are seen running from this point to the periphery of the membrane ; later the redness is diffused, but the posterior half of the membrane is always affected first and more markedly than the anterior half. Inflammatory exudation causes bulging of the membrane which may lead to a perforation in the posterior half.

Complications. In some cases recovery takes place with perforation of the membrane, or occasionally without. Incomplete recovery leads to : (*a*) Deafness, which may later be improved by inflating the middle ear through the Eustachian tube. (*b*) Continued discharge ; this is sometimes associated with granulation (polypus) which projects into the perforation and prevents drainage. If the discharge persists for five or six weeks the mastoid will probably be infected ; but before a mastoid operation is performed infected foci in the nose or naso-pharynx must be excluded ; removal of adenoids may bring the suppuration to an end. (*c*) Facial paralysis from pressure on the seventh nerve, through a congenital aperture in the Fallopian canal. (*d*) Paralysis of the sixth cranial nerve which may be accompanied by pain in the frontal and temporal regions and is perhaps the result of a serous meningitis. (*e*) Mastoiditis, which is recognised

by pain behind the ear, tenderness on pressure over the mastoid—especially its tip—and swelling of the soft tissues over the bone. Bulging of the deepest part of the external auditory meatus is a valuable sign. In advanced cases there is much swelling over the mastoid process and above the ear with redness of the skin. Mastoiditis may lead to (*f*) abscess on the lateral sinus dura which may compress the sinus and later cause thrombosis, (*g*) extradural abscess in the middle fossa which is rare, (*h*) cerebral abscess which has been known to occur without pus formation in the mastoid, (*i*) suppurative meningitis.

Treatment. The patient will be kept in bed ; drugs are given to relieve the pain such as acetyl salicylic acid, pulv. ipecac. co., and morphia if necessary. Injections of anti-streptococcal (anti-scarlatinal) serum may be given in doses of 12 c.c. on two or three succeeding days intravenously or intramuscularly. Drops of glycerine and carbolic or 4 per cent. cocaine in camphor water are instilled into the ear ; warmth by means of an electrically heated pad or wool or hot-water bottle or fomentations over the ear may be used. Alternatively small ice bags kept permanently over the mastoid relieve the pain and inflammation. It may be advisable to incise the tympanic membrane, especially in acute cases, with much pain or high temperature. Treatment of mastoiditis is outside the scope of this book.

REFERENCES

1 E. P. Poulton and F. A. Knott .. 1936 *Practitioner*, January.
2 M. Hovel .. .. 1924 *Brit. Med. Journ.* **i.**, p. 497.
3 Sir St. Clair Thomson .. .. 1924 *Lancet*, **ii.**, p. 948, and *Med. Res. Counc. Spec. Rep. Ser.* **83.**
4 Sir St. Clair Thomson .. .. 1922 *Lancet*, **ii.**, p. 164.

DISEASES OF THE ORGANS OF CIRCULATION

In the working of the normal heart, two kinds of structures are concerned: the muscular contractile walls of its cavities, which drive the blood, and the valves, which control the direction of its flow. The power of rhythmical contraction is inherent in the heart muscle. The researches of the last few years have shown us the points in the myocardium at which stimuli to contraction commonly arise, the paths of conduction of stimuli from auricle to ventricle, the normal rate of such conduction, and the fact that contraction, though usually initiated in the auricle, and passing to the ventricle, may, in certain circumstances be started in the ventricle. After each ventricular systole there is a period of rest from contraction, which is broken by the systole of the auricle, and this is immediately followed by the systole of the ventricle. Three structures are involved in this process: one a small elongated mass of nerve tissue and muscular fibre and cells situated near the attachment of the superior vena cava to the auricle, called the *sino-auricular node;* another, a small mass situated in the septum of the auricles, near the opening of the coronary sinus, called the *auriculo-ventricular node;* the third, a special band of muscular fibres known as the *auriculo-ventricular bundle.* This band arises in the auriculo-ventricular node and measures about 2·5 mm. in breadth: it passes from the auricular septum into the ventricular septum, lying at first below the *pars membranacea septi,* and there divides into two portions, which lie one on each side of the septum ventriculorum; the right branch passes into the moderator band. Each branch is distributed extensively in the wall of its own ventricle, terminating in Purkinje's fibres, which lie beneath the endocardium in nearly all parts of the ventricles. The auriculo-ventricular node and the auriculo-ventricular bundle are sometimes called *junctional tissues.* In the normal action of the heart, the stimulus starts in the sino-auricular node, and is transmitted to the auricles. The wave of contraction which is slightly preceded by an electrical wave, called the excitation wave, spreads out radially from the S.A. node, travelling with equal velocity in all directions. The A.V. node then becomes stimulated. The excitation from the A.V. node spreads down the A.V. bundle along its various ramifications, and is spread out in the Purkinje network over the endocardium of the ventricles, and from here it spreads at right angles into the muscle of the ventricle.

The heart muscle is supplied by two sets of nerve fibres: (1) from the vagus; (2) from the sympathetic. Their function is to modify the beat. Very little is known about the sympathetic apart from the fact that its stimulation accelerates the heart and strengthens the beat. Branches from the vagus end both in the S.A. and A.V. nodes. Stimulation causes the seat of origin of the excitation wave (pacemaker) to move from the upper to the lower end of the S.A. node. Other effects are described under Bradycardia.

EXAMINATION OF THE HEART

Like the lungs, the heart is accessible to examination by the eye, the hand, and the ear. It comes into close proximity with the chest wall between the anterior margins of the lungs, over an area corresponding to the lower half of the sternum

on the left of the middle line, and the inner portions of the fourth and fifth left costal cartilages and the spaces below them. The *impulse* of the heart can be determined by inspection and palpation; the *præcordial area*, or the area of chest wall over the heart, can be made out by percussion, and the *heart sounds* can be studied by auscultation.

INSPECTION

In healthy persons, not very fat, the heart can be seen to beat over an area of about ½ inch in diameter in the fifth intercostal space, from ½ inch to 1 inch within a line drawn vertically down from the nipple, or from 2½ to 3 inches from the middle line in an average-sized adult; this beat is called the *impulse*, or *apex beat*. In disease sometimes no impulse can be seen, either from feebleness of beat, or because the heart is overlaid by lung. The right auricle, when dilated, can sometimes be seen beating to the right of the sternum. Inspection also shows bulging of the chest wall in some cases of great enlargement of the heart.

A slight visible *systolic retraction* of intercostal spaces is not uncommon in healthy persons; a more marked retraction occurs with hypertrophy of the heart.

PALPATION

The position of the impulse can usually be more closely defined by palpation than by inspection. In hypertrophy of the left ventricle it may be displaced outwards and downwards; in extreme dilatation it may be felt in the axilla. The beat may be forcible or heaving and quick and irregular. It may not be palpable at all. Examination by X-rays shows that the left border of the heart usually corresponds with the point furthest to left, where a definite forward and horizontal lift is imparted to the fingers (**63**), and not with the outer and lower part of the area over which the vibrations can be felt, which is commonly outside the area of the heart, as shown by X-rays. In one case observed by the writer an apparent impulse was produced in the fourth space by the upper part of the left ventricle. A *systolic* impulse may be produced in the epigastrium by a hypertrophied right ventricle, by the aorta, whether aneurysmal or conducted by tumour, or by a pulsating liver. A dilated right auricle may be felt beating to the right of the sternum. In some cases of aortic aneurysm the hand placed over the base of the heart can appreciate a shock described as the *diastolic shock*, or *diastolic rebound*, which can be readily felt because the aneurysm compresses the lung and comes into closer contact with the thoracic parietes.

In some cases of valvular disease, over a limited area in which a murmur can be heard with the stethoscope, a *thrill* (*frémissement cataire*) can be felt by the hand. It is usually accompanied by a murmur, but occasionally the murmur is absent, because the vibrations are so coarse (*i.e.* their rate is so slow) that they can only be felt, not heard. It is most common in mitral stenosis, and accompanies a large proportion of auriculo-systolic murmurs, and some mid-diastolic murmurs. Thrills with other murmurs are much less common and occur in other valvular lesions, such as pulmonary stenosis (congenital), aortic stenosis, and occasionally aortic regurgitation and mitral regurgitation. Aneurysms and pericarditis may also give rise to palpable vibrations.

PERCUSSION

While the greater part of the chest is resonant to percussion, from the presence of the lung, there is a small area of *superficial* or *absolute dulness*, which corresponds to that part of the anterior surface of the heart which is not covered by lung. Around this dulness is an area of *deep* or *relative dulness*, the outer limit of which corresponds to the outline of the heart, and therefore maps out its actual size. Above it reaches to the third space; to the left it reaches to the

impulse; and to the right it can often be made out half an inch beyond the right border of the sternum. The sternum itself is resonant. The relative dulness is best obtained by means of moderately light percussion. The room must be quiet. X-ray examination shows that the border of the heart usually corresponds to the point where the note first undergoes a considerable change in resonance. The lower limit of the heart's dulness cannot be discriminated from that of the liver, and the outline is assumed to lie between the impulse and the lowest point of the right border of the dulness.

The position of the heart varies slightly with the position of the patient. The area of its projection on the chest wall extends rather lower, but it is less wide in the vertical than in the horizontal position.

When the lungs are distended, as in emphysema, it is usually quite impossible to tell the size of the heart by percussion, and in addition the impulse is often too weak to feel. An important cause of the enlargement of the area of relative dulness is distension of the pericardial sac with liquid. Exceptionally, the area may be resonant from the presence of air in this sac. The area of præcordial dulness is shifted upwards, downwards, or to either side by anything which displaces the heart in these directions.

AUSCULTATION

Heard with the stethoscope the sounds of the heart resemble the syllables "lubb dup"; the *first* sound duller and longer, and the *second* sound sharper and shorter. The first sound is due partly to muscular contraction, and partly to sudden stretching of the auriculo-ventricular valves after closure; the second is due to sudden stretching of the semi-lunar valves after they close. In the case of both valves, the flaps normally float together immediately after the blood has stopped streaming through the orifice (**1**). The first sound is heard best near the apex of the heart, and the second is heard best at the base.

Modifications of the Sounds. The heart sounds may be accentuated or diminished in loudness, or increased in number, or their time relations may be altered.

Accentuation arises from several causes, amongst others from retraction of the lung, so as to bring the heart closer to the chest wall. Accentuation and dulling or muffling of the first sound results from ventricular hypertrophy, while accentuation without dulling is common in mitral stenosis. Accentuation of the second sound in the second *right* intercostal space results from increased arterial blood pressure, whereby the valves are stretched with unusual force after closure (Plate 10, B (2)); and accentuation of the second sound in the second or third *left* space results similarly from the pulmonary valves.

Diminution of the sounds results from feeble action of the heart, from its being unusually covered by lung, as in emphysema, or from its being surrounded by pericardial effusion. The heart sounds may also be diminished if the valves are imperfect so as to allow regurgitation of blood with production of *murmurs*.

Reduplication of the *second* sound is commonly heard at the base of the heart, especially in the pulmonary area, and it is occasionally conducted to the apex. It occurs in cases of valvular disease where there is congestion of the lungs and increased pressure in the pulmonary circuit. It is due to the fact that the pulmonary and aortic valves do not close quite synchronously. It is probable that reduplication of the *first* sound, heard at the apex, may sometimes be due to asynchronous closure of the A.V. valves. In *canter-rhythm* there is very well marked reduplication of the first or second sound at the apex, so that there is a triple rhythm of two types, "te-lubb dup" and "lubb dup-te." There are two causes for canter-rhythm: (1) The extra sound is due to the same cause as often produces an early mid-diastolic or an auriculo-systolic murmur in this position; *i.e.* it is an indication of mitral stenosis; (2) it is due to heart block (*q.v.*), and may

short, or it may be rumbling and continue through most of diastole, and this suggests a high degree of stenosis. The auriculo-systolic murmur gets gradually louder, and ends in an accentuated first sound. It may be represented by "r-r-rup." It is possible to have both mid-diastolic and auriculo-systolic murmurs present at the same time (C and D), or an auriculo-systolic murmur may be accompanied by a reduplicated second sound.

What is here stated of the aortic and mitral valves may be said, *mutatis mutandis*, of the pulmonary and tricuspid valves.

The relation of the murmurs to the rhythm of the heart and the flow of blood through it may be tabulated as follows :

Orifice.	Lesion.	Murmur.	
Aortic or Pulmonary.	Obstruction.	Systolic.	
	Regurgitation.	Diastolic.	
Mitral or Tricuspid.	Obstruction.	Diastolic	Early. Mid. Late (Pre-systolic or auriculo-systolic)
	Regurgitation.	Systolic.	

Of these the pulmonary regurgitant and tricuspid obstructive murmurs are very rare ; and murmurs due to pulmonary obstruction are less frequent than the remaining five, although a systolic murmur over the region of the pulmonary artery is quite common in association with changes in the quality or quantity of the blood, and is known as a hæmic murmur.

Obviously, the eight possible lesions above indicated (obstruction and regurgitation at each of the four orifices) cannot be distinguished solely by the relation of their murmurs to the sounds of the heart. But we find help towards their discrimination in the different points of the præcordial area at which they are best heard. These are determined not by the actual position of the valve below the surface, but by the direction of the current of blood which is flowing past the orifice, and in which the sound vibrations are produced. The flow of blood in the aorta from mid-sternum towards the right clavicle, in the pulmonary artery from the sternum upwards towards the left, and in the heart from auricle to ventricle, conveys each murmur along a special path ; and the reflux of blood through the aortic valves into the ventricle, and through the mitral valves into the auricle, acts in a similar way in the case of regurgitant murmurs. The term *area* (mitral area, aortic area) is often applied to the part of the præcordia or adjacent chest wall where a particular murmur is commonly heard, and in auscultating the heart for valvular disease these areas must be successively examined.

Aortic obstructive murmurs are heard with greatest intensity at the junction of the second right costal cartilage with the sternum, and at the extremity of the second right intercostal space (aortic area) ; they can be traced upwards towards the inner half of the right clavicle, and into the vessels of the neck, and they are sometimes heard in the right supraspinous fossa.

Aortic regurgitant murmurs are heard over the aortic area ; they are traceable down the sternum or along the left-hand side of it, towards the apex of the heart, *i.e.* along the line of the regurgitating stream of blood. They are usually loudest to the left of the sternum, and sometimes this is the only place where they can be heard.

Mitral obstructive murmurs are heard most loudly at the point of impulse of the heart against the chest (mitral area) ; though sometimes audible more or less imperfectly between this point and the sternum, they are always best heard at the apex, and are often strictly limited to an area of an inch or an inch and a half in diameter. The stethoscope should always be placed over the actual heart beat, as found by examination, and not only over the spot where the impulse should be normally found. They are heard best if only very light pressure is used.

Mitral regurgitant murmurs are mostly heard with greatest intensity at the

apex of the heart, but they are commonly widely diffused over the præcordia towards the sternum and the base of the heart, though as a rule they are heard more loudly when traced outwards to the left. In the axilla they often lose in loudness, but they are again heard at the angle of the left scapula.

Pulmonary obstructive murmurs are heard with great intensity in the second left intercostal space at its inner end (pulmonary area), and can be traced outwards in that space, and upwards towards the left clavicle.

Pulmonary regurgitant murmurs are heard at the junction of the third left costal cartilage with the sternum, and thence downwards over the right ventricle, along the left border of the sternum.

Tricuspid obstructive murmurs are sometimes heard, with a pre-systolic or mid-diastolic rhythm (like mitral obstructive murmurs) at the left side of the sternum, over its junction with the fourth costal cartilage.

Tricuspid regurgitant murmurs are heard at the lower half of the sternum, over an area corresponding pretty closely to the part of the heart left exposed between the two lungs; but they are often limited to the base of the ensiform cartilage (tricuspid area).

The murmurs due to congenital defects in the heart and aortic aneurysm are described later.

The Character of the Murmur. The quality of the sound is most often blowing; it is sometimes rushing, sawing, or rasping. Sometimes murmurs have a distinctly musical quality. Half-detached fragments of valve playing in the blood current, perforations in valves, and loose chordæ tendineæ sometimes cause such murmurs. In some cases a murmur, though not strictly musical, has a different pitch at one point from that which it has an inch away.

Murmurs vary with the position of the patient, probably from the effect of gravity upon the velocity of the blood currents. Thus in the recumbent position there is often an increase in the loudness of aortic, mitral and tricuspid systolic murmurs. Conversely the erect position often intensifies mitral obstructive and aortic regurgitant murmurs; but there is no hard and fast rule.

The Significance of Murmurs. It is a remarkable thing that, considering the large changes in calibre of the passage through which the blood goes—veins, auricle, ventricle, artery—no murmurs are usually produced in the heart. It is easy to imagine that a small alteration of no pathological importance might make all the difference, and cause a murmur.

As the result of experience gained in the War, especially by Lewis and his co-workers, views on the importance of murmurs have changed considerably. Where diastolic murmurs are present, indicating aortic regurgitation or mitral stenosis, the practice is not to place the man in a high category for service. However, the presence of a systolic murmur should be entirely disregarded, since it has been found that the proportion of men who eventually turn out to be unfit is the same among those who have a systolic murmur as among those who have no murmur at all. No doubt the reason of this is that systolic murmurs heard in apparently healthy men may sometimes be exocardial, but where actual mitral regurgitation is present the lesion may be so well compensated that there is no detectable difference in the heart's efficiency, in the absence of other symptoms.

Murmurs not Dependent upon Actual Disease of either of the Four Valvular Orifices. The above descriptions apply to the sounds which result from obstructions and leakages at the four valvular orifices. But abnormal sounds may be heard over the præcordial area, which arise in other ways. Some of these are called *functional murmurs*, to contrast them with those due to structural disease of the heart.

Hæmic Murmurs. In anæmic states such as chlorosis, pernicious anæmia, and after great losses of blood, a systolic murmur is heard over the cardiac area. It is often harsh in quality, and is heard loudest in the second left intercostal space,

and is traceable outwards along that space and towards the left clavicle—that is to say, in the direction of the flow of blood in the pulmonary artery. This murmur is often loudest in the recumbent position, and diminishes or even disappears when the patient stands up. In severe anæmia a murmur may also be heard at the apex, and also behind. A possible explanation is that the increased velocity of the blood stream from the increased "minute volume" in anæmia causes turbulent motion or gives rise to the murmur.

Exocardial Murmurs. These are sounds of blowing character which are caused not by changes in the interior of the heart, but by sound vibrations produced outside the heart. Some of these are due to the alteration in size of the heart at each beat, which causes movements of the air in the neighbouring part of the lung, and so gives rise to a series of short respiratory sounds with a cardiac rhythm (*cardio-pulmonary*). The most common of these is a short, high-pitched, systolic murmur, often limited to the apex, which is heard in nervous or excited persons when they are under medical examination. Such a murmur is sometimes heard at the left scapula behind, as well as in front. Its exocardial origin is by some thought to be proved, if it disappears on firm pressure with the stethoscope. But pericardial friction sounds, which are certainly produced outside the heart, and may be mistaken for internal bruits, are often increased by pressure. A systolic apex murmur, audible only during inspiration, or as long as the lung is kept expanded, is probably often cardio-pulmonary.

Other exocardial murmurs are produced by displacement of the heart, as when it is compressed by pleural effusion, or by deformities of the thorax; and others by morbid conditions of the lung and pleura immediately adjacent to the heart, and mostly on the left side. Very extraordinary murmurs are sometimes heard when a large pulmonary cavity is in close contact with the heart, the air being driven suddenly out of the cavity with each cardiac impulse.

Friction Sounds. Rubs or friction sounds are exocardial sounds arising from the movement of inflamed and roughened pericardial surfaces over one another during the heart's movements. In character, they are generally rough and grating, and hence are readily distinguished from the blowing murmurs above described. The pericardial rub may be a single sound during systole or a double sound, one in systole and one in diastole; or it may be a triple sound of a shuffling character which is very distinctive. It is not usually in time with the heart sounds. It commences at almost any part of the præcordial area, and may spread over the whole of it. It is sometimes rendered louder by pressure of the stethoscope. Pleuro-pericardial friction has already been described.

ESTIMATION OF THE CAPACITY OF THE HEART FOR EFFORT

The most important of all examinations of the heart is the estimation of its reserve power, by which is meant finding out its response to exercise. In its simplest form this consists in asking the patient to take some exercise, such as walking quickly, running along the level or upstairs, or doing some simple exercises with dumb-bells, and observing whether he is abnormally breathless or exhausted after it, whether he becomes pale, whether his expression becomes anxious, and whether he develops anginal pain. The history of the patient is also of great importance in this connection, as, for instance, that from a boy he was never able to join in games at school, or that since an attack of rheumatic fever or influenza or diphtheria he has never been able to run; or that he never does run for a train, because he gets too short of breath; or that he never runs upstairs, and so on.

The response to exercise bears little relation to the loudness of the murmurs. This fact was observed when recruits were being examined for the army. Many men were found with loud præcordial murmurs who had always believed themselves healthy, with hearts which responded to exercise perfectly normally. On the other hand, in cases of aortic regurgitation the most severe cases often have

the softest murmurs. Estimating the size of the heart and its shape and the extent to which the muscle is hypertrophied will give a better measure of the extent of the lesion which has to be compensated. Palpation and percussion may be employed, but the most certain information can be obtained by the X-rays. The measurements must be taken orthodiagraphically.

The late Dr. G. H. Hunt, who made a large number of observations on the pulse-rate before and after exercise, believed that it was of value in estimating the cardiac efficiency in disease. The number of heart beats during the first two minutes immediately following the cessation of a given amount of work is measured and compared with the pulse rate at rest by taking the ratio. Thus, supposing the pulse rate at rest was 70 and after exercise 160 beats were counted, the ratio would be 2·29. The exercise consists in going up and down a step 13 inches high. In normal trained individuals who carry out this exercise thirty times a minute for three minutes the pulse ratio is approximately 2·5. The exercise for the patient is so chosen (*e.g.* ten, fifteen or twenty steps a minute for three minutes) that the pulse ratio is found to be 2·5. Suppose the rate was 20, then the efficiency is calculated on $\frac{20}{30}$, *i.e.* $\frac{2}{3}$ the normal. It is, however, advisable also to take into account the rate at which the pulse falls after the exercise.

EXAMINATION OF THE HEART BY MEANS OF X-RAYS

By this means the size of the heart can be accurately determined. The method is of special importance in cases of emphysema, where percussion is usually not trustworthy. Since the rays come out from a point by reflection from the anticathode, they are not parallel, and so the shadow on the screen is larger than the heart actually is. To correct this the heart must be measured "orthodiagraphically." The diaphragm is stopped down, and the tube is moved about so that the edges of the heart are seen and marked in the middle of the narrow field on the screen.

Another method is to place the patient 6 feet in front of the tube and take a radiogram. At this distance the divergence of the rays will not be sufficient to cause any serious error.

Although examination of the heart by X-rays is a big subject, and cannot be dealt with here fully, a few of the more important points may be mentioned.

In Fig. 12, I. represents the shape and topographical anatomy of the normal heart. Note that the aortic arch forms a prominent knuckle projecting above to the right.

II. represents the normal with the patient in the right anterior oblique position, the rays coming through from the back.

In Plate 11 (mitral stenosis) the shape is characteristic; there is no aortic knuckle as in the normal and the dilatation just below is not due to dilatation of the left auricular appendix, which is always quite small, but to the infundibulum of the pulmonary artery, which is dilated and often forms a projection, but the left ventricle is smaller than usual; hence, the apex tends to be pointed, and the left border of the heart is more vertical than usual. The auricles are dilated and this is well seen in the oblique position, as in II., after swallowing barium; the œsophagus becomes curved. The left auricle is often very dilated (aneurysmal dilatation) and extends further to the right than the left auricle.

In Plate 12, A, which represents a case of compensated aortic regurgitation, the left ventricle is rounded and the apex displaced downwards and outwards. There is excessive pulsation at the apex. The aorta is dilated and the knuckle very prominent.

In pure congenital pulmonary stenosis the right ventricle is hypertrophied and the right auricle dilated, and the left ventricle is displaced upwards and is quite small (Plate 12, B). There is very often a dilatation of the origin of the pulmonary artery, but the cause of this is obscure. When there is also deficiency of the septum the shape of the heart is normal, though it may be large.

dizziness, disturbances of vision, nausea, vomiting and pyrexia. The drug must certainly be stopped if there are signs of heart failure. When the auricular fibrillation has been abolished it is as well to continue with small doses of quinidine (0·8 gramme per diem) for some weeks; the amount can be gradually reduced and the drug eventually omitted. A relapse, which is not uncommon, should be treated along the same lines.

In general, patients feel more comfortable when the heart's rhythm is normal, and for this reason there is an advantage in quinidine over digitalis, which does not abolish fibrillation. Quinidine may be given both in permanent and in paroxysmal auricular fibrillation. Thyro-toxic fibrillation cases do well with quinidine if the hyper-thyroidism has been efficiently treated. Quinidine and digitalis should not be given simultaneously.

PULSUS ALTERNANS

In this form of abnormal heart beat there is a regular alternation of small and large beats, but, unlike the pulsus bigeminus, or coupled beats, in which the interval following the smaller beat is longer than that following the larger beat, the intervals throughout are almost exactly uniform. If the difference between a small and a large pulse beat is not very marked, it may be unrecognised by the finger, and the sphygmograph may be necessary to demonstrate the condition. If the difference is pronounced, that is, if the alternate weak beats are very small, they may be missed by the finger, and the pulse may be thought to be abnormally slow, that is, slower by one-half than it actually is. The condition may also be recognised by taking the blood pressure with a sphygmomanometer. At a certain pressure the weaker beats are eliminated, and the pulse at the wrist apparently drops to half its original rate. Pulsus alternans is not so readily diagnosed from the electro-cardiogram; but in Fig. 31, III., on p. 240, it is present, as shown by the alternate lessening of the R.S. excursion.

This abnormality is certainly due to defective contractility or exhaustion of the myocardium; it is increased or made manifest by exercise; it may be temporary and disappear. But if it is continuous it points to a persistent cause for the defect of contractile power, as, for instance, myocardial degeneration. Experience shows that pronounced cases rarely last more than two years, and not infrequently death is sudden. The prognosis is worse if alternation is observed when the pulse is slow. It is not so bad if the condition only appears when the heart is beating rapidly.

Treatment. The heart must be rested in order to conserve its power. Digitalis has been found of value in those cases where the pulse is quick, especially if œdema is present. Its administration slows the pulse and abolishes the alternation.

INFREQUENT ACTION

(*Bradycardia*)

Although seventy in the minute is often regarded as the normal frequency of the radial pulse and heart, a pulse of sixty per minute is quite common. A pulse of fifty is normal in some individuals, and the rate in these slow-pulsed persons may fall to forty-eight in the cold hours of midnight or early morning. A slow pulse rate is observed in starvation or under-nutrition, and is, no doubt, associated with the lessened metabolism that occurs.

In examining for this condition it is, of course, essential to observe the heart as well as the radial pulse, as there are several conditions in which the beat of the heart may not get through to the wrist, such as pulsus alternans or pulsus bigeminus. Bradycardia might be suspected if the pulse only were felt, whereas the heart would be beating at a normal rate.

Many conditions of bradycardia are due to vagal stimulation, which may be produced reflexly. The slow pulse of cerebral compression, jaundice, conva-

lescence after influenza and other acute infective diseases is due to this. The same is the case with the slowing of the whole heart that causes the fainting attack so commonly due to emotion or prolonged standing, and possibly the fainting attacks in aortic disease.

The alternate slowing and quickening of the heart during respiration (sinus arrhythmia) is also due to vagal action, and the rather uncommon " phasic irregularity," where the whole heart slows periodically, independently of respiration and without apparent reason.

Sino-auricular block is another uncommon condition producing bradycardia, but sino-auricular block itself may be due to vagal stimulation. A fairly common cause of prolonged bradycardia is to be found in auriculo-ventricular block, especially where the block is complete.

VENTRICULAR FIBRILLATION

By means of the electro-cardiograph the condition of fibrillation has been recognised as occurring in the ventricle as well as in the auricle.

It is observed as a rule immediately before death, though not necessarily as the cause of death; but in animals, and on rare occasions in man, it has ceased in time for recovery to take place. It appears to be the cause of death in lightning stroke, and is believed by some to be the explanation of some of the fatal cases of chloroform anæsthesia.

COMPENSATION OF THE HEART

In disease the heart frequently works under some disability. When by natural processes the strength of the heart is increased to overcome the disability, the heart is said to be *compensated*. The strength of the heart is increased by increasing the thickness of the muscular walls; this is called *hypertrophy* which may or may not be associated with dilatation of the cavities as well.

When the disability under which the heart is working is small, hypertrophy will take place to such an extent that, whatever work it is called upon to perform, its response will be as effective as in a normal person. The patient will not become more than usually short of breath after the severest forms of muscular exercise, and the breathlessness will disappear as quickly as usual after the exercise is finished. Such a disability may be said to be *fully compensated*.

If the disability, which includes damage to the heart itself, is of a higher grade, the patient may be comfortable when at rest or during mild exercise, but may become more than normally short of breath when the exercise is more severe, and this breathlessness may persist for some time. In this case the heart is compensated for mild exercise, but is uncompensated for severe exercise. The term *partial* or *incomplete* compensation may be used for such a case.

In still more severe cases, where the heart is failing, the patient exhibits breathlessness and other symptoms, even when lying at rest in bed. In this case complete failure of compensation has occurred, and the various chambers of the heart become dilated to a greater extent than they were previous to the failure of compensation.

HYPERTROPHY

Hypertrophy is the natural response of the body to an increased amount of work thrown upon the heart, and can take place so long as the nutrition of the muscle is well maintained by a proper supply of blood. When hypertrophy of the ventricles takes place without increase of the corresponding cavities (dilatation) it is called *concentric hypertrophy*, and this may be left-sided or right-sided, depending on which side of the heart this extra work falls, or both sides may be equally affected. The causes of left-sided hypertrophy without dilatation of the left ventricle are—(1) disease of the aortic valves with narrowing of the orifice;

so as to leave some residual blood, but nothing is known for certain about this in man, although it may occur experimentally in the " heart-lung preparation " (Starling).

Pathology. There are two kinds of dilatation. (1) There is the compensatory dilatation of aortic and mitral regurgitation, due to the fact that the particular chamber of the heart accommodates the extra quantity of blood that regurgitates, as well as the normal quantity that is delivered to it from the lungs and is sent on into the general circulation. This is compatible with a perfectly healthy myocardium. (2) There is the dilatation due to yielding of the ventricular walls that spells the onset of failing compensation and is often associated with myocardial disease (*q.v.*). Starling's experiments suggest that this second type of dilatation may also be a compensatory mechanism, enabling the heart to beat more forcibly because the greater the relaxation of the cardiac muscle-fibre, the stronger the beat. This is called the " Law of the Heart."

Slight dilatation of the heart occurs normally during muscular exercise, the effect of this being to increase the output of blood at each beat. It is, however, quite certain from X-ray evidence that immediately after exercise the heart normally contracts down so as to become slightly smaller than its resting size. On the other hand, it has been found that in cases of incipient cardiac failure the heart shows dilatation after muscular exercise.

Morbid Anatomy. The effects on the size and shape of the heart vary with the cavity concerned. In general dilatation the heart becomes more globular, and is widened transversely. The dilated left ventricle increases to the left; when the right ventricle is much dilated, the triangular shape of the heart is lost, it becomes more globular, and the apex is formed partly by the right ventricle instead of being formed entirely by the left. The thickness of the walls will depend on the presence or absence of accompanying hypertrophy. In dilatation with thinning, the ventricular walls may be reduced to $\frac{1}{8}$ inch, and even less at the apex, which is commonly the thinnest part. The auriculo-ventricular orifices share in the dilatation, and incompetence of the valves often results. The auricles may undergo very considerable dilatation, and this is often accompanied by some hypertrophy of the auricular walls.

Physical Signs. The increased size of the heart, as indicated by enlargement of the præcordial dulness or of the shadow of the heart produced by X-rays, may be due to hypertrophy or dilatation or both of these combined. However, it is probable that any considerable enlargement of the heart observed by these methods is chiefly due to dilatation. Any enlargement to the right of the sternum is due to auricular dilatation, because the auricular wall, even if hypertrophied, is quite thin; and it is nearly always *right* auricular dilatation. But in several cases of mitral disease, with enormous enlargement of the left auricle, the latter has actually formed the right border of the heart (**11**); because the left auricle always enlarges towards the right. It is often possible to feel the beat of the heart by placing the fingers in the intercostal spaces over the dilated auricle. Dilatation of the left auricle may cause dysphagia by pressure on the œsophagus and apparently, in one case seen by the writer, paresis of the left diaphragm by pressure on the left phrenic nerve. It may compress the lower part of the left lung or the left bronchus, or cause paralysis of the left vocal cord. The left auricle may be observed on the X-ray screen when the patient stands in the oblique position, facing the tube, with his right shoulder towards the observer. The rays pass through the posterior mediastinum, between the vertebral column and the left auricle. The œsophagus, if outlined with barium, is seen to be displaced.

Dilatation of the ventricles causes an increase of the præcordial dulness and of the X-ray shadow to the left of the sternum. In extreme cases the shadow reaches the left wall of the chest, and the impulse can be felt in the axilla; but it may be diffuse and weak. Dilatation of the left ventricle is often accompanied

by a systolic murmur, due to mitral regurgitation, and dilatation of the right ventricle often causes tricuspid regurgitation.

FAILURE OF COMPENSATION

Failure of compensation may affect both sides of the heart simultaneously, or may be right-sided or left-sided ; the recognition of the latter is comparatively recent.

Pathology. X-ray observations on the healthy subject have shown that there is more blood in the heart and lungs at the end of inspiration than at the end of expiration, and that the heart and lungs become engorged with blood on attempting a forcible inspiration with the glottis closed (Müller's experiment), and emptied of blood on attempting a forcible expiration also with the glottis closed (Valsalva's experiment), as shown in Plate 13. These observations can only be explained by temporary inco-ordination between left and right ventricles. Normally, over a given time, the output of the right ventricle into the lungs must be equal to the output of the left ventricle into the systemic circulation, or else the lungs would either be deprived of or engorged with blood. Deprivation takes place in Valsalva's experiment, because the right ventricle has to act against the high positive pressure in the lungs and temporarily fails relatively to left ventricle. In Müller's experiment the right ventricle is helped by the negative pressure and more blood is pumped into the lungs than can be disposed of by the left ventricle. This engorgement indicates relative left-sided failure.

Observations on a patient with myocardial degeneration by means of a closed circuit respiration apparatus have shown that such an engorgement of the heart and pulmonary circuit, due to acute left-sided failure, took place during muscular exercise and disappeared again within the first minute or two of rest—a state of affairs which was relieved by treating with oxygen (**10**). It has been suggested that an acute left-sided failure of this nature is comparatively common and leads reflexly by vagal action to spasm of the bronchi, and in extreme cases, when pulmonary œdema has followed the congestion, to prolonged rattling expiration interrupted by short inspiratory gasps; this is a protective mechanism because the prolonged expiration increases the pressure in the lungs, hindering the relatively over-active right ventricle, while the extremely dangerous period of lowered intra-pulmonary pressure is made as short as possible.

Morbid Anatomy. In *left-sided failure* the lungs are affected. In early stages there is simply undue fulness of the venous radicles in the lung ; there is often, in addition, a transudation of serum into the air vesicles and minute bronchial tubes, so that on section of the lung a quantity of yellowish or almost colourless frothy liquid flows from it ; and in advanced cases the most affected parts of the lung become solid, tough, airless, dull brown in colour, from the presence of hæmatogenous pigment, and uniformly smooth. This condition has been called *heart-lung*, or *brown induration*. Both induration and ordinary œdema especially affect the bases of the lower lobes. As a result of local interference with the circulation, some transudation of fluid into the pleural cavity (hydrothorax) often occurs, and there is more or less proneness to inflammatory lesions of the lung, either in the form of bronchitis, pneumonia, or pleurisy. None of these effects is necessarily bilateral ; the exudations tend to affect the side on which the patient most often lies.

In *right-sided failure* there is a general œdema of the subcutaneous tissues called *anasarca*. In the horizontal position the congested and dropsical area begins in the trunk and tends to spread peripherally as the blood increases in volume. There is also *ascites* and peritoneal dropsy. In the upright position the veins of the trunk are relieved to some extent of their accumulated blood by gravity at the expense of the legs, which thus become a part of the congested area, and the ankles swell by increased output. The head and upper parts shrink

from increased lymph absorption. In the same way if the head and arms hang down these parts swell and the legs shrink. In a very advanced case the congested area has extended up the legs, so that both legs all the way up and the abdominal wall are enormously swollen. In fact, the veins of nearly the whole of the body may be thus affected. It looks as if the body employed this method of storing up superfluous fluid to protect its vessels against abnormal plethora, since the kidneys cannot get rid of it owing to their congested condition (**54**).

The hepatic veins open into the inferior vena cava so close to the right auricle that the influence of cardiac disease upon the circulation of the *liver* can be readily understood. The organ enlarges considerably, and becomes darker in colour, and in advanced conditions acquires a peculiar appearance of red, yellow, and white mottling, to which the name of *nutmeg liver* has been applied. On section the centre of each lobule is seen to be occupied by the enlarged hepatic vein rootlet transversely divided, and the adjacent central zone of the lobule is dark red or purple; outside this is a zone of yellow colour from the retention of bile within it; while the external zone of the lobule is of white or grey colour which the microscope shows to consist of cells in a state of advanced fatty degeneration.

The *kidneys* are congested, becoming in consequence larger and dark-coloured; but from long-continued congestion a certain amount of fibrous tissue may develop, and by its irregular distribution and contraction it may produce a granular condition of the surface.

The *spleen* becomes hard and darker than normal, and, though varying in size, is often small. The congestion of the *stomach* and *intestine*, like that of the spleen, is, of course, secondary to that of the liver, since the veins derived from these organs empty themselves into the portal vein. The mucous membrane becomes congested, and after death considerable distension of the vessels, and sometimes hæmorrhages into the substance of the mucous membrane, may be seen.

DISEASES OF THE MYOCARDIUM

MYOCARDITIS

Myocarditis, or inflammation of the muscle of the heart, may be either acute or chronic. *Chronic myocarditis* can only be recognised in its final stage of fibroid change, and is included in the description of fibroid degeneration (*see* next page).

Acute myocarditis occurs mostly in connection with pericarditis or endocarditis as a part of rheumatic fever and is described later. But the myocardium may be affected in any acute fever, the symptoms due to diphtheria (*q.v.*) being very characteristic. A more local inflammation of the myocardium results from coronary thrombosis and from malignant endocarditis, where ulceration of a valve extends to its base, and then invades the muscle; or where vegetations or semi-detached fragments set up ulceration in adjacent parts of the endocardium by friction or contact, and this involves the myocardium.

A third form is *suppurative myocarditis*, which is chiefly the result of pyæmia. Small abscesses occur in the substance of the heart, mostly in the wall of the left ventricle, and may approach so near to the pericardium as to rupture into its cavity and set up acute pericarditis. This form of myocarditis is often secondary to acute osteomyelitis, and the treatment is that of the primary disease, but the prognosis is practically always hopeless.

MYOCARDIAL DEGENERATION

Pigmentary Degeneration. (*Brown Atrophy of the Heart*). The heart is smaller than normal, and the muscular fibre, instead of having a full red colour, is of a dull brownish-red, and softer and more friable than is natural. Under

the microscope the fibrillæ are seen to contain a number of minute yellow granules. It occurs in senile and cachectic conditions, being common in fatal cases of malignant disease of other organs.

Fatty Degeneration. This change in the muscular fibres must be distinguished from the deposit of fat about the heart. In the latter the ordinary adipose tissue is deposited beneath the pericardium, and invades the muscular fibres because the connective tissue cells between the fibres become loaded with fat. In the former, or true fatty degeneration, the muscular fibrillæ themselves are the seat of minute fat granules, which replace the true sarcous elements and rob the muscle of so much of its contractile tissue. This true fatty degeneration occurs in different forms: the muscular wall may be uniformly affected, or the fatty changes may be limited to a small patch, or to the layer underlying the pericardium, as described under Myocarditis, or it may consist of streaks and lines on the inner surface of the heart. When the affection is general the heart is of softer consistence, more easily lacerated, of pale pink or buff colour, and often somewhat larger than normal, from yielding of the affected muscular tissue. When the fat is deposited in lines or streaks it gives a characteristic appearance, the lines of pale yellow colour being often arranged upon the darker red muscle, like the markings of a tabby cat. They are seen mostly on the musculi papillares, on the posterior wall of either ventricle, and on the septum in the right ventricle. Fatty degeneration is common in hypertrophied hearts, and may be present even when the muscle has quite a normal colour.

Ætiology. The causes of fatty degeneration of the heart are general and local. It may be the result of a general tendency to degeneration, such as occurs at an advanced age, and is accompanied by obstruction of the coronary arteries due to atheroma or syphilitic changes, by which the nutrition of the heart wall is impaired. On the other hand, fatty degeneration is seen constantly in pernicious anæmia, and often in other forms of anæmia, in purpura and scurvy, and in cachectic conditions, such as phthisis and cancer; in poisoning by phosphorus, by some mineral substances (lead, antimony, arsenic), and in chronic alcoholism. In most of the acute febrile diseases the consistency of the heart is sometimes altered, as the result of a finely granular condition of the muscular fibres, which is probably not to be separated from fatty degeneration. This is the case in enteric and typhus fevers, in yellow fever, diphtheria, small-pox, and measles. Fatty degeneration also arises from myocarditis, and is seen in connection with long-standing valvular disease and renal disease.

Fatty overgrowth or *infiltration* of the heart has previously been described as a separate disease, in which not only is the outside of the heart loaded with fat, but fatty streaks are seen penetrating into the muscle wall. This is characteristic of *obesity* and is described under this head.

Fibroid Degeneration. In this form of degeneration, the muscular tissue of the heart is replaced by white fibrous or connective tissue. The change is in most instances partial, so that streaks and patches of a white, yellowish-white, or grey colour are seen deep in the muscular substance. It affects the lower third of the ventricle, the lower third of the septum, the musculi papillares, and sometimes the bases of diseased valves. Only occasionally is the ventricle almost entirely converted into fibrous tissue, but even here some traces of muscular fibre may be found on microscopical examination. The heart affected with fibroid disease is generally hypertrophied, and it may be dilated, or the subject of adherent pericardium; the affected part of the heart's wall is often thinner than normal, and it may be bulged out into a distinct aneurysm.

Ætiology. Fibroid degeneration often results from rheumatic myocarditis, and in more pronounced cases the co-existence of pericardial or endocardial lesions will sometimes show its inflammatory origin (*chronic myocarditis, interstitial myocarditis*). On the other hand, fibrosis of the heart is often due to obstruc-

tion of the coronary arteries, and may be associated with fatty degeneration. In these circumstances the blood supply is insufficient for the nutrition of active muscle. The latter atrophies, and is replaced by fatty or fibrous tissue. If the coronary obstruction takes place fairly quickly, fatty degeneration occurs. If the obstruction is more chronic, fibroid change predominates. Fibrosis may also be secondary to coronary thrombosis or infarction. It is also commonly associated with chronic bronchitis, emphysema, Bright's disease, and arterio-sclerosis. Fibroid degeneration may be due to alcoholism or long-continued congestion.

Syphilis. The lesions of this disease occur as arteritis, as fibrous scars (*syphilitic myocarditis*), as fibroid masses, or as a distinct gumma, which may be cheesy, and even softening in the centre, affecting the muscular substance of the heart in the same way as the voluntary muscles and causing some surrounding inflammation. A gumma is seated usually in the walls of the ventricles. It produces no characteristic symptoms apart from those considered under the heading of Myocardial Degeneration. Sometimes the A.-V. bundle is affected, leading to Adams-Stokes' syndrome.

Tubercle. Tubercles not infrequently form in connection with inflammation of the pericardium, when they are found as whitish-grey or yellowish granulations, mostly in the substance of the pericardial lymph or false membrane uniting the layers of the cavity, or sometimes actually under the layer of the visceral pericardium. They occur in the course of general tuberculosis, and there may be secondary advanced tuberculosis elsewhere. The diagnosis can only be made from the appearance of pericarditis in those circumstances; but it must be remembered that a pericarditis, which is not tuberculous, may also arise in the course of phthisis. Isolated deposits of tubercle are exceedingly rare.

Symptoms of Myocardial Degeneration. In early cases the patient complains of breathlessness on exertion. There may be præcordial pain, which may be noticed after exercise, or there may be definite anginal attacks. The patients may suffer from cerebral attacks, with unconsciousness and convulsions, but these attacks are probably due to some abnormality of the cardiac mechanism, such as heart block, or vagal stimulation. Appetite is often poor, and the patient may complain of indigestion. Sometimes these are the only symptoms complained of, and on inquiry the history of shortness of breath on exertion points to the heart as the primary cause of the gastric symptoms.

The physical signs attributed to myocardial degeneration are feeble cardiac impulse with faintness of the first heart sound, which may become equal to or less than the intensity of the second sound over the aortic area. This diminution of intensity gives a tic-tac character to the sounds when examined with a stethoscope, and this is further emphasised by a relative shortening of the diastolic interval, so that the sounds become more evenly spaced. The heart is dilated.

The symptomatology of a group of cases showing myocardial changes has been very carefully studied (**12**). The cases are met with very commonly. The patients are elderly, and suffer from shortness of breath, coming on at first after exertion, but later on they are more or less permanently dyspnœic. In some cases there is Cheyne-Stokes breathing, and in some other cases there are sudden attacks of extreme breathlessness, which come on particularly at night-time, and which are described by the term *cardiac asthma;* these attacks of paroxysmal dyspnœa may often be the dyspnœic phase of a rather irregular Cheyne-Stokes breathing. There may or may not be orthopnœa present. Cyanosis is conspicuously absent, and if present at all its amount could hardly be considered enough to account for the dyspnœa. The rate of the heart is usually increased. The mechanism of the beat may be normal, but common irregularities such as those due to heart block, auricular fibrillations, extra-systoles, and alternation may be present. The heart is increased in size. Murmurs

may be present. The body temperature tends to be subnormal. The advanced signs of cardiac failure, such as anasarca, congestion of the lungs and liver, may be present. There is usually some retention of urea in the blood, but the values are not extreme—at most 0·1 per cent., and usually 0·05 per cent. (normal 0·03). Albuminuria with casts may be present and unless there are signs of venous stasis, the urine is increased in volume. Post-mortem examination shows that there is advanced coronary sclerosis of the heart, and there may be fatty degeneration. The kidneys show thickening of the vessels and some fibrosis, often of a patchy nature. The glomeruli are often congested, and some are hyaline, but there is no extensive obliteration of glomeruli, as occurs in chronic interstitial nephritis when the patient has died from uræmia. Sometimes these patients are described as cardio-renal cases, but it seems clear that although the kidneys always show some changes, and are termed senile arteriosclerotic kidneys, these are not the essential cause of the disease. The urea retention never reaches a fully uræmic figure of 0·2 or 0·3 per cent. Hence they are best described as cases of myocardial degeneration, giving rise to cardiac asthma or paroxysmal dyspnœa.

The CO_2 in the arterial blood is increased in the dyspnœic cases, and the oxygen content of the arterial blood may be low. Consequently, it has been suggested that the dyspnœa, which may be extreme, is brought about by bronchial spasm (**14**). On this view, the term *asthma* can be used for this type of case. However, in pure cardiac dyspnœa, *e.g.* mitral stenosis, and when there is Cheyne-Stokes breathing, the CO_2 is low from increased respiration (**41**), although in some cases it may be a little raised and the oxygen lowered from pulmonary congestion which hinders the free interchange of gases in the lungs. Recent experimental evidence points to the paroxysm being, at any rate in some cases, caused by acute pulmonary congestion and œdema from relative failure of the left ventricle (**13**). The **Treatment** is considered on p. 276.

RUPTURE OF THE HEART

Apart from injury, this is mostly a consequence of fatty degeneration or fibroid changes; these may be coronary thrombosis leading to hæmorrhage into the myocardium and destruction of part of the wall of the heart; in a very small proportion of cases, its cause is abscess, malignant endocarditis and aneurysm. It occurs in old people, and not infrequently follows muscular efforts. The left ventricle has been the seat of the rupture in three-fourths of the cases on record. The patient is suddenly seized with intense cardiac pain, followed quickly by pallor, unconsciousness, a few convulsive twitchings, and death. In rare cases life has lasted some hours, or even days, with pallor, cold sweats, feeble pulse, and sighing respiration.

ANEURYSM OF THE HEART

Aneurysms of the heart may be acute or chronic.

Acute aneurysms arise from ulcerative endocarditis of the ventricle wall, in the manner which will be described under Malignant Endocarditis, and this is a rather frequent cause of aneurysm of the *pars membranacea septi*, or undefended space, as well as of the valves. Aneurysms of the pars membranacea are sometimes congenital. In either case, the sac opens towards the left ventricle. The condition is not recognisable during life.

Chronic aneurysms of the heart commonly arise in connection with fibroid degeneration. The cavity affected is weakened at one spot by this conversion of its muscular fibre into fibrous tissue, and dilates under the pressure of the blood into a sac. The left ventricle is their usual seat, and only a few cases are on record of aneurysms of the other three cavities. In two cases out of three they occupy the apex; they form rounded sacs, of which the communication from the

is no invasion of the blood stream by the streptococcus, and by the time the acute rheumatism begins on the 16th day the streptococcus has disappeared from the throat, though in fatal cases of pericarditis it has been grown from the spleen and pericardial lymph glands (**50**). This sequence of events would be compatible with the view that the acute rheumatism was an allergic manifestation due to " sensitisation " during the original streptococcal attack ; but it might also be argued that the hæmolytic streptococcus was not itself the primary cause of the acute rheumatism, but facilitated the introduction of a secondary invader, for instance, an ultra-microscopic virus, which was the direct cause of the disease ; there is recent evidence of this.

Morbid Anatomy. The chief structural changes of rheumatic fever result from carditis, polyarthritis, chorea and subcutaneous nodules. The reaction, which consists in the formation of an inflammatory node, is essentially the same in all these cases, though the appearance depends on the locality affected. The reaction is most easily studied in the heart.

Acute Myocarditis. The first change occurs in an arteriole ; at one point the lining cells swell and multiply and become the centre of a brisk inflammation with round cell infiltration, chiefly polymorphs. The arteriole becomes sealed with clotting and destroyed. Later the round cell infiltration disappears, and we get eventually a group of large multinucleated cells embedded in a background of fibrin constituting the *Aschoff's node.* These cells are fibroblasts and are later converted into ordinary fibrous tissue, forming a permanent but inconspicuous scar. In the muscle fibre cells fatty granules and droplets appear first of all near the nucleus, and later there is localised necrosis which may be toxic in origin or due to cutting off the blood supply when the arteriole becomes destroyed. The nodes appear most commonly in the left ventricle, deeply embedded in the muscle, near the root of the aorta and the mitral ring.

Acute Endocarditis. In rheumatic endocarditis this " nodal " inflammation results in the formation of very slight swellings of subendocardial tissue near the edge of the valves on the auricular side of a mitral cusp, or the ventricular side of an aortic cusp, so as to form a number of beadlike elevations, usually described as *vegetations ;* and these occupy at first the line where the valve touches its fellow on closure, and not the free edge of the valve. Later the endothelium of the valves over the inflamed area becomes loosened, and fibrin and polymorphonuclear leucocytes are deposited from the ventricular blood. With subsidence of the inflammation slight scarring again takes place ; but in long continued inflammation or after repeated acute attacks gross deformity of the valves is produced, which is described in the section on chronic endocarditis. The appearances of pericarditis are also described later.

Arthritis. The joints have been found in fatal cases to contain a turbid synovia, with shreds of fibrin. Leucocytes are present, but the fluid is never purulent. The synovial membrane itself is vascular, and covered with a layer of lymph. Probably the synovial changes are even slighter than this when such rapid subsidence takes place as is often witnessed. In the tendon sheaths have been found opaque serum and greenish-yellow lymph.

The genesis of the subcutaneous rheumatic node, so characteristic of rheumatism, is exactly the same as that already described for the heart, but on a larger scale. It begins with focal arterial inflammation ; then there is multi-nucleated fibroblastic infiltration which evolves into a small scar in the course of a few weeks.

Symptoms. There is often a previous history of one or more attacks of tonsillitis ; and the tonsils are seen to be enlarged, or to contain deep crypts, or to exude pus on pressure, or adenoids may be present. The first symptoms of the rheumatism may be those of a multiple arthritis or synovitis, lesions which are obvious because painful and accompanied by pyrexia ; in other cases, and especially in children, the first lesion is inflammation of the cardiac valves, myocardium or pericardium (rheumatic carditis), which may be entirely latent

but may be associated with a history of vague pains, perhaps called growing pains, which have not confined the child to bed. Sometimes a child attacked by the articular form of rheumatism is found to have a cardiac lesion obviously of old date, not dependent upon the present synovitis, but without any history of a preceding synovitis, or there may have been a history of *chorea* (*see* later).

The *joints* may be affected quite suddenly. The knee is often first attacked, and then the ankle, in other cases the wrist or the shoulder. Whichever is first attacked, the disease may soon spread to other joints of the body, so that the shoulder, elbow, and wrist, the hip, knee, and ankle, may all be inflamed at the same time or successively. Occasionally in adults the joints of the fingers and toes or the sterno-clavicular joint, or even the vertebral joints, are affected. The extent of the disease is very variable. In one only two or three joints may be inflamed, in another a great number; and an important feature of rheumatic fever is the way in which some inflamed joints will quickly recover while others become involved; and these last will get well while fresh joints suffer, or those first affected become again inflamed.

A joint attacked by rheumatic fever is swollen, hot, tender to touch, and painful. The swelling is most manifest in the knee, where effusion can easily be recognised, in the ankle and in the wrist. The colour may be a bright pink; it rarely covers the whole swelling, and may be in patches. The tenderness is sometimes extreme, so that a slight shock on the bed, and any clumsy handling of the joint, will cause intense pain. It may persist after spontaneous pain has subsided. In the shoulder, hip, and elbow joints, pain and tenderness are the chief evidences of rheumatism, as slight swelling is not easily recognised, and redness is generally absent. On the whole the arthritis is more painful in adults than in children. It is common enough for the muscles of the limbs to be tender on palpation, due presumably to a myositis, which is similar in nature to the myocarditis; in fact, in a boy under the writer's care, there was intense muscular tenderness without any involvement of the joints at all.

In the vast majority of cases the synovitis clears up without leaving any sign of previous inflammation; but occasionally, especially if the same joint is repeatedly attacked, permanent alterations may be seen, with wasting of the muscles. These may be associated with rheumatic nodules, and resemble very closely acute rheumatoid arthritis. Histologically the lesions in rheumatoid arthritis are indistinguishable from those of acute rheumatism, so that it is possible that they may eventually prove to be different manifestations of the same disease. It has been stated that the synchondroses are also sometimes involved in rheumatic fever. Undoubtedly the sheaths of the tendons about certain joints are often inflamed, especially those about the wrists and ankles; and some of the redness that extends on to the dorsum of the foot and hand may be due to their inflammation. In a boy seen by the writer there were subperiosteal nodes round the mandible.

With this multiple arthritis there is associated some *pyrexia* which subsides as the inflammation of the joint subsides and recurs with any recurrence of the arthritis. There is sometimes hyperpyrexia. Profuse *sweating* is a characteristic of acute rheumatism. The sweat may often be seen in clear vesicles at the orifices of the sweat pores, called *sudamina;* when the vesicles contain a point of pus, and are surrounded by a pink areola, they are known as *miliaria*. The fever is not generally accompanied by much cerebral disturbance, and delirium is not a marked feature in uncomplicated rheumatic fever. The *tongue* is furred and the bowels are constipated. The *urine* is scanty, high-coloured, and acid; it contains only occasionally a trace of albumin.

Rheumatic Carditis. In a large proportion—between a third and a half—of the cases of rheumatic fever beginning with arthritis, the *heart* is found to be affected by endocarditis and myocarditis and less often by pericarditis. While the descriptions of the pericarditis is deferred till later, it must be pointed out

that such symptoms of carditis as are present are due to the myocarditis rather than to the endocarditis. They are usually quite slight, and sometimes absent altogether. The onset of carditis may be marked by an increase in the pyrexia. A persistent tachycardia is common. In severe cases there is shortness of breath and exhaustion after exercise, and these may be the earliest symptoms of the disease. Exceptionally pronounced heart failure shows itself within a few months of the rheumatic attack. The patient is often, but not always, anæmic.

The earliest physical sign is represented by a slight prolongation, or roughness, or some want of clearness of the first sound in the mitral area on auscultation. Within twenty-four hours it may lengthen into a distinct murmur, or soft blowing sound, which accompanies, and may later on entirely replace, the first sound. It indicates acute infection of the heart, and is certainly due to mitral regurgitation. There may be minute pin-point vegetations on the valves, but it is difficult to see why these should give rise to incompetence. The more probable explanation is, that, owing to myocarditis, there is dilatation of the mitral ring leading to incompetence. These murmurs may disappear as the patient gets better. The mitral regurgitation commonly leads to an accentuated pulmonary second sound. Acute heart block also occurs, and in some cases a reduplicated first or second sound or a prestolic murmur heard at the apex may be due to the auricles contracting perceptibly before the ventricles in this condition, but all these physical signs may also be due to the rush of blood through the mitral valve as described below. A less common murmur, also heard at the apex, in rheumatic fever in children is mid-diastolic in time. This is certainly not in all cases due to mitral stenosis, as post-mortem examination has on more than one occasion disclosed a healthy valve. It is probably due to "relative stenosis," *i.e.* a normal valve opening into a dilated ventricle, and so producing a fluid vein and eddies. It is similar to Flint's well-known murmur in aortic regurgitation. The presence of this murmur in children usually means a severe grade of infection, and it often leads on in later years to a fully developed mitral stenosis. If the aortic valve is affected, the second sound may become imperfect, and a diastolic murmur is developed, but this lesion is much less frequent than the others.

Pleurisy is sometimes seen when the heart is severely affected, and especially in association with pericarditis. A rub is heard, and there may be pain. When situated between the pericardial and visceral pleura, pleuro-pericardial friction may be present (*see* p. 127). There is not usually sufficient exudation to require tapping; but occasionally it may be extensive and give rise to physical signs at the left base, resembling the pressure of a pericardial effusion on the left lung—impairment of note, deficient vesicular murmur, or weak high-pitched bronchial breathing. *Acute pulmonary œdema* and *broncho-pneumonia* occur in children occasionally (Poynton). Acute nephritis not uncommonly occurs simultaneously.

Besides the sudamina and miliaria already mentioned, urticaria and different forms of erythema may occur, especially *E. multiforme* and also purpura (*peliosis rheumatica*). *E. nodosum* is also associated with rheumatism. It may be of streptococcal origin (*see* later), but is most commonly tuberculous.

Subcutaneous nodes are also more common in children than in adults, and are found in the neighbourhood of joints, and over bony ridges and prominences, where little fat intervenes between the skin and bone—for example, over the elbows and knees. They are not painful and seldom tender; they are freely movable under the skin, and slightly on the fibrous structures beneath them. They disappear in a a few weeks.

Course. If untreated, the symptoms in the joints may last from ten to fourteen days, when they will often subside; if treated by salicylates, the pains and fever are often gone within a week. In any case, however, rheumatism shows a great tendency to *relapse*, the joints being affected in a precisely similar manner after an apyrexial painless interval of from two days to a fortnight. Occasionally recovery is delayed by the persistence of the inflammation in one

joint for weeks or months ; pain, swelling, and stiffness are prominent troubles, and the joint has ultimately to be treated, with rest, splints, and local treatment. Another cause of delay in convalescence is the rapid progress of a carditis, so that the patient passes at once from rheumatism into pronounced heart disease, with murmurs of aortic or mitral disease and failing cardiac muscle and even pericarditis. Death takes place in the course of an attack from carditis, very rarely from hyperpyrexia.

Diagnosis. This usually presents no difficulty, the sudden occurrence of joint pains, with redness and swelling, fever and profuse sweating, being mostly decisive, especially if it occurs in young persons with previous good health, or, on the other hand, with a previous history of rheumatic fever or of heart disease. Where one joint alone is affected, *acute osteomyelitis* must be considered. Here the constitutional symptoms are more severe ; there is great tenderness, especially when pressure is exerted on the bone. *Acute pyæmia* with suppurative arthritis is uncommon, and there is usually some obvious focus of infection, such as a septic uterus after childbirth. The joints when attacked take a long time to clear up. *Gonococcal synovitis* is also more persistent than rheumatic fever, and is only rarely accompanied by cardiac complications, and the inflammation particularly tends to involve fasciæ ; but in early stages it may be readily mistaken for acute rheumatism. Acute multiple arthritis may also occur in many specific infections, *e.g. enteric fever, dysentery,* and *pneumococcal infections, relapsing fever,* etc. The reaction of the patient to salicylates is a valuable indication of acute rheumatism. The diagnosis from *gout* will be given with the description of that disease.

The diagnosis of rheumatism in a child who has not had a multiple arthritis depends on the recognition of sore throat or septic tonsils, and a cardiac lesion or chorea. The diagnosis of an acute endocarditis and myocarditis requires some care, as the murmurs of recent acute endocarditis and myocarditis may be confounded with the murmurs of old *valvular disease,* and with *pericardial* friction sounds. The chief point to note is that the murmur in question is generally soft in quality, systolic in time, and strictly limited to the mitral area. There may be tachycardia and an accentuated pulmonary second sound. A functional or hæmic murmur is generally loudest over the pulmonary artery, and often harsh in quality. The murmur of chronic valvular disease is often loud or harsh, heard over a large area, and accompanied by some alteration in the size or shape of the heart.

Prognosis. The immediate mortality of acute rheumatism is small. The possible dangers have been indicated above. The temperature and pulse rate and alteration in the murmurs give the best clinical indications as to whether the disease is still active. The sedimentation rate of the red cells provides valuable additional help. Using Westergren's method, if the cells fall more than 10 mm. in the first hour, or more than 20 in two hours, the disease is still active (**42**).

Prevention. A clay soil is usually regarded as predisposing to rheumatism, and low-lying situations in river valleys should be avoided. Children who are rheumatic should change their clothing if it becomes damp. The most important point is to treat all possible sources of infection ; in this connection the nose and sinuses and throat should be examined with care, especially in children, while in adults dental infection in particular should be looked for. A study has appeared on the subject of tonsillectomy carried out on eighty-five children with various rheumatic manifestations (**43**). In most cases the tonsils had been inflamed more than once, and in all cases the tonsillar lymph glands were enlarged. The cases were followed up over an average of three and a half years after tonsillectomy. The tonsillar lymph glands became impalpable in 59 per cent. of cases. Of patients who had had rheumatic fever, there was no recurrence in 84 per cent. As regards chorea, there was no recurrence in 50 per cent. of cases. As regards myositis and joint pains, there was no recurrence in 77 per cent. of cases. In a

few cases a second operation was necessary to remove the tonsils completely. On the other hand, in a series of 428 cases, including chorea, at Great Ormond Street, the beneficial result of tonsillectomy was very doubtful (**45**), and this agrees with other authorities (**47**). The following conclusions may be drawn: In rheumatic children complete removal of the tonsils by means of enucleation is desirable when the infection of the tonsils is impairing the child's health and there are repeated sore throats and chronic glandular enlargement; the operation should be carried out after an acute infection has subsided.

Treatment. For the efficient treatment of even mild cases of rheumatism complete rest in bed is absolutely necessary until all pain and swelling of the joints has disappeared and all active inflammation of the heart has subsided. It is difficult to be certain when this is actually the case, so that patients, particularly if they are children, may be kept in bed many weeks to be on the safe side. In any case the patient should not be allowed to get up till the pulse and temperature have fallen to normal and have remained so for some days. Another useful indication is the character of the murmurs. As long as these show any change from day to day it means that there is active inflammation present. Possible foci of infection should be looked for and dealt with (*see* p. 276). Tonsillectomy is dealt with above.

In severe cases the joints will be so painful that the patient cannot do otherwise than lie still. The joints should be protected from every risk of injury. Sometimes it is desirable to raise the bedclothes from the limbs by a cradle; and some local relief to the pain may be obtained by wrapping them round with cotton wool, upon which, in severe cases, a little anodyne, such as belladonna or opium liniment, may be sprinkled, or methyl salicylate (artificial oil of wintergreen) may be spread on the joint and covered with guttapercha tissue. In the past a strict milk diet has usually been prescribed, but on general principles it is much better to allow a more varied dietary, as in other febrile conditions.

The drug now almost universally employed is sodium salicylate. When the patient is fully under its influence the pains disappear, the redness and swelling of the joints subside, and the temperature falls two or three degrees—it may be to the normal. If the drug is then lessened or discontinued, the pains will most likely return; if the dose is maintained, the rheumatism may be practically cured from that time; but the treatment, both by drug and diet, will have to be continued for ten days or more, at the end of which time some relaxation may be cautiously allowed. An efficient dose of either salicylic acid or its sodium salt is 20 grains, and of salicin 30 grains, every four hours during the first twenty-four or thirty-six hours; but in less severe cases a smaller quantity may suffice. Some give a smaller dose every hour for the first four or five hours, and then diminish the frequency to every two hours. If the attack is very severe, it may be desirable to give a 20-grain dose every two or three hours for the first day. If too much is given, the patient suffers from headache, deafness, tinnitus aurium, and slight delirium, which cease when the drug is withdrawn. Occasionally vomiting, a slow or irregular pulse, albuminuria, epistaxis, hæmaturia, or suppression of urine with uræmia has occurred. As a rule, the earlier toxic symptoms coincide with the subsidence of the pains; but, this having been obtained, the frequency of the dose must be reduced to four times or three times a day, at which rate it should be continued until five or six days have elapsed from the last pain or the last abnormal temperature, when the drug may be stopped altogether.

There is no material difference in the effects upon rheumatism of the three drugs under consideration. The sodium salt is generally preferred, and it is frequently combined with an equal quantity of sodium bicarbonate. Sometimes these drugs are not so successful; the pains continue in abated form, or relapses frequently occur. Salicylate of quinine (2 to 6 grains) may then be useful; or recourse may be had to the old alkaline treatment—potassium bicarbonate or acetate, 20 grains every four hours—or to potassium bicarbonate with quinine. Compounds containing salicylic acid, such as salol, salophen, and acetyl sali-

cylic acid (aspirin), have some influence upon the pains of acute rheumatism. The last has been largely used in 10- or 15-grain doses in cachet.

It is not known at present how salicylates act. Many authorities believe that they have no specific action on the infection itself. It has, indeed, been suggested that there is a disadvantage in abolishing the pyrexia and the joint pains, because an indication of the progress of the infection in the heart is thereby lost, and a certain measure of pyrexia may be a useful defence against the infection.

The treatment of hyperpyrexia must be prompt and energetic, as dealt with under Heat Stroke.

CHOREA

(Sydenham's Chorea, Chorea Minor)

Chorea (χορεία, a dancing) is characterised by irregular involuntary movements of different parts of the body. The popular equivalent, St. Vitus's dance, has reference to the occurrence in the Middle Ages of epidemics of dancing mania, when patients were cured by a pilgrimage to the shrine of St. Vitus—Chorea Sancti Viti. But the complaint in those epidemics partook rather of the nature of hysteria, and though the name *chorea* is still sometimes used to indicate some other forms of abnormal movement, it is, as a rule, reserved for the disorder now to be described.

Ætiology. Chorea is one type of acute rheumatism, and so it has the same ætiology. It is mostly a disease of childhood: nearly half the cases occur between the ages of five and ten, and another third between ten and fifteen. It is more frequent in girls than in boys, in the proportion of two or three to one. Fright or mental shock or strain, such as work for school examinations, may be an aggravating cause of the disease. Among adult patients pregnancy is a common antecedent; some of them have had rheumatism, and others chorea in childhood.

Morbid Anatomy. The brain shows hyperæmia; but there are not enough changes to suggest that bacterial invasion is the cause of chorea. Lumbar puncture rarely discloses any increase in lymphocytes.

Pathology. The facts in favour of chorea being a rheumatic infection are—the frequent occurrence of endocarditis and its almost universal presence in the fatal cases; the association with rheumatic fever and its various manifestations during life.

It seems necessary to give up the view, previously held, that chorea was a bacterial invasion of the brain, except in a few of the worst cases (chorea insaniens), where a streptococcus has been cultivated. Recent work points to the disease as being due to a lowered content of ionic calcium in the body and especially in the cerebro-spinal fluid—below 5 mg. per cent.—and this rises to above 5 mg. when the child recovers (**51**). On this view chorea is closely related to tetany, and, just as in tetany, it is found that the excitability of the muscles to electrical stimulation is increased. Thus the minimum exciting current, enough to produce a visible twitch in the supinator longus, with the active electrode applied to the motor point of the muscle was below 2 milliamperes, the normal being above this figure (**52**).

Symptoms. The symptoms of chorea may be present alone or may be accompanied by any of the manifestations of acute rheumatism already described. The most prominent feature of the disease is the action of the muscles: they are in a condition of (1) involuntary movement, (2) ataxy or inco-ordination, and (3) slight degree of actual weakness or paresis. The patient is in a constant state of movement, whether lying, sitting, or standing; and the movements, which affect nearly all the muscles of the body, are jerky, irregular, and devoid of purpose. The fingers are opened and shut, the wrist suddenly extended or flexed, or the shoulder lifted. The facial muscles are twitched, the eyebrows suddenly elevated, the head or the eyes rotated to one side, and the chin elevated

or depressed. In the lower extremities the movements are often less; the toes are twitched, or one knee gives way. In the muscles of the trunk, one notices half-rotation of the body to one or other side, sudden retraction of the abdomen, or jerky action of the respiratory muscles.

The irregularity is more marked on voluntary movements. If the hands are stretched out in front, the child is quite unable to hold them steady; on protruding the tongue, it is put out with a jerk, and perhaps withdrawn suddenly, and the muscles of the jaws act capriciously at the same time; in walking the legs are thrown about, the body is jerked round, and the shoulders are lifted. In the same way it may be seen that the muscles relax with great readiness; after grasping an object, one or two fingers quickly yield, and soon the hand and arm will drop. The movements are increased when the patient is watched, or if she becomes excited; they cease during sleep.

The child's disposition is apt to be altered; she becomes fretful, irritable, capricious, or excited, while intellectually she has a weak memory and is unable to fix the attention.

Varieties. Sometimes the symptoms are very slight, and remain so for some time; the fingers are only twitched a little, irregular movements are scarcely noticed, but the child drops things that she attempts to carry. In some cases the movements are limited to the arm and leg of one side only (*hemichorea*). In others there is decided paralysis, with only slight choreic movements; the arm hangs by the side, and can with difficulty be raised; the fingers are twitched occasionally, and the grasp is extremely feeble (*paralytic chorea*); there may be a *choreic hemiplegia*. Rarely all four limbs are affected, the child lying quite helpless, while each limb drops like a log on being raised from the bed. Speechlessness, mental weakness, maniacal and melancholic conditions also occasionally occur, and are generally temporary.

Exceptionally the movements are very violent; standing or sitting is impossible, and the patient is confined to bed, where she throws herself about in the wildest contortions, striking the hands and arms against the sides or head of the bed, and rubbing the elbows, shoulders, buttocks, hips, knees and heels, so as to produce serious abrasions of the skin. Feeding becomes difficult or impossible, as everything placed to the mouth of the patient is jerked aside or spilt; and even if it gets into the mouth it may be rejected by the want of co-ordination for deglutition. These cases (*chorea gravis*) sometimes progress with great rapidity; the patient appears to be exhausted by the constant movement and the want of sufficient nutriment; rapid emaciation takes place, the face is flushed, the eyes sunken but bright, the lips and tongue dry, the pulse rapid, and ultimately death may occur, being preceded often by some rise of temperature and by cessation of the movements. In fact, the patient may lie for some hours before death perfectly tranquil, and give the impression that convalescence has begun. In some the mind is severely affected, and the patient becomes delirious, or even wildly maniacal. Such violent cases are much more frequent in persons between the ages of fifteen and twenty-five, and a large proportion are in pregnant females.

Duration. The duration of chorea is very variable. The majority of cases last from six weeks to three months; not infrequently slight twitching may occur for many weeks or months after the severer manifestations have subsided, and the symptoms may again after a time become aggravated. In the end most cases recover. The violent cases are usually of short duration; if death takes place, it is often within two or three weeks from the first symptom, or from the time when the movements become violent; if recovery ensues, the movements become quieter after a few weeks, though complete cure may be delayed some time. Chorea is very apt to recur even after its entire subsidence; second and third attacks are frequent. These may be of shorter duration than the primary attack, but are not different in other respects.

Sequelæ. The disease sometimes leaves behind it a liability to sudden

starts, which in the course of months subside. Epilepsy has also been observed, and after recovery a tic may remain.

Diagnosis. This rarely presents any difficulty. Movements closely resembling those of chorea may occur as a part of *hysteria;* they are generally more rhythmical, more localised, and may recover quickly. *Habit spasm* may be present in children, and is closely allied to the above; the movements are localised, voluntary in character, more under control and less constant than those of chorea. There are jerky movements in *Friedreich's ataxia;* but the gait is different, the history is a very long one, and other signs are present.

Prognosis. In children it is favourable, apart from the condition of the heart; in young adults it is much more uncertain.

Treatment. The treatment of acute rheumatism should be consulted. The child should be kept quiet in bed, and everything tending to worry or annoy should be kept from her. The diet should be plain, nutritious, and abundant. Calcium aspirin (7 to 10 grains), and chloretone (5 grains) three times a day are beneficial. Arsenic is usually given, but there is no evidence that it is of any value. In violent cases food may have to be given through a nasal tube. Favourable results have recently been obtained with parathormone injections, which raise the calcium in the cerebro-spinal fluid—5 minims night and morning for a child of ten, 3 minims for a child of three.

ENDOCARDITIS

Endocarditis, like so many other inflammatory processes, is always due to the action of micro-organisms or their toxins. As a rule the parts first affected are the valves of the left side of the heart: the lesion is often confined to them, and may completely subside, or if any traces are left they consist of structural damage to the valve, of which the later consequences are solely dependent on the mechanical failure of the valve. This is a simple *acute endocarditis,* while the term *chronic endocarditis* is applied to the permanent deformities and changes in the valves which result from a simple acute endocarditis and may be made worse by later acute attacks; but the term is also used for an inflammatory process, which is chronic from the beginning. In other cases, more extensive changes take place in the valves, micro-organisms are present and may be conveyed by the current of blood to remote parts of the body, and so set up fresh foci of disease—*malignant endocarditis.*

ACUTE ENDOCARDITIS

Ætiology. Acute endocarditis is, in the great majority of cases, an infection due to the virus of acute rheumatism, which has just been dealt with. Myocarditis is usually associated with it. Acute endocarditis also occurs in scarlet fever, diphtheria, typhoid, and other infectious diseases. It may occasionally occur during the progress of Bright's disease, syphilis and other chronic maladies. It may occur after local injuries, such as the rupture of a sigmoid valve, or of the chordæ tendineæ, and as the result of unnatural friction of one part of the heart with another. The passage of currents of blood through abnormal apertures may cause the local inflammation of the endocardium. In patients dying from any infective disease it is very common to see minute vegetations on the valves, particularly the aortic valves, indicating a terminal infection of the blood stream.

No separate account of acute endocarditis is necessary, as it has been dealt with under acute rheumatism and other infective diseases.

CHRONIC ENDOCARDITIS

(Chronic Valvular Disease of the Heart)

Relative Frequency of Valvular Lesions. The relation of endocarditis to the two sides of the heart is of very great importance. If endocarditis occurs

during fœtal life, it is believed to attack the pulmonary or tricuspid valves ; but it is extremely rare for endocarditis acquired during life to attack the valves on the right side of the heart *only*. It occurred only once in 20,000 post-mortem examinations at Guy's Hospital. On the other hand, right-sided endocarditis associated with left-sided endocarditis is not so very uncommon (**18**). The commonest occurrence is for the valves on the *left* side to be affected alone. Disease of the mitral valve is more common than that of the aortic valve, since rheumatic fever, which pre-eminently attacks the mitral valve, is the commonest antecedent of valvular disease. Regurgitation by itself, as shown by an apical systolic murmur, is the most frequent event at the mitral orifice, though there is doubt as to whether the regurgitation is due to disease of the valve or a dilated mitral ring. A combination of obstruction and regurgitation comes next in frequency, and pure obstruction is least frequent. However, the majority of cases of mitral disease of whatever kind coming to autopsy are found to have stenosis. This is due to the fact that stenosis is the natural result of prolonged inflammation of the mitral valve. At the aortic orifice, regurgitation is very much commoner than obstruction. In rheumatic cases aortic disease is commonly associated with mitral disease. A higher proportion of the cases following scarlet fever have aortic disease than of those that follow acute rheumatism. Pure aortic disease is due to syphilis, and not commonly to acute rheumatism. On the right side of the heart the tricuspid regurgitation that is quite commonly met with is due to dilatation of the muscular ring secondary to left-sided failure, and so is not really a valvular lesion at all.

Compensatory dilatation and hypertrophy affect primarily the particular chamber of the heart with which the affected valves are in relation. However, when failure of compensation occurs the other chambers of the heart become involved. For instance, if the left ventricle dilates, the muscular ring from which the mitral valve is suspended shares in the dilatation. This causes mitral regurgitation. This leads to engorgement of the left auricle and of the lungs with rise of the pulmonary blood pressure. To overcome this resistance the right ventricle hypertrophies. If dilatation of this chamber occurs, it leads to tricuspid regurgitation with engorgement of the abdominal viscera. Valvular disease is often associated with fatty and fibroid degeneration of the myocardium. This degeneration may be due to the same cause as produced the original valvular disease, *e.g.* rheumatic fever, syphilis, etc., or it may be the direct result of lack of nutrition of the heart muscle. There is a tendency at the present day to consider the state of the myocardium as the all-important factor in determining the onset of cardiac failure in valvular disease, and it is probably correct that although valvular disease unaccompanied by myocardial changes may cause symptoms of breathlessness and exhaustion after exercise, indicating relative failure of compensation, complete failure of compensation will be hardly likely to occur if the condition of the myocardium is sound. At the same time the heart should be regarded as a whole. It is really impossible to separate the effect of valvular disease from that of myocardial changes, if both are present together.

AORTIC DISEASE

There are two main causes of aortic valve disease. In the first place, there is acute rheumatism. Here disease of the aortic valves was in 62 per cent. of cases associated with disease of the mitral valves ; in 38 per cent. the aortic valves were affected alone. In the second place, there is syphilis. This disease usually produces primarily an aortitis, and the aortic valves become involved in the same process, while the mitral valves are usually not affected. In a series of 296 cases of aortic disease acute rheumatism was responsible for 67·5 per cent., with men and women in about equal proportion. Syphilis (three men to one woman) for 18·6, atheroma (nearly all elderly men) for 6·8, other causes for 7·1 per cent.

Morbid Anatomy. The changes in the aortic valves consist in thickening

towards the base of the cusps with fibrous tissue, and to a less extent of the free edge, with shortening of the radial measurements, so that the cusps cannot meet to cover the orifice. See also Hypertrophy of the Heart.

Since the three cusps are discrete, chronic inflammation usually causes them to shrink independently of one another, so that there is aortic regurgitation with thickening of the endocardium owing to friction by the regurgitant stream. There may be some thickening at the three points on the wall of the aorta where the valve segments meet, and they are commonly slightly adherent at these points, but not enough to cause stenosis of the opening. It is rather uncommon for the valves to be so fused together or thickened from calcified or bony deposits so as to present an obstruction to the flow of blood—a great contrast to the case of the mitral valve. But, when there is stenosis, there is also usually some regurgitation as well. Exceptionally the fusion is so complete as to allow only a small opening for the passage of blood into the aorta, and yet the valve closes well. The lesions may be aggravated by frequent and continued strains upon the circulation, especially from the excessive use of the arms, such as arises in blacksmiths, sawyers, and others with laborious occupations. Sudden rupture of a valve also sometimes takes place, when it has been softened by inflammation.

AORTIC STENOSIS

Pathology. In Cohnheim's classical experiments on animals a ligature was passed round the aorta and gradually tightened. The lesion was compensated for by the greater power of the muscular contractions of the ventricle, *i.e.* the output of the heart per minute, and the arterial and venous pressures remained the same, but the intra-ventricular pressure was much increased, the heart rate was slowed, while the actual duration of the contraction of the ventricle was increased in the endeavour of the heart to force its content of blood into the aorta against this artificially increased resistance. It was only when the constriction reached a certain limit that the heart suddenly failed.

Exactly the same conditions are present in aortic stenosis caused by disease, except that here, since the lesion has been produced gradually, the heart has had time to adapt itself. The increased work that falls on the heart causes a primary hypertrophy of the left ventricle. With a stationary lesion this is sufficient by itself to empty the ventricle completely through the narrow opening at each systole. Only when compensation begins to fail is there a dilatation of the ventricle, which spreads to the other chambers of the heart.

Symptoms. In pure *aortic stenosis*, which is an exceptional condition for reasons already explained, the murmur is systolic, audible in the second right intercostal space near the sternum, traceable up towards the right clavicle, and audible in the carotid arteries, and it is usually accompanied by a rough systolic thrill felt at the same spot. The pulse is often characteristic; the obstacle interposed in the current of blood prevents the full effect of the ventricular contraction upon the column of blood in the systemic arteries, and the pulse can be felt to have lost its suddenness and to rise quite slowly. The pulse tracing is then *anacrotic*, that is, the percussion wave is lower than the succeeding tidal wave, and appears as an elevation on the ascending limb. In the extreme variety of this form this wave is rounded off, or entirely absent, and the tracing resembles that shown in Fig. 41, A (p 308). The pulse is infrequent and sluggish when palpated (*pulsus tardus*). When the aortic stenosis is fully compensated the patient may have no symptoms. In other cases pain in the chest and a feeling of oppression may be noticed. When compensation begins to fail, shortness of breath and signs of venous congestion will be observed.

AORTIC REGURGITATION

Pathology. If one of the aortic valves is experimentally damaged in an animal, compensation takes place at once, just as in aortic stenosis. The output

is regurgitation. But there is also shortening of the valve circumferentially, leading to stenosis, and the longer the inflammation lasts the greater the stenosis. These two types of shortening often co-exist, producing a double lesion. Slight inflammation will not cause enough circumferential shortening to cause clinical stenosis, though there may be regurgitation. Severe inflammation may lead to regurgitation alone, stenosis alone, or more commonly to the two combined. The presence of stenosis always means a severe infection of the valve. Post-mortem examination also shows that in mitral disease the cordæ tendineæ are thickened and shortened—so shortened, indeed, that the valve curtain is continuous with the musculi papillares, and these themselves are invaded by the fibrotic change. In some cases of stenosis there is circumferential shortening without much shortening from above downwards ; in other cases both types of shortening exist, so that only a narrow slit presents itself on the auricular side in the dense surface of the valve. A distinction is thus drawn between *funnel-shaped* and *buttonhole* orifices ; and the former appears to be very much more frequent in children (8 to 1, Allbutt), the latter in adults (25 to 1).

Mitral stenosis is to be regarded as the final result of chronic infection or of repeated attacks of acute infection on the valve, which lead to adhesion and shrinking and thickening of the cusps. It requires some years for its development. This explains the fact that it is not often met with in children, though it is met with from puberty onwards. Mitral regurgitation, on the other hand, is a less severe form of valvular inflammation, also due to rheumatism.

Symptoms and Physical Signs. There are certain general symptoms and signs, largely due to venous congestion, which are common to both mitral regurgitation and stenosis, and these will be considered here. The early symptoms are noticed particularly after exercise. They are shortness of breath and a feeling of exhaustion ; to these may be added pain over the heart, palpitation and swelling of the feet ; and this earlier stage may last for several years. The transition to a later stage is often coincident with the occurrence of one of the previously described forms of irregularity of the heart's action, such as premature beats, and especially auricular fibrillation, when the pulse which was previously regular, though rather frequent, becomes grossly irregular both in rhythm and force. When the later stage is reached, the symptoms are in great part the result of the circulatory disturbances, and of the *retardation* of the blood flow, the effects of which upon the organs of the body have been described (*see* p. 252). Thus, as a result of the passive congestion of the lungs the patient suffers from cough, from mucous expectoration, from occasional hæmoptysis, which may arise from the pulmonary infarcts above described, from orthopnœa at night or continually, and from dyspnœa on the slightest exertion. On examination the right auricle will be found to be dilated, with impairment of note and pulsation for an inch or more to the right of the sternum ; the second sound in the pulmonary area will be accentuated, while epigastric pulsation will indicate hypertrophy of the right ventricle. Crepitations will be heard at the bases of the lungs, and in advanced cases there will be dulness, with deficient vesicular murmur, and deficient tactile vibration. General venous stagnation is shown by a rich red colour or actual cyanosis of the lips, cheeks, ears, and extremities, by the filling and pulsation of the large veins in the neck, and by the occurrence of anasarca. The congested liver is large and smooth, reaching perhaps to the level of the umbilicus, and it is tender if the congestion has been acute, and it may pulsate ; the skin is slightly jaundiced, the yellow tinge of the forehead combining with the deep red of the lips and cheeks to give a very characteristic appearance to the sufferer. There will be dyspeptic symptoms. The secretion of the kidneys is also affected, the urine being scanty, reduced perhaps to 10 or 15 ounces daily, high-coloured, depositing large amounts of urates and containing albumin and fibrinous casts ; the quantity of albumin is generally small, and varies inversely as the efficiency of the heart. Drowsiness or restlessness, and in advanced cases occasionally delirium, show the

effect upon the circulation of the brain. Death takes place ultimately from cardiac failure, from œdema of the lungs and exhaustion, or from malignant endocarditis, or other complication (*see* also p. 275).

MITRAL REGURGITATION

Pathology. Since at each systole blood passes back into the left auricle, compensation for this lesion consists in a primary dilatation of the left ventricle and left auricle for the following reason. During systole the auricle receives blood that has leaked back through the mitral valve, but it also receives its normal quota from the lungs, so that it must dilate. All this blood passes into the ventricle, which must also dilate to receive it. The extra work involved in filling up the auricle and ventricle falls to a large extent on the right ventricle, which, in consequence, undergoes secondary hypertrophy, so as to hold more blood, and enable the full quota to be delivered to the aorta at each beat. Hypertrophy of the left ventricle will not be so obvious as in aortic regurgitation, because no work will be done in respect of the blood that regurgitates through into the auricle, since in the latter the pressure is low.

Physical Signs. These are displacement of the impulse outwards, the blowing systolic murmur heard loudest at the apex, which has already been described.

MITRAL STENOSIS

Pathology. In pure mitral stenosis, the primary effect on the heart is hypertrophy of the left auricle, but later on this leads to dilatation as well, especially when there is incipient heart failure. The right ventricle hypertrophies so as to cause a rise of blood pressure in the pulmonary system which acts against the resistance of the narrowed valve. As compensation begins to fail, not only is there congestion in the lungs, but the left ventricle receives less than the normal quantity of blood. The cavity becomes smaller, and the ventricle wall may actually atrophy to some extent, and the aorta become narrower than usual in long-standing cases. Most cases of mitral stenosis are associated with some degree of mitral regurgitation.

Physical Signs. The murmurs of mitral stenosis and their mode of production have been described (*see* p. 221). They are often localised to the apex and are commonly accompanied by a thrill (*see* p. 217). The variation of the murmurs may be summed up as follows: When the heart is beating slowly and the stenosis is slight, an auriculo-systolic murmur is heard due to the hypertrophied auricle. If fibrillation supervenes, the murmur disappears entirely. If the action is slow, but the stenosis greater, murmurs are heard all through diastole; they consist of mid-diastolic and auriculo-systolic murmurs. Sometimes the mid-diastolic and auriculo-systolic murmurs alternate frequently in the same case; either may be replaced by what is apparently a reduplicated second sound audible at the apex (*see* p. 218). In the case of auricular fibrillation, the murmurs occupy the earlier parts of diastole when the pause between the beats is long, or occupy the full diastolic interval when the latter is short. When the heart's action is quick both with normal rhythm and in auricular fibrillation, the murmurs tend to occupy the whole diastolic interval, but it is often very difficult to hear them at all. There may only be an accentuated first sound, and the second sound may be inaudible at the apex.

In early stages the heart is not enlarged; but in later stages general cardiac enlargement takes place when either tricuspid or mitral regurgitation supervenes.

Symptoms. Mitral stenosis often gives rise to hæmoptysis quite early owing to congestion of the lungs, and also to attacks of giddiness and faintness due to cerebral anæmia, and is more often than mitral regurgitation the cause of hemiplegia from embolism of the cerebral arteries. This arises from thrombi in the

left auricle, which are formed owing to the stagnation of blood in the later stages of the disease. The other general symptoms have been described.

RIGHT-SIDED VALVULAR DISEASE

Tricuspid Regurgitation. Though tricuspid incompetence is a very common condition, it is usually due to the dilatation of the right ventricle, which is associated with mitral disease, pulmonary stenosis, myocardial disease, or with other conditions causing obstruction in the lungs (emphysema, bronchitis, asthma, fibroid phthisis). Much more rarely is it due to organic disease, similar to that which attacks the mitral valve. It is commonly accompanied by the evidence of dilatation of the right auricle, and by the various degrees of œdema, anasarca, and venous congestion which indicate a difficulty in the return of blood to the right heart and lungs. These have already been enumerated under the later symptoms of mitral disease. The murmur of tricuspid regurgitation has been already described (*see* p. 222) ; it is sometimes accompanied by a systolic thrill over the lower end of the sternum. The pulsation of the internal jugular vein, which occurs in these circumstances, may be very pronounced, causing an extensive undulating movement of elevation and subsidence at the side of the neck between the ear and the clavicle posterior to the course of the carotid artery. The external jugular vein may pulsate at the same time. The force of the right ventricular contraction may also be transmitted to the hepatic veins, so as to cause *hepatic venous pulse*, or *pulsating liver.* The organ is commonly much enlarged, and can be felt throbbing over its whole surface ; and the pulsation is sometimes even conveyed behind into the right loin under the last rib, so that the liver can be felt to expand between the hands placed in front and behind.

Tricuspid stenosis is less common, and is generally observed in conjunction with disease of some other valve, especially mitral stenosis. No special group of symptoms can be referred to it apart from those seen in tricuspid regurgitation.

Disease of the pulmonary valves is mostly congenital if of old standing, and if acute it is the result of malignant endocarditis. *Pulmonary stenosis* combined with deficiency of the intra-ventricular septum is the usual condition in the former case, and is described later. (*See* Congenital Malformations.)

Pulmonary regurgitation sometimes occurs as a result of mitral stenosis, the valves yielding before the great pressure in the pulmonary artery ; a diastolic murmur is heard along the left side of the sternum.

Malignant endocarditis may cause a double (systolic and diastolic) murmur at the pulmonary orifice like that of aortic disease, the respective murmurs having the positions previously noted. The symptoms under such conditions have already been detailed (*see* Malignant Endocarditis).

DIAGNOSIS, PROGNOSIS, AND PREVENTION OF CHRONIC VALVULAR DISEASE

Diagnosis. In the diagnosis of valvular heart disease many questions have to be considered. It has to be determined (1) whether a murmur is due to a valvular lesion or to some other cause, endocardial or exocardial, the former including change in the muscular walls ; (2) at which orifice it arises, and if there are two, whether one is dependent on the other ; and (3) what is the functional capacity of the heart, *i.e.* its response to exercise and the condition of the several cavities of the heart. Very important information as to the heart's position, action, and valvular working can be got by the eye and the hand ; and these should always be used in conjunction with the stethoscope. The Röntgen rays will also assist in the estimation of changes in the size and shape of the heart's cavities (*see* Fig. 12, p. 225).

1. The murmurs of valve disease are apt to be confounded with those due to

other conditions. *Anæmia* produces a harsh systolic murmur over the pulmonary area. Seeing the rarity of organic pulmonary disease, this is mostly distinctive enough, but with very considerable anæmia murmurs extend over the whole præcordial area, arising, no doubt, at other orifices besides the pulmonary. As in such cases the patients are short of breath, with a tendency to palpitation and to swelling of the feet, the diagnosis may be difficult. The marked pallor of the anæmic cases, the absence of history of rheumatism or other precursor of heart disease, and the diminution of the murmur under the use of iron tonics, are points which will help. But anæmia may also undoubtedly itself be a cause of mitral regurgitation; the deficient quality of the blood causes malnutrition of the wall of the ventricle; this dilates, the mitral orifice yields, and regurgitation is the result. This is, indeed, an actual lesion, and the murmur is immediately due to structural changes in the orifice, if not in the valve itself; but inasmuch as they are primarily due to a condition of the blood which, together with its results, is curable, this murmur is often spoken of as *functional* or as *hæmic*. The diagnosis must, at any rate, be made between this and chronic valvular disease, and it can generally be effected by a consideration of the preceding and associated circumstances—viz. the absence of rheumatism and the decided anæmia.

Aneurysm of the aorta frequently gives rise to a murmur at the base of the heart which may be mistaken for that of aortic obstruction. Indeed, a simple systolic murmur in the aortic area, unaccompanied by regurgitant murmurs, is much more often due to aneurysm than to stenosis of the valves. Abnormal pulsation to the right of the sternum and increased area of dulness should be sought for as further evidence. If the murmur is localised at a point not strictly corresponding to the known areas of valve disease, aneurysm is still more probable.

Pericarditis often gives rise to a to-and-fro sound, very like the murmur of double aortic disease. It is, however, usually rougher, less uniform in loudness over a large area, not strictly localised to the usual area of aortic disease, and perhaps here and there not strictly synchronous with the two periods of the heart's beat. A short history of acute illness, unusual pain, or distress at the heart, increased area of præcordial dulness in an upward direction, and absence of splashing pulse, point to pericarditis.

Another difficulty arises from *exocardial* murmurs, which are sounds synchronous with the heart's action, but produced outside the heart. But the recognition that a murmur is endocardial and produced at a valvular orifice does not carry with it the diagnosis of disease of the valve. Ventricular dilatation not only from anæmia, but from any cause whatever, may lead to an apex systolic murmur; and such an occurrence is most common in Bright's disease, in alcoholism, and in arteriosclerosis, and acutely in the myocardial disorders of infectious disease.

Chronic renal disease may bring about hypertrophy of the heart, and even dilatation and murmur; and the case will then closely resemble one of mitral disease with secondary albuminuria. The difficulty is increased by the fact that the kidneys in a state of chronic congestion from heart disease may become granular; and that a heart dilated, as a result of extreme arterial tension in renal disease, will cause secondary stagnation in the venous system, like one affected with primary mitral disease. In primary heart disease one must look for the history of rheumatism or other cause of endocarditis. The urine has the characters described (*see* p. 271), and the pulse is small and of low tension. But in renal disease the urine is more likely to be pale, though also scanty, and to have a more uniform quantity of albumin; and the pulse is one of high tension. In enlargements due to arteriosclerosis and to alcohol, conditions which are often combined, the arterial tension is variable, and albumin is often absent; the diagnosis may have to depend on the history or associated conditions.

Conversely a valvular lesion is sometimes present when no murmur can be heard ; this is most frequently the case in the later stages of mitral constriction, when the strength of the auricle is failing.

2. The diagnosis of the different forms of valvular disease one from another depends for the most part on the character of the murmurs, and the extent to which they are audible over the præcordial area. A murmur may be conveyed beyond the area of one valve into the area of another, when it will be necessary to compare carefully the intensity of the sound at different points. Aortic regurgitation and mitral regurgitation are nearly always indicated by their characteristic murmurs. Mitral obstruction frequently exists without its characteristic murmur, as above stated. Pre-systolic murmurs and diastolic murmurs, when heard at the exact impulse (and not heard at the base), are very strong evidence of mitral obstruction. But murmurs identical with these are sometimes heard at the apex in association with aortic regurgitation—Flint's murmurs (*see* p. 269)—with adherent pericardium, and with a dilated ventricle under other conditions. The explanations of these anomalies are various : vibrations of the anterior mitral cusp from impaction upon it of the aortic regurgitant current, or from its being driven in upon the auriculo-ventricular current ; mingling of the above two currents ; the formation of a " fluid vein " in consequence of the dilatation of the left ventricle, while the mitral orifice is of normal size, a condition sometimes called relative stenosis. The last is the more likely explanation.

3. The estimation of the heart's response to exercise is perhaps the most important point in diagnosis. The amount of breathlessness or exhaustion after exercise is observed (*see* p. 223). The size of the heart provides a useful guide as to the extent of the valvular defect. This may be determined by palpation and percussion. X-rays may be used, and also the electro-cardiograph to indicate the proportion of right- and left-sided hypertrophy (*see* p. 249).

No diagnosis can be made without an examination of the heart and lungs ; but it is interesting to note that there is often in children and young people a superficial resemblance between mitral disease and phthisis, since the former may produce marked pallor, emaciation, and hæmoptysis.

Prognosis. A study of 1,000 cases of heart disease in ex-service men reviewed after ten years (**20**) showed that the most important elements for a bad prognosis are a poor exercise tolerance and a large heart. Thus with moderate enlargement and poor tolerance about half the cases die within ten years, a few survive unchanged ; while with great enlargement 76 per cent. and congestive failure 97 per cent. die within ten years, 80 per cent. being the rate of survival of these two grouped together.

Of the whole series, 22 per cent. have lived uneventfully and unchanged through the ten years, and this figure is probably on the low side. Half the cases have died, mostly of congestive failure, and this failure was associated with infective endocarditis in 26 per cent. of failure cases and with auricular fibrillation (30 per cent.), while bronchitis and other infections were also noted. Sudden death accounted for 17 per cent. of all the deaths.

When the cases are grouped according to auscultatory signs, 35 per cent. of those without obvious valvular disease die within ten years ; the death rate of aortic stenosis and syphilitic aortic regurgitation is 60 per cent. (or 58 per cent. excluding aneurysm) ; the death rate of uncomplicated non-syphilitic aortic regurgitation is 33 per cent., of combined regurgitation and mitral stenosis 30 per cent., of mitral stenosis 37 per cent. (excluding fibrillation 29 per cent.) ; with early mitral stenosis the death rate is 10 per cent., with developed stenosis 39 per cent., with slight aortic regurgitation 16 per cent., with free regurgitation 45 per cent. Hence the nature of the valvular lesion is less important than modifying factors. There are two factors, dealt with elsewhere, which are of special importance in prognosis—auricular fibrillation and subacute bacterial endocarditis, *q.v.*

Although this series of cases excludes children and women, it is of special value because it comprises, so to speak, a whole section through a diseased population—ambulant as well as bedridden ; in the last edition it was necessary to be content with an analysis of patients who had died in hospital ; this is now replaced by more complete statistics. Some points may be specially emphasised—the unimportance of a mitral systolic murmur. In the case of soliders invalided with the effort syndrome the presence of a mitral regurgitant murmur was of no value as an indication whether the man would be able to return to full duty or not. Mitral stenosis is a serious lesion, as it is the end result of chronic or repeated acute attacks of rheumatic mitral disease. In slight cases, however, it may remain stationary for years if the infection is arrested. The combination of aortic regurgitation and mitral stenosis does not make the prognosis worse. Repeated attacks of acute rheumatism in childhood or other infections are dangerous, because they may lead to further damage to the myocardium or valves ; the liability to mitral stenosis, and of elderly patients to auricular fibrillation ; the fact that the *immediate* prognosis in congestive failure is improved if there is fibrillation, but the ultimate prognosis is worse ; the liability to sudden death of the aortic group and to bacterial endocarditis in non-syphilitic aortic regurgitation ; the added seriousness of pregnancy.

Prevention. Since most of the cases of heart disease in young children are due to acute rheumatism, prevention consists in counteracting this disease, as already described.

In older subjects the teeth should be examined, particularly in people who already have chronic valvular disease, as any infection they may pick up may lead to infective endocarditis. Pyorrhœa alveolaris, when there is a free discharge of pus, is not so dangerous, but care should be taken to exclude abscesses hidden away at the roots of the teeth, from which the pus is not discharged, and which may lead either to an acute attack of endocarditis, or to a chronic smouldering infection with progressive deformity of the valves.

Another very important point in prevention is to ensure that the child who has suffered from the mildest rheumatic manifestations is put to bed whenever there is any indication of acute infection, such as a sore throat, tonsillitis, or a common cold, because there is always the chance that the heart may be simultaneously affected. In fact, it is the greater care taken about children of the better classes in this respect that probably ensures their relative freedom from severe heart disease compared with children of the working classes.

Of the specific infections syphilis is the commonest cause of heart disease, and early intensive anti-syphilitic treatment should be carried out, if the disease is contracted.

Arterial disease leads commonly to myocardial degeneration, and the appropriate prophylaxis (*q.v.*) should be undertaken.

TREATMENT OF CHRONIC CARDIAC DISEASE

The following remarks apply not only to chronic valvular disease of the heart, but also to cases of adherent pericardium and myocardial degeneration.

Before considering treatment it is necessary to find out (1) whether there are early signs of cardiac failure—distress, breathlessness and substernal or præcordial pain after exercise ; (2) whether the later signs are present—engorgement of the veins in the neck and of the liver, cyanosis, and œdema ; (3) whether the heart is enlarged, and whether there are signs of valvular disease or myocardial changes ; (4) whether there is any cardiac irregularity, particularly auricular fibrillation ; (5) whether there is evidence of active infection in the heart (Lewis).

The principles of treatment consist in ordering the life of the patient, so that the work the heart is called upon to do is well within its capacity.

In early cases of cardiac failure the patient's symptoms are the main guide. It is necessary to find out the amount of work that causes the onset of undue

fatigue, or distress, or breathlessness, or of cardiac pain. In the perfectly healthy individual these symptoms are only experienced after the most severe muscular exercise. Recent experience has taught that there are many individuals with systolic murmurs audible over the præcordium who have no history of rheumatic or other infection, and show no enlargement of the heart, who can take the most severe muscular exercise with no more distress than the normal person experiences. Such persons need not be restricted in regard to the exercise they take. When, however, there is reason to suspect aortic regurgitation or mitral stenosis, it is wise not to allow the patient to call forth his whole cardiac reserve, even if violent exercise can be undertaken with no more than the normal amount of distress. Only the milder forms of exercise should be permitted. The same thing applies to cases of mitral regurgitation and aortic stenosis when there is definite cardiac enlargement.

In patients who exhibit symptoms after moderate exercise, such as running or walking upstairs or uphill quickly, or walking quickly along the level, the exercise causing the symptoms should be forbidden. At the same time such exercise as can be tolerated should be allowed. It is bad practice to under-exercise his heart. However, the patient should be told to remain quite still supposing the symptoms come on while out for exercise.

Rest in bed is indicated in all cases where actual infection is present, in all cases of advanced cardiac failure, in cases showing signs of venous congestion, in cases of auricular fibrillation where the heart is rapid, and it is required to administer a full course of digitalis, and, most important of all, in patients who show signs of distress when standing or walking leisurely. The patient should lie recumbent, unless there is orthopnœa, when he should be propped up in bed. Complete quiet and freedom from anxiety and excitement should be enjoyed. All unnecessary movement should be forbidden, and, in particular, sleep should be encouraged, as this is the condition that gives the heart its most complete form of rest. This is one of the most important points to be attended to in the treatment of any cardiac patient, whether some exercise is allowed or not. Nine to ten hours in bed should be aimed at, even though the number of hours of actual sleep is less than this. Whisky, 1—2 ozs., may be given as a soporific, or paraldehyde in doses of 1—2 drachms. The diet should be sufficient, simple, and readily digestible; it may be mixed solid and liquid, in quantity at any one time not to overload the stomach, and of a nature not to cause flatulence or distension. Fluids should not be given in excess and salt intake should be cut down if there is œdema. In obesity a low calorie should be given, since obesity is a common cause of raised metabolism. Heart disease has also recently been treated by thyroidectomy in order to lower the metabolism and diminish strain on the heart.

When a patient has obtained relief after rest in bed for some time, exercise should only be begun gradually. Graduated exercises may be given by allowing him to move his arms and legs while still in bed. Another plan, when the patient is up, is to increase the amount of walking from day to day until his exercise tolerance is reached.

In cases of advanced cardiac failure with congestion of various organs and œdema, there are three main lines for treatment: (1) Removal of œdema fluid or bleeding; (2) administration of oxygen; (3) of drugs, especially digitalis.

(1) If much fluid is present in the pleural cavity, its removal by tapping will bring great relief. If there is much anasarca, the legs may be punctured in ten or twenty places with a large flat surgical needle, or drained by Southey's tubes. The patient should sit upright in a chair for twelve or twenty-four hours with the legs down, so as to allow the fluid to gravitate into them. They must be cleaned scrupulously and painted over with a weak solution of iodine. The fluid is allowed to run down into a bath, which should be surrounded with a blanket for warmth, but the blanket must not touch the legs where they have been

punctured. In ascites the abdomen may be tapped, and by these proceedings the pressure on the circulation is diminished. The indications for *venesection* are severe orthopnœa, and cyanosis with distended veins. This means that there is a fall of general arterial blood pressure and a corresponding rise in venous pressure, so that the right side of the heart has become so engorged that it has difficulty in contracting upon its contents. In such circumstances, auricular fibrillation is often present; the withdrawal of blood to the extent of 20 or 30 ounces by a cut into the median basilic vein relieves the distress by diminishing the blood flow to the heart. A still more rapid effect may be obtained in extreme cases by opening the external jugular vein at the bottom of the neck. In this case the blood will flow from the central end if the venous pressure is high, and the right side of the heart will receive direct relief. It is not always easy to obtain enough blood by a simple cut into the vein. A more effective method is to use a short wide hollow needle connected to a closed bottle by means of rubber tubing. Suction can then be applied to the bottle.

(2) Oxygen should be given in all cases of heart failure with secondary pulmonary complications and in myocardial degeneration, particularly when it is probable that the coronary arteries are sclerosed. It is usually not effective in the heart failure of rheumatic origin in young subjects. Dyspnœa and cyanosis are the best indications, but when in doubt its effect should be tested, using a mask and valves. It may be given by nasal catheter; but a tent is recommended (*see* p. 156).

(3) The *drugs* which act directly upon the heart in a favourable sense are comparatively few. Digitalis is the most valuable and the one whose action has been most studied. In auricular fibrillation its use has already been described (*see* p. 244). In these cases the ventricle is beating rapidly and irregularly, and digitalis acts like a specific. The pulse is slowed. The urine is increased in volume, and the œdema disappears. But in other cases, even when auricular fibrillation is not present, digitalis may be used with success, especially for its diuretic action. The powdered leaves are often combined with mercury in the form of a pill which is used for such cases. It cannot be said that its action is so certain as in auricular fibrillation. Digitalis may be given by mouth in powder, infusion, or tinctures or as one of its active principles, digitalin or digitoxin. In serious cases 2 drachms of the infusion or 10 or 15 minims of the tincture may be given every three or four hours at first, and after twelve or twenty-four hours less frequently or in smaller doses. The dose of digitoxin is $\frac{1}{250}$ grain to $\frac{1}{64}$ grain. Given in these doses, digitalis takes two or three days to produce its full effect. Much more rapid action is obtained by giving massive doses by mouth, a treatment that may be carried out when there is auricular fibrillation. Toxic symptoms arising during digitalis treatment are described on p. 245.

Some other drugs have an action like that of digitalis. The most important of these is strophanthus (dose, 2 to 5 minims of the tincture). The active principle of strophanthus, strophanthin, is valuable where there is no time to be lost in cases of serious failure. $\frac{1}{250}$ grain may be given intravenously. It may also be injected intramuscularly or subcutaneously. The treatment of auricular fibrillation by quinidine has already been described (*see* p. 246). Strychnine has been regarded in the past as a valuable cardiac tonic. A carefully controlled series of observations has shown that strychnine has no effect either in acute or chronic cardiac failure (**21**). Oubaine ($\frac{1}{4}$ mg. intravenously, or 1 mg. by mouth, once or twice a day) has been recently used for myocardial degeneration in France, to increase the tonicity of the left side of the heart.

Other symptoms and complications may have to be treated. If dropsy does not yield to digitalis, *theobromine sodium salicylate* (diuretin), in doses of 10–20 gr. t.d.s., is the best drug of the purin series to use, either in the form of tablets or in a mixture well flavoured with syrup of ginger. These drugs probably act by increasing the permeability of the glomerular membrane or perhaps increasing

the number of active glomeruli. They do not involve an increased oxygen consumption by the kidney; but they may obviously be ineffective if the glomerular capillaries are engorged and perhaps suffering from anoxhæmia. *Urea* may also be tried in doses of 5–15 grams. Urea filters through the glomeruli; and is also excreted by the tubules, so that the osmotic pressure of the tubal fluid remains high and less water is reabsorbed by the tubules lower down and so is excreted. Finally, salyrgan, an organic mercury compound (up to 2 c.c. intramuscularly) and neptal (up to 1 c.c.) once or twice a week are much more effective diuretics than the old-established Pil Hydrarg. They are still more effective when combined with the oral administration of ammonium chloride in doses up to 100 grains in the twenty-four hours. The latter acts by producing an artificial acidæmia so that the colloids give up some adsorbed fluid, and this fact must be remembered when there is some associated nephritis, where acidæmia may be present already. Pain over the heart is often severe, and may be relieved by belladonna plasters, by small doses of morphia internally, or by subcutaneous injection of gr. $\frac{1}{4}$. Cough may be treated with small doses of expectorants and sedatives (*see* Treatment of Bronchitis), and vomiting by effervescing salines. In aortic disease with hypertrophy, one of the most distressing symptoms is the violent action of the heart and the throbbing of the great vessels in the neck and over the body generally: and this may be much relieved by the use of a small dose of tincture of aconite (1 to 3 minims), by bromides, or by a small dose of morphia. Pulmonary hæmorrhage is rarely sufficient to threaten life, and does not require styptics. In cases of sudden arrest or weakening of the heart's action, especially during anæsthesia, when death is imminent, life may be restored by injecting 1–3 c.c. of 1 in 1,000 adrenalin into the right ventricle from a syringe. The needle, 3 inches long, is passed directly backward above the fifth costal cartilage, close to the left side of the sternum, slightly inwards. Its arrival in the ventricle at a depth of $1\frac{1}{2}$ to 2 inches is indicated by withdrawing a little blood before making the injection.

In myocardial disease of elderly subjects and often in aortic disease, paroxysmal attacks of breathlessness cause much distress. Oxygen provides relief, and is preferable to repeated subcutaneous injections of morphia, which also give relief (**25**). On the view that the breathlessness is due to incipient pulmonary œdema from relative left-sided failure (*see* p. 252), the author has used with success Plesch's method of raising the pressure of air in the lungs as described under pulmonary œdema.

Syphilitic myocarditis should be treated over an extended period with antisyphilitic remedies. Deep subcutaneous injections of sulfarsenol (0·3 to 0·48 gram) may be given weekly. A course consists of 6 grams, and six weeks are allowed to elapse between the courses. During the course yellow iodide of mercury, gr. $\frac{1}{8}$, may be given three times a day as tabloids, and increased to 8 or 12 a day. Potassium iodide may be given between the courses.

Heart Disease and Pregnancy. The question not uncommonly arises as to whether pregnancy should be allowed in patients who on auscultation are found to have murmurs characteristic of mitral regurgitation, mitral stenosis or aortic regurgitation. Pregnancy should be permitted: (1) if there is evidence that the valvular defect is of long standing and that there has not recently been any inflammation in the valves; (2) if the response to effort is good; (3) if the heart is not enlarged or unduly excitable; (4) if the rhythm is normal; (5) if in aortic regurgitation there is no great difference between the systolic and diastolic blood pressure, and the apex beat is not too far out or too forcible; (6) if in mitral stenosis no persistent crepitations are heard in the lungs after coughing or deep breathing, indicating commencing œdema. No attention should be paid to the occurrence of extra systoles in pregnancy; but the presence of auricular fibrillation should be looked upon as an absolute bar (Mackenzie). If pregnancy has been begun against advice the case must be carefully watched and pregnancy

terminated if unfavourable symptoms present themselves. When the heart shows some signs of functional inefficiency the patient should rest, propped up in bed, taking deep breaths at intervals during the day so as to aid the circulation through the lungs. Induction of labour during the later months of pregnancy is often a long business, and so is more of a strain on the heart than if labour comes on spontaneously. In such a case Cæsarean section may be considered, especially as sterilisation by resection of parts of the Fallopian tubes can be performed at the same time. Mackenzie states that no degree of heart disease in a married woman is a bar to sexual connection, supposing she feels the desire for it, and ability to perform it.

MALIGNANT ENDOCARDITIS

(Infective, Septic, Ulcerative or Bacterial Endocarditis)

Ætiology. Acute rheumatism is an antecedent of malignant endocarditis, but the proportion of cases (fifty-three out of 160—Osler) is less than that in which rheumatism is related to simple endocarditis; in some of these the symptoms have developed in the course of the rheumatic fever, and in others they have arisen in the stage of chronic valvular disease, which predisposes to the occurrence of infection. On the other hand, malignant endocarditis may occur even though the valves are healthy, especially after exposure and hard muscular work. This has been verified by war experience (**19**). Besides rheumatism, its predisposing cause may be found in acute pneumonia, in the eruptive fevers such as scarlatina, in puerperal processes, in the existence of open wounds on the surface of the body, in septicæmia and pyæmia. Purulent discharges from the mucous membranes (urethritis, vaginitis, pyorrhœa alveolaris) may give rise to the disease, but the latter is more likely to arise when for some reason the pus is held back, and there is no free drainage. This is particularly likely to occur in the chronic tonsillitis of children, or dental abscesses in the case of adults. Of 1,000 ex-servicemen with cardiac disease subacute bacterial endocarditis attacked 12 per cent.; it was responsible for death in 32 per cent. of non-syphilitic aortic regurgitation cases, but in only 6 per cent. of mitral stenosis (**20**).

Various micro-organisms are found in the organs in infective endocarditis. Streptococci, *i.e. S. viridans*, similar to those found in the mouth or large intestine, are most common; staphylococci, meningococci, pneumococci, the *Bacillus pneumoniæ* of Friedländer and the bacilli of tubercle, diphtheria, and typhoid and the gonococcus and anaerobic bacilli are found occasionally. From some centre of infection the organisms find an entrance into the blood and are thence deposited on the valves. Streptococci are often found in the blood during life in the acuter forms of the disease.

Morbid Anatomy. In this form of endocarditis the tissue of the inflamed valve is softened, and breaks down, so that erosions or ulcerations take place, and, as a result of this, fibrin is deposited upon the roughened surface, and accumulates into irregular masses of vegetations, which may reach the size of a hazel nut. By suitable methods the micro-organisms can be demonstrated on the surface, and more or less deeply in the substance of the vegetations, where they form considerable masses in acute cases, while beneath the infected surface there is a zone of polymorphonuclear infiltration; when the disease is chronic the micro-organisms are far fewer and processes of repair by means of fibro-blasts are more obvious. Several important changes result from these processes in the valve. The valve itself may be perforated, or strips of tissue may be partly separated and hang loosely in the blood current, or portions may be completely detached. Sometimes a part of the valve is so weakened by the destructive process that it yields before the pressure of the blood, and a saccular dilatation, or *aneurysm*, of the valve is formed, projecting on the opposite side. Another result is the occurrence of endocarditis, or endarteritis, in adjacent parts from a strip of the valve playing backwards and forwards

in the blood currents with the systole and diastole of the ventricle, and striking alternately the walls of the cavities in front and behind. At the spot struck infection takes place, and causes a fresh patch of inflammation of the lining membrane.

But the most important effect of malignant endocarditis is the infection of the whole arterial system by particles detached from the valves being carried to remote parts ; and it is to this process, combined with the presence of organisms in the detached fragments, that the special features of this disease are due. Embolism may take place in almost any part of the body. It is especially common in the vessels of the spleen and kidneys, but it happens also in the vessels of the brain, alimentary canal, skin, retina, and lungs, and the larger arteries supplying the limbs, such as the radial, ulnar, tibial, brachial, and others. The local results of these impactions are : (1) Obstruction of the circulation ; (2) necrosis or hæmorrhage, or both, within the area of distribution of the obstructed vessel, and the formation of infarcts ; and (3) suppuration in the same area from the septic influence of the micro-organisms, when the process is acute (*see* Embolism).

The effects upon the various organs, as they may be seen in different cases of malignant endocarditis, are—softening and abscess of the brain, and meningitis ; retinal hæmorrhages and optic neuritis ; diffused swelling, infarction, and abscess of the spleen. There are three ways in which the kidneys may be affected : (1) there may be acute toxic nephritis ; (2) there may be an acute focal embolic nephritis giving rise to *flea-bitten kidneys*, which are often large and speckled with hæmorrhagic points upon a white ground. Microscopically there are intra-capsular hæmorrhages of varying size which gradually become organised and a patchy œdema of the interstitial tissue, without lipoid ; (3) by infarction. There may also be hæmorrhages under the skin, hæmorrhagic infarctions and abscesses of the lungs, pleurisy and empyema.

Malignant endocarditis, like simple endocarditis, affects chiefly the left side of the heart ; but the proportion of cases in which the right side is involved is much larger than in the simple form. In the majority of cases malignant endocarditis occurs on valves showing the effects of previous simple endocarditis.

Symptoms. The symptoms and course of the disease present the greatest variety. In some cases the symptoms at first are simply the occurrence of fever with afternoon rises of temperature, or perhaps sweating, in a patient living an active life, though perhaps known to have valvular disease, more or less perfectly compensated. The temperature may be high, reaching 102° or 103° ; but it is generally remittent or intermittent, and sometimes with remarkable regularity for long periods. There is often free perspiration, and there may be an occasional rigor. The pulse is rapid, ranging from ninety to 120, or even higher. If the heart be auscultated, a murmur will generally be heard at one or other orifice, mostly, however, on the left side. Still it must not be forgotten that in these cases murmurs may be entirely absent. The spleen is commonly enlarged and albuminuria and hæmaturia may be present, and there is a secondary anæmia. The case occasionally resembles an acute nephritis. Where there is a previous history of rheumatism, or known cardiac disease, there may be abnormalities in the size and action of the heart.

In a considerable number of cases there is a close resemblance to *typhoid fever*, chiefly on account of the almost spontaneous occurrence of fever, with headache and enlarged spleen, either from the general infection or from embolism ; but there are no rose spots. Thus, the patient may have been perfectly well until he complains of some such symptoms as usher in other severe febrile diseases, pain in the head, or in the back and limbs, or a definite rigor or rigors. Then follow severe pyrexia, with its usual conditions—high temperature, quick pulse and respiration, dry tongue, loss of appetite, thirst and malaise. Frequently, within a few days, the patient is prostrate, apathetic, drowsy, and at night

delirious ; but the time of appearance of this symptom, determined presumably by the virulence of the toxin, is variable. The condition of the bowels varies, but there are often loose yellow motions, with much resemblance to those of typhoid fever ; and the abdomen may be distended. The duration of these cases is generally from ten days to two or three weeks, that is, much less than in cases of subacute infective endocarditis.

In another group of cases rigors are a prominent symptom, occurring once, twice, or more times in the day, and the resemblance to *pyæmia* from wounds is very close ; in fact, in a case of osteomyelitis, for example, due to *Staphylococcus aureus*, the infective endocarditis may cause no characteristic symptoms, and the lesion may be only disclosed at autopsy. In again another group the organisms invade the cerebral meninges, and the symptoms of meningitis form the prominent feature.

In any case of the disease, to the symptoms dependent upon septicæmic infection may be added those due to the obstruction by embolism of arteries or arterioles. Sometimes embolism of a large vessel in the brain will occur, and cause hemiplegia ; if a vessel in the leg or arm is obstructed, there will be loss of the pulse at the wrist or ankle ; but neither gangrene nor coldness need occur, unless a very large vessel is involved. More frequent are embolisms of the small vessels in the viscera ; there is thus often enlargement and tenderness of the spleen, due in part to infarcts, and the spleen may weigh from 20 to 30 ounces. Infarcts also occur in the kidney, accompanied, it may be, with pain, and the appearance of albumin or blood in the urine. In some cases petechial hæmorrhages appear under the skin, the petechiæ being generally small, and situate on the trunk, about the groins and axillæ ; exceptionally a *purpuric* condition may be present for months. Sometimes small painful erythematous swellings appear on the skin, particularly on the flexor surfaces of the fingers, last a few days and disappear again ; or there is deep-seated pain, and a larger tender lump can be felt beneath the skin in the deeper tissues of the limbs or body, lasting a few days. These are known as *Osler's spots*, and are especially diagnostic in the subacute disease. These are presumably embolic events. Hæmorrhages are often seen in the retina, and there may be also hæmoptysis or epistaxis. Some inflammatory conditions are probably also referable to embolic processes, such as the form of nephritis already mentioned (*see* p. 281), though whether as the result of vascular obstruction or of the introduction of micro-organisms may be doubtful ; albuminuria from nephritis or infarct is frequent. Optic neuritis is sometimes present.

There is a particular group of more or less chronic cases known as *subacute bacterial endocarditis* or *endocarditis lenta* (**19, 23, 24**). The disease arises insidiously. The patient becomes progressively pale and anæmic, suffers from lassitude, and there are often slight rises of temperature, often not above 100° F. Clubbing of the fingers is characteristic, and there is enlargement of the spleen. Petechial and other embolic symptoms are found occasionally, *e.g.* there may be slight albuminuria, and centrifugalisation of the urine may disclose the presence of blood cells. Osler's spots are specially characteristic of this form of the disease.

The duration of malignant endocarditis is very variable. Some cases last six or seven months with little else than a constant pyrexia ; cases of a pyæmic or severe typhoid type, and those with meningitis, are often fatal in a few weeks or days. Death occurs commonly from cardiac failure or uræmia, or embolism.

Diagnosis. This rests upon the pyrexia of remittent or septic type, the existence of valvular disease, and the evidences of embolism above enumerated ; marked anæmia and optic neuritis, if present, are also valuable signs. But a murmur may be wanting throughout the whole illness ; and even if present the valvular disease does not exclude the possibility of influenza, typhoid, or tuberculosis. Thus the diagnosis may often have to depend upon the occurrence of

emboliams. Malignant endocarditis is frequently mistaken for *typhoid fever*, and agglutinatosis tests should be carried out. In some of the subacute cases the spleen may be so enlarged, and the anæmia so considerable, that *splenic anæmia* is simulated ; this is all the more likely if there are petechiæ or hæmorrhages from the mucous membranes and if the murmur is not unmistakably organic. *Malaria* may also be suggested by septic endocarditis. A continued pyrexia without obvious signs may be due to commencing *miliary tuberculosis* as well as malignant endocarditis ; but after a time local signs peculiar to one or the other ought to be observed.

The blood should be examined for streptococci and other organisms.

Prognosis. This is exceedingly bad, and the recovery of a well-marked case of either typhoid or pyæmic form is rare. On the other hand, attacks of subacute bacterial endocarditis have subsided, but they may occur again after a varying interval.

Prevention. Cases have arisen after the removal of septic teeth. The safest way for dealing with multiple extraction is to get the dentist to scale and clean up all the teeth very carefully, repeat this in a week's time, and then some days later to carry out all the required extractions at one time. The danger of removing teeth one or two at a time over a long period is that the wounds are liable to be infected by the septic teeth remaining behind in the mouth.

Treatment can obviously be little more than palliative in the majority of cases. As in pyæmia, if there is any wound or sore, it should be rendered aseptic, and an attempt may be made to influence the disease by frequent doses of quinine (5 grains), sodium sulphocarbolate (10 to 20 grains), or sodium benzoate 20 grains). In a few cases good results have followed the subcutaneous injection of an antistreptococcal serum, or of an autogenous vaccine. But it is sometimes impossible to find any micro-organisms in the blood ; and even when they are found, and a vaccine can be prepared, it is with rare exceptions useless. A more promising line of treatment when an organism has been isolated is to inoculate a relative and carry out an immuno-transfusion from the relative to the patient. The general rules for nursing and dieting in febrile states are applicable. Profuse diarrhœa may be checked, if required, by astringents. The delirium is rarely so violent as to require any special treatment. Stimulants are naturally given, as the heart's action early tends to be seriously affected.

EFFORT SYNDROME

(*Disordered Action of the Heart, Soldiers' Heart*)

During the late war the effects of the war strain upon the heart of the soldier have been constantly the subject of observation and study. Thousands of soldiers were at different times invalided for symptoms suggestive of a weak or diseased heart, and in such cases the nature of the cardiac or other lesion, the best method of treatment, and the prognosis as to the patient's future in relation to military service, whether discharge or return to duty, had to be considered. The subject is dealt with in a report by T. Lewis to the Medical Research Committee (Special Report Series, No. 8, 1918) ; and in this important report are given the results of the study of 1,000 soldiers returned as sick during training or on active service for actual or supposed defects of the cardio-vascular system.

Ætiology. There is a definite symptom complex, called the "effort syndrome," which occurs under a number of different conditions, such as tuberculosis, exophthalmic goitre, valvular disease of the heart, and in other conditions where there is no obvious lesion in the body. It is this latter type of case that is known as "disordered action of the heart"—a name that is

objected to, because it points solely to the heart, and thus gives a bad impression to the patient. Lewis is inclined to think that the heart action itself is only a subsidiary feature in the disease.

Before study and treatment it is necessary to separate off those other diseases causing the same symptoms. In particular, valvular disease of the heart is held to include cases exhibiting aortic or mitral diastolic and pre-systolic murmurs, but not those with systolic murmurs, whether at the base or apex, owing to the uncertainty of the significance of this type of murmur. Systolic murmurs in soldiers only exceptionally mean valvular disease, and often the amount of damage to the valve is but slight. Further, patients who are invalided on the ground of systolic murmurs alone are found when tested to be fit for active service in nearly all cases.

The malady is found chiefly in men of sedentary occupation, and especially among the more intellectual class of workers. Temperamentally they are unusually sensitive. There is a prevalence of teetotalism among them (53 per cent. in 454 cases). A history of venereal disease is very uncommon; on the other hand, there is often the certainty of self-abuse.

The action of the vagus is probably abnormal, as shown by the variation in the pulse rate during respiration, and occasionally there is profound slowing of the pulse, with fainting fits.

The sympathetic system is more easily stimulated and depressed by adrenalin and apocodeine than normal; this suggests that sympathetic stimulation may account for the cardiac acceleration.

There is no evidence that hyperthyroidism is the cause. Experiments have shown that these patients are just as tolerant to thyroid administration as normal people.

The high incidence of rheumatic histories in the patients (23 per cent.), in spite of the absence of physical signs in the heart, suggests the possibility of early myocardial change as the cause in many cases However, there is no indication of heart block immediately after exercise, as indicated by the electro-cardiograph, which is usually a valuable sign.

Blood cultures are negative.

It does not seem probable that tobacco smoking is the cause of the condition, though it has been proved that tobacco increases the pulse rate in these cases more than in normal people. In the first place, it is as commonly met with in Sikh soldiers, who do not smoke, as in other Indian troops. Again, the consumption of tobacco is not usually inordinate, and, curiously enough, the heavy smokers return to duty in a higher percentage of cases than the light smokers do, but the non-smokers do best of all. An obvious explanation is that the light smokers are not so much accustomed to tobacco as the heavy smokers. There is no doubt that tobacco smoking aggravates the condition.

It is possible that some toxæmia may be at the bottom of the condition; the symptom complex is very similar to that met with in early tuberculosis, and there is often a history of previous infection. In 50 to 60 per cent. of cases infections are legitimately suspected to have played a large part in the production of the malady

Symptoms. The " effort syndrome " consists of the following symptoms: *Breathlessness.* This is a constant feature, especially on exertion. A respiration rate of sixty to eighty is by no means uncommon during the waking hours. During sleep the rate is normal, and it is usually not increased when the patient is lying at rest in bed. *Pain.* This occurs in about three-quarters of the cases, and varies in character from uneasiness over the præcordia to pain of anginal distribution; it is especially associated with exercise. *Exhaustion* is an almost constant symptom; it is provoked by sustained effort, and is far in excess of that due to fatigue in healthy men. *Giddiness and Fainting.* Giddiness is almost constant, and is associated with change of posture and with effort. Attacks of

fainting are less common. *Palpitation* is frequent, especially with exercise. It is usually due to rapid and vigorous heart beats, and not often to extra systoles, or other well-defined cardiac irregularity. However, extra systoles do occur, and sinus arrhythmia with respiration is not uncommon. *Headache* is almost constant. *Sweating and coldness of the extremities* is common. The response to pilocarpine is greater than normal. Irritability of temper, sleeplessness, inability to fix attention, shakiness, tremor of the hands, and flushing are common. A disinclination to take alcohol in any form (sometimes for conscientious reasons, but as commonly for reasons of distaste) is to be reckoned as a frequent and remarkable association.

The following are the physical signs :—*Increased heart rate*, especially marked in response to emotions, exercise, or alteration of posture, *i.e.* changing from recumbent to erect position. A notable and widely recognised sign is the slow return of pulse rate after effort. *Blood pressure* is usually normal when the patient is at rest, but there is an exaggerated response to emotion or effort, and high readings are often obtained. *Diffuse apex beat* is common, and this may or may not be associated with increased force of the impulse. It is commonly regarded as a physical sign of dilatation of the heart, but X-ray examination by the orthodiagraph shows that there is no enlargement of the heart, so that the physical sign is untrustworthy, in fact the heart is small (**56**). The *deep reflexes* are usually exaggerated. The *urine* in 60 per cent. of cases is hyperacid, the quantity being reduced, and the ammonia and amino acids are increased. In 20 per cent. the volume is also reduced, and the urine deposits phosphates. The ammonia is normal in amount, but the amino acids are increased. Speaking of the urine generally, calcium oxalate crystals are often found, and spermatozoa are found in large numbers in the morning urines in 15 per cent. of cases. The *blood* shows a leucocytosis, the average being 12,100 c.m., the lymphocytes being increased. A much larger leucocytosis than normal is observed after exercise, the lymphocytes being increased, and the severity of the symptoms runs parallel with the leucocytosis. The electro-cardiograms show no abnormality.

Prognosis. The following criteria decide whether the patient will in future only be fit for sedentary work : a history of rheumatic fever, persistently severe breathlessness on exertion, præcordial pain sufficiently severe to prevent exercise, a pulse rate of 120 and more even in recumbency, symptoms which have been present for many years, even though of only moderate severity. A method of testing patients is for them to walk up a flight of thirty steps ; indications to be looked for are an anxious expression, a respiratory rate of thirty-five or over, which persists while the patient lies and is interrogated from time to time, a pulse rate which fails to fall within five beats of the pre-exercise level on lying for two minutes.

All the men who are not excluded so far are treated with graduated exercises ; selected army exercises are used, with which the men are mostly familiar, and these are supplemented by route marches in light or full kit. The exercises are arranged in seven groups of increasing severity, and a patient moves to a higher grade every three or four days. The exercises last fifteen or thirty minutes daily. The men are classed for duty on the highest grade of exercise they are able to stand without distress. The average period required for classifying the men is a month and a half. Of 220 soldiers discharged from the hospital, 182 (83 per cent.) were still fit for duty in one capacity or other three months afterwards.

Prevention. A long and gradual training is advisable in recruits whose occupations have been sedentary, for these form a very high proportion of the patients, a longer convalescence from febrile affection or affections of the bowel, with a graduated system of retraining.

Treatment. This consists in clearing up local foci of infection (extraction of carious teeth, removal of tonsils, etc.). The removal of a latent dysentery

infection by emetine bismuth iodide has several times ameliorated the condition. If the symptoms are recent, a period of rest from drill and exercise is desirable, but rest in bed is harmful, and should always be avoided, except in severe præcordial pain, headache, or giddiness. Occupation is clearly called for, especially in the open air, such as gardening. They should be encouraged by the assurance that their malady is curable, and that improvement is visible. No particular attention should be paid to the heart. Tobacco increases the resting pulse rate and the symptoms after exercise. Bromides are valuable in the early stages. The most important treatment is by graduated exercises. Digitalis is valueless.

CONGENITAL MALFORMATIONS

Malformations of the heart arise from defects in its development, which is normally not complete until the closure of the ductus arteriosus and foramen ovale some days after birth. Arrest of this process in any stage will lead to a congenital malformation. It has occurred so early as to leave the heart with only two cavities—an auricle and a ventricle ; or with three cavities—a ventricle and two auricles. But these are very rare cases, and the children mostly live but a short time after birth. One of the commonest lesions is a combination of pulmonary stenosis and deficiency of the interventricular septum. The stenosis is caused either by union of the pulmonary valves, or by a constriction of the ring just below them, or of the infundibulum itself, or by an imperfect septum dividing the infundibulum from the ventricle. Such conditions are regarded by Keith as invariably due to defects in development or to want of expansion of the bulbus cordis, and never to intra-uterine endocarditis. If the outlet of the right ventricle is thus obstructed in early fœtal life, the pressure in that cavity is relieved by overflow into the left ventricle through the still unclosed septum ; and this opening then becomes permanent. According to the stage of development at which the arrest has taken place, the deficiency may be a very large one or a mere perforation in the upper part ; and in this latter case the aperture occupies the *pars membranacea*. When the deficiency is a large one, the aorta frequently arises from the right ventricle, or from both right and left ventricles, and the foramen ovale and ductus arteriosus may one or both be pervious. Both pulmonary stenosis and patent interventricular septum may occur independently of one another. In a few rare cases the communication between the two ventricles has been below the anterior aortic valve (over which arises the right coronary artery) instead of the right posterior valve ; it is then in front of the pars membranacea and opens into the infundibulum of the right ventricle (**27**).

Constriction or obliteration of the aortic orifice or of one auriculo-ventricular orifice sometimes occurs, and similarly interferes with the course of the circulation and the normal development of the heart ; and complete transposition of the aorta and pulmonary artery and other complicated transpositions of vessels have been found.

The ductus arteriosus and the foramen ovale may remain unclosed without any obvious reason—probably, however, from a temporary obstruction to the circulation at the time of birth ; but more or less patency of the foramen ovale occurs in about 30 per cent. of healthy persons, a mere fissure or narrow valvular opening being insufficient of itself to allow of any free passage of the blood from one cavity to the other.

Instead of three sigmoid valves in the aorta or pulmonary artery there may be only two, or there may be four. This change may exist in association with other deformities, but if alone it is less likely to give rise to difficulties at birth than to lay the foundation of disease in later life.

Pathology. No more is really known of the cause of arrested or faulty development of the heart than of congenital malformations in other parts of the

body. One of the most characteristic symptoms of congenital heart disease is *cyanosis*, and the disease has been called the *morbus cæruleus*. Some recent observations have thrown light on the cause of cyanosis in general (**14**). (1) It is due to slow circulation of blood in the peripheral capillaries, so that the returning venous blood contains less oxygen than usual; (2) it is due to the arterial blood not being fully saturated with oxygen. Of course both these factors may be combined, and the cyanosis is intensified if the red cells of the blood are increased. There seems little doubt from determinations of the oxygen content of blood taken direct from the radial or brachial artery through a fine needle that, although in marked cases there may be some arterial unsaturation, it is the peripheral stasis factor that is chiefly responsible for the cyanosis of acquired heart disease. The arterial blood may contain less than the normal quantity of oxygen (*a*) if there is a hindrance in the lungs to the exchange of gases, such as may occur in œdema, pneumonia, bronchial spasm, or chronic pulmonary disease; (*b*) if the polycythæmia is extreme, because the blood may not remain long enough in the pulmonary capillaries for all the corpuscles to become normally saturated; (*c*) if the arterial blood is a mixture of blood from the lungs and from the systemic veins, as may occur with a deficient septum ventriculorum or patent foramen ovale, associated with congenital pulmonary stenosis. Slowness of the blood through the lungs, such as occurs in acquired heart disease, will by itself tend to complete saturation of the arterial blood, because there is plenty of time for oxygen to be taken up. It was found in certain cases of congenital heart disease with marked cyanosis that the arterial blood was only 70 to 80 per cent. saturated with oxygen. When the patient breathed pure oxygen for half an hour through a mask and valves, the saturation was raised to just over 90 per cent. This is compatible with the arterial blood being composed of a mixture of pulmonary and venous blood, because it was impossible to saturate it completely by giving oxygen. At the same time the peripheral stasis factor is also present in congenital heart disease and increases the cyanosis.

The common lesion is the association of pulmonary stenosis and deficient septum. The stenosis may be so extreme that very little of the blood can reach the lungs by this route. Nearly all of it passes into the aorta and mixes with blood from the left ventricle. In these extreme cases the bronchial arteries are dilated and a fair supply of blood reaches the lungs by means of the anastomoses of these arteries with the small branches of the pulmonary artery. In one case the pulmonary valve was found to be entirely closed and no systolic murmur was heard over the pulmonary area; the patient was extremely blue. The heart was only slightly larger than usual, since all the blood travelled into the aorta, and there was no extra resistance (**14**, Case 15). Where the pulmonary valve is patent, though stenosed, less blood will pass into the aorta; the right ventricle may be hypertrophied and dilated, and there will be a systolic murmur and perhaps a thrill in the pulmonary area. In certain cases a patent foramen ovale may act instead of a deficient septum in short-circuiting the blood. A patent foramen ovale or a patency of the septum will be of no functional significance if the pulmonary valve is normal, because there will be nothing to prevent the blood going through the lungs in the ordinary way. At most a little blood may pass through from the left to the right ventricle, and so travel through the lungs a second time. A patent ductus arteriosus associated with a pulmonary stenosis and deficient septum will provide an extra path for the mixed arterial blood to pass through the lungs; if present by itself it will be of little functional significance.

Symptoms. Cyanosis when present is most marked in the prominent parts of the face—the cheeks, lips, nose, and ears—and in the fingers and toes. In slighter cases it is only richer red than natural; in the severest cases it is purple almost to blackness, and any exertion at once increases the distension of the vessels and deepens the colour. It is a remarkable fact about this disease that,

though the cyanosis may be extreme, there is no shortness of breath while the patient is at rest. The chronic stagnation will cause thickening of the parts affected, and the nose and lips are coarse, while the ungual phalanges of the fingers or toes are thickened much beyond the rest of the fingers, or "clubbed" (*see* later). The blood shows in a remarkable degree the great excess of red corpuscles (*polycythæmia*) which is met with in many forms of cyanosis; thus the corpuscles have been found to number from 8,000,000 to 9,000,000 per cubic millimetre, and the hæmoglobin may reach 110 to 160 per cent. of the normal. The patient sometimes suffers from attacks of giddiness, faintness, convulsions, and loss of consciousness. He is incapable of much exertion, from the readiness with which dyspnœa supervenes; and he is also peculiarly susceptible to cold or exposure, and easily suffers from attacks of catarrhal bronchitis. In later stages œdema of the legs, ascites, enlarged liver, and albuminuria are found; or the patient succumbs to bronchitis; or tuberculous disease of the lung is the cause of death.

Physical Signs. Most commonly a systolic murmur is heard, loudest over the pulmonary area in congenital pulmonary stenosis, but it may also be heard over adjacent spaces. It may be accompanied by a thrill. Dulness may extend to the right of the sternum in consequence of the dilatation and hypertrophy of the right side of the heart. In pure pulmonary stenosis this is very marked. If deficiency of the septum is the only lesion, there is a systolic murmur of maximum intensity in the third left space near the sternum, conducted outwards, and often a thrill; but no cyanosis. A patent ductus arteriosus often causes a prolonged murmur running through systole into diastole, and waxing and waning in loudness. (*See* Plate 10, E, p. 220.)

The various types of congenital heart disease may give characteristic appearances when examined by X-rays. Thus in the rare pure pulmonary stenosis the shape of the heart is characteristic (*see* Plate 12, B), owing to hypertrophy of the right ventricle, and dilatation of the right auricle. There may be dilatation of the pulmonary artery beyond the obstruction; the reason for this is quite obscure, but it has been several times observed at post-mortems. In the usual combination of septal defect with pulmonary stenosis both left and right sides of the heart may be enlarged; but, on the other hand, there may be no recognisable change in the shape of the heart.

Prognosis. Congenital malformations are always unfavourable. Cases of severe defect live but a few hours or days; others of slighter degree survive five, ten, or twenty years; and even persons with very ill-developed organs have occasionally reached middle age. In any given case the prognosis must depend upon the evidences of cardiac efficiency rather than the nature of the malformation.

Treatment. This is the same as for chronic cardiac disease.

DISEASES OF THE PERICARDIUM

PERICARDITIS

Ætiology. Inflammation of the pericardium may result from a general blood infection, or it may occur from local irritation or from infection directly spreading from the neighbourhood.

Among the first class of cases, acute rheumatism is its most frequent cause; but it also occurs in Bright's disease, in pyæmia, in leukæmia, in tuberculosis, in influenza, in general pneumococcal infection, and in other conditions of septicæmia and toxæmia. Its local causes are the growth of cancer nodules into its cavity, the rupture into it of abscesses and hydatid cysts, and the contiguity of a source of infection, such as empyema or pneumonia.

Morbid Anatomy. If we take as the type the pericarditis which

occurs in the course of acute rheumatism, we find the following changes: In early stages the membrane loses its smooth, glossy surface, and becomes more vascular, so that it is injected with a fine network of vessels. Some shreds of lymph from the exudation of corpuscular elements and fibrin from the blood vessels are next seen, and a complete layer forms upon the pericardium. Ultimately the two opposed surfaces of the sac may be separated by a layer of lymph $\frac{1}{8}$ or $\frac{1}{4}$ inch in thickness, which is sufficiently soft to allow the parietal and visceral membranes to be peeled from one another, and the lymph is often of such a consistence that the separation of the surfaces leaves a curiously honeycombed or reticulate appearance. Generally, at the same time, some serum is formed, of yellow colour, and turbid from corpuscular elements. This may accumulate to a considerable amount and further separate the two layers of the pericardium, while it allows the formation of long, shaggy processes of lymph, stretching from surface to surface. After a time the fluid generally disappears, and the lymph is either itself absorbed, or it becomes organised, and unites the parietal and visceral layers of the sac more or less completely together, causing adherent pericardium.

In other infections, and especially in pyæmia or septicæmia, the fluid contents of the pericardium are pus, instead of serum, constituting *purulent* or *suppurative pericarditis*. This is often secondary to abscess of the cardiac muscle, which is known frequently to result from acute necrosis of the long bones. Sometimes the new-formed vessels in the inflammatory formation rupture, and small petechiæ or larger patches of hæmorrhage cover the surface of the membrane, forming *hæmorrhagic pericarditis*. And, occasionally, tubercles are formed both in the new tissue and in the original membrane covering the heart's surface; this is known as *tuberculous pericarditis*, and forms part of a general tuberculosis.

The micro-organisms of pericarditis vary with its origin. Streptococci, staphylococci, pneumococci, and tubercle bacilli have been most often found. Poynton and Paine found their rheumatic diplococci in the pericarditis of rheumatism.

Effect on Circulation. Cohnheim's animal experiments show that the effect on the circulation depends on the tension in the pericardial sac. If fluid is injected slowly when the pressure reaches a definite point the arterial pressure falls, and the venous pressure rises. This is an expression of a diminished efficiency on the part of the heart as a pump, the output of blood at each beat being diminished. The higher the tension in the pericardium, the smaller the output.

Physical Signs. Since pericarditis so frequently arises in the course of some infectious disease, like rheumatism, its symptoms may be entirely masked by those of the disease which it accompanies, and its presence may be only revealed by the alteration in the heart sounds, and other physical signs which it produces. These, however, are generally characteristic. Firstly, there is the *pericardial rub*, which has been described under the examination of the heart. It may be soft to begin with, but after a few hours the sound becomes louder and harsher and rougher, and then the friction can often be felt by the hand placed over the præcordial region.

If liquid is effused into the pericardium, as is frequently the case, the præcordial dulness is increased. It extends upwards to the upper border of the third rib, the upper border of the second rib, or even to the clavicle; towards the right for 1 inch or more beyond the sternum; and towards the left it may reach right into the axilla. The præcordial dulness has a more or less triangular shape, with its broad base upon the diaphragm, and a rounded apex at the upper part of the sternum and the left upper intercostal spaces.

As the liquid increases, the impulse of the heart becomes diffuse. An important distinction must here be mentioned between pericarditis and pleurisy in the effect of effusion of liquid on the occurrence of a friction sound. In pleurisy the effusion of liquid results in the disappearance of the pleuritic friction sound. In pericarditis the friction sound persists commonly throughout the illness, even to the

period of greatest distension of the sac, and during the subsequent absorption of the liquid. This is probably because the fluid collects chiefly behind the heart, as the patient lies on his back, leaving the two inflamed layers of pericardium rubbing against one another in front.

A pericardial effusion often compresses the base of the left lung, causing a dull note on percussion and bronchial breathing on auscultation.

Another result of pericarditis in some cases is inhibition of the action of the diaphragm. Either abdominal respiratory movements cease, or there is a little recession during inspiration, with upward movement of the higher abdominal viscera and of the heart, collapse of the bases of the lungs, and it may be distension of the stomach and colon.

Symptoms. The local symptoms which may accompany pericarditis and pericardial effusion are pain, anxiety or distress at the præcordia, tenderness on pressure over that region, shortness of breath, with shallow respirations and short hacking cough. The pulse may not at first be much affected, but it tends soon to be quick. Occurring in the course of a febrile disease like rheumatism, pericarditis may not notably add to the existing pyrexia, but with its rapid onset occasionally there is considerable elevation of temperature—for instance, to 105° or 106° ; and in other cases it may be accompanied by the usual conditions of pyrexia, loss of appetite, dry tongue, thirst, and scanty urine.

In the worst cases the cardiac feebleness increases, the pulse becomes irregular and fluttering, or may take the form of the *pulsus paradoxus* (*see* p. 226), præcordial pain is severe, and the face becomes drawn and pinched and the patient dies primarily of cardiac failure, sometimes with convulsions and coma. But in the majority of instances the symptoms gradually subside ; the dulness diminishes while the rub often remains till a late stage. The changes of pericarditis occur rapidly, effusion may reach its height in two or three days, and subsidence may be well established in three or four more.

Suppurative, tuberculous, and hæmorrhagic pericarditis are not essentially different in their symptoms and physical signs.

Diagnosis. Under ordinary circumstances this presents no difficulties, the double or triple friction sound being very distinctive. The diagnosis of pericardial effusion is not always easy, because it may be simulated by a *dilated heart*, caused by the same rheumatic poison as has led to the pericarditis. The signs which support the diagnosis of effusion are extension of dulness to the left beyond the heart's impulse and upwards to the second rib or higher, and signs of compression at the left base. The Röntgen rays may show the shadow of the heart and pericardium extending right out to the left costal wall, and up into the first space, and to the right as far as the nipple, with little or no pulsation, and with a large effusion the heart's shadow is sometimes seen within a ring of lighter shadow due to the distended pericardium alone.

Prognosis. Pericarditis is not, on the whole, an immediately fatal disease. It may be so mild that it is only detected by the stethoscope in the course of a routine examination, and in a large proportion of the cases occurring in rheumatic fever the inflammation subsides. The adhesion of the layers, which so often results, may become a danger in itself. On the other hand, the commonness of " milk spots " found on the surface of the heart at post-mortems suggests the possibility that slight attacks of pericarditis frequently occur, and subside completely. Milk-spots are often regarded as merely due to friction ; but it is difficult to see how the latter can occur without some degree of inflammation. Possibly some are the result of bruising from trauma. In Bright's disease, and in association with other chronic cachexial conditions, pericarditis often occurs towards the end of the illness, and then may appear to be the lesion determining death ; but even in such circumstances the physical signs may completely disappear before death, or, if they persist, the fatal result may not seem to be hastened thereby. A grave prognosis must be given in suppurative pericarditis,

and the occurrence of a pneumococcal pericarditis in the course of pneumonia or empyema is generally fatal; but Sir F. Taylor knew a case of double empyema with pericarditis recover. Pericarditis in acute rheumatism is often accompanied by, and masks, some inflammation both of the endocardium and of the myocardium, the ill effects of which become developed afterwards.

Treatment. The treatment of pericarditis is mainly palliative. Like other acute inflammations, it must be met by complete rest in the recumbent or semi-recumbent posture, by nutritious easily digestible diet, and by abstinence from excitement. In the case of rheumatic fever, these conditions are probably already provided in the treatment of the initial disease. For very severe pain six or eight leeches may be applied to the præcordia. The præcordia may be covered by a layer of cotton wool, or a warm linseed-meal poultice, or antiphlogistine or thermogen wool may be applied. Morphia may be given if necessary. If the circulation is failing, or the heart becomes irregular, small doses of tincture of digitalis should be given frequently, with brandy or ammonia. A rheumatic effusion rarely if ever requires aspiration; but this must be considered if there is a possibility that pus is present. D. C. Taylor, from experience at Lewisham Hospital, after anæsthetising the skin and subjacent tissues with 2 per cent. novocaine, recommends inserting a fine needle backwards and a little downwards in the 6th intercostal space at the left side of the sternum, in order to avoid wounding the internal mammary vessels, until the diaphragm is felt—to be sure of this the patient is told to take a deep breath; it is withdrawn a little and then pushed straight back for about an inch from the surface. He then washes out the cavity several times with 20 c.c. of 1 in 2,000 flavine, and the aspiration is repeated every other day or a rib may be resected.

ADHERENT PERICARDIUM OF RHEUMATIC ORIGIN

Morbid Anatomy. Reference has been already made to this condition as arising from rheumatic pericarditis. The degree to which the two surfaces may adhere varies much in different cases; there may be merely a few filaments running from the surface of the heart to the parietal pericardium, or there may be complete union of the pericardial sac to the surface of the organ, and every intermediate condition occurs. When the union is complete, the tissue uniting the two surfaces may form only a thin layer; or it is a dense, firm, fibrous, more or less vascular coat, $\frac{1}{4}$ inch or even $\frac{1}{2}$ inch in thickness. Hypertrophy and dilatation are usually present, because the muscular substance of the ventricle has been injured by the occurrence of myocarditis at the same time as the pericarditis; there is usually mitral stenosis. In many cases there is not only obliteration of the pericardial sac, but the external surface is firmly fixed to the surrounding pleura and to the sternum. In fact, the mediastinal tissues are matted together to form dense fibrous tissue (*mediastinitis fibrosa*).

Symptoms and Physical Signs. Cardiac pain, palpitation, and dyspnœa are prominent. Physical signs cannot be relied upon to reveal the presence of the adhesion itself; but when the more extensive external adhesions are also present, one or more of the following physical signs may be recognised: (1) systolic retraction at the point corresponding to the apex of the heart; (2) systolic retraction of the lower end of the sternum; (3) systolic retraction of the third, fourth, and fifth intercostal spaces to the left of the sternum; (4) systolic retraction of the lower ribs at the side or back of the left chest (Broadbent's sign). These are not very reliable; certainly systolic retraction of intercostal spaces is not peculiar to adherent pericardium. The commonly associated mitral stenosis must be carefully looked for. Death is caused by heart failure with extensive œdema.

X-rays may give valuable indications of adherent pericardium. They consist in alterations of the normal movement and shape of the heart on breathing deeply

or leaning to one side, and alterations in the movement of the central part of the diaphragm on breathing, due to adhesions with the pericardium and mediastinum.

The **Prognosis** and **Treatment** of pericardial adhesions must be considered chiefly in reference to the changes in functions of the heart which result from them (*see* pp. 275, 276). The treatment is that of heart disease in general.

CHRONIC CONSTRICTIVE PERICARDITIS

Pick's Disease

This disease, first noted by Lower (1669), Chevers (1842), Wilks (1870) and Pick (1896), has just recently been again brought to light (**73**).

Ætiology. Tuberculosis, pneumonia with pleurisy and pericarditis or sepsis may be responsible; but the cause is often unknown, since the onset is insidious; there may be a history of pericarditis, but not of acute rheumatism.

Morbid Anatomy. There is chronic fibrous thickening of the parietal pericardium, often with calcification, pockets of fluid, obliteration of the sac and/or external pericardial adhesions. Since, owing to the constriction, the heart cannot fill in diastole, "inflow stasis" results, and there is ascites, often with a frosted "sugar loaf" liver or spleen, and pleural effusion. The heart itself is healthy.

Symptoms. The onset is insidious; there are dyspnœa, ascites, an enlarged, but not a tender or pulsating, liver, engorgement of the jugular veins, pulsus paradoxus, low blood pressure, and sometimes œdema of the legs and pleural effusion. The size of the heart is normal or a little increased. Broadbent's sign is not present. The electrocardiogram is of low voltage with flattening or inversion of the T-waves in leads I. and II., and occasionally auricular fibrillation. The serum proteins may be low.

Diagnosis. Mitral stenosis with or without adherent pericardium is differentiated by careful examination for the murmurs. Polyserositis is a different disease. Portal cirrhosis and nutritional œdema must be differentiated.

Prognosis. The disease is chronic, sometimes with remissions; it may run a rapid course or last for many years. Six out of 10 cases have been cured after operation, and one other relieved.

Treatment. Delorme's operation of pericardial resection is the only cure.

HYDROPERICARDIUM

This term denotes the presence of an excess of serum in the pericardial sac, and is generally used to distinguish the passive secretion of dropsy from that of inflammatory effusions already described under Pericarditis. The pericardium naturally contains a very small quantity of serum, and after death from any cause it is common to find a few drachms of pale yellow fluid in it. The causes of serous effusion, apart from inflammation, are those of general dropsy, such as Bright's disease, and such local interference with the venous circulation of the pericardium as valvular disease of the heart itself, chronic lung disease, and pressure of growths upon the veins which return blood from the pericardial surfaces. The liquid contained in the sac resembles that of dropsical effusion into the other serous cavities, being pale yellow, or more or less pink from exudation of blood-colouring matter, with a small quantity of fibrinogen and from 1 to 3 per cent. of albumin.

The **Physical Signs** of hydropericardium are the same as those of effusion in pericarditis. As a rule, no special **Treatment** directed to the pericardium is required where the condition forms part of a general dropsy, or where it results from local interference with the circulation; the general dropsy or the valvular

disease must be dealt with. In rare cases the effusion may be so rapid or abundant as to require paracentesis of the pericardium.

PNEUMO-HYDROPERICARDIUM

This signifies the presence of gas and liquid together in the pericardium. Gas in conjunction with liquid has been observed as a result (1) of gas gangrene, and (2) of the communication of the pericardial sac with air-containing cavities. This communication may be traumatic, as in the case of a juggler who, in attempting to swallow a blunt sword, perforated the pericardium from the œsophagus; as in the case recorded by Flint, where the pericardium was punctured by a stab through the pleura; and after the operation of paracentesis pericardii. Or the communication may be effected by disease; and cases are on record of cancer of the œsophagus ulcerating into the pericardium, of a phthisical cavity opening into it, and of a hepatic abscess communicating at the same time with the pericardium and with the stomach. Gas can never be observed alone in the pericardium, as its entrance from without is almost immediately followed by pericarditis with liquid effusion.

The **Physical Signs** of pneumo-hydropericardium are resonance on percussion over the præcordial area and splashing, churning, or gurgling sounds, synchronous with the movements of the heart.

HÆMOPERICARDIUM

In slighter degrees, the effusion of blood into the pericardium occurs in so-called hæmorrhagic pericarditis, from the rupture of the new-formed vessels; but larger quantities, when not directly traumatic, result from rupture of the myocardium, of an aneurysmal sac, or of vessels in a cancerous growth. Scurvy and allied conditions may also give rise to pericardial hæmorrhage.

Symptoms. When sudden effusion of blood into the pericardium takes place, the patient is seized with more or less oppression of the chest, pallor, syncope, unconsciousness and death in quick succession; or with pallor, feeble pulse, and orthopnœa he may remain for twenty-four or thirty-six hours before the fatal termination; or presumably, with a less degree of hæmorrhage, death may be still further delayed, and a pericarditis may develop which contributes to the final result. Walshe refers to cases, probably of a scorbutic nature, or at any rate not dependent on rupture of aneurysms, or of the heart itself, in which recovery has taken place.

The **Physical Signs** are those of a large pericardial effusion, extensive præcordial dulness, and enfeeblement or absence of the heart sounds. The **Diagnosis** would be assisted by a knowledge of the previous existence of aneurysm, or attacks of angina pectoris.

Treatment. Absolute rest and judicious use of stimulants would give the only chance.

ANGINA PECTORIS

This name is commonly given to an intense pain beneath the sternum produced in the heart or aorta, which comes on with great suddenness, and occasionally proves fatal. There is probably no fundamental distinction between this severe pain and other milder pains produced in the heart, which are sometimes designated "angina minor," or better—simply "cardiac pain."

Ætiology. It may occur in boyhood, but it is uncommon before the age of thirty, increases in frequency with every year, and is most common between the ages of fifty and seventy-five. It is more frequent in men than in women, in the proportion of about four to one. Heredity also has an influence. It is common in aortic disease, rare in mitral stenosis. Tobacco is not uncommonly respon-

sible. Focal sepsis, especially in the gall bladder or at the apices of the teeth, is another factor. The immediately exciting causes are: (1) Physical exercise, especially going uphill or against the wind, and, later on, even the mildest forms of exertion; (2) a large meal; very often these two factors are combined; (3) emotional excitement, whether depressing or exhilarating, and mental strain; and (4) exposure to cold. The last is important, since undressing at night in a cold room may bring on an attack in bed. Occasionally the attack begins during sleep.

Pathology. When death has taken place in an attack, the heart has generally been found relaxed, with its cavities full of blood. In the majority of cases, some disease of the heart or aorta has been found, and mostly of the following kinds: myocarditis, pigmentary, fatty or fibroid degeneration of the myocardium; syphilitic aortitis, atheroma, or dilatation of the aorta; atheroma or calcification or shrinkage of the aortic valves; and arterio-sclerosis or calcareous deposit in the coronary arteries, or their obliteration from endarteritis or thrombosis. Coronary embolism may cause death rapidly, with the most severe anginal symptoms. In some cases of death from angina the heart muscle and coronary arteries have been found to be perfectly healthy.

Mackenzie's view is that angina depends on the cardiac muscle (**29**). In this connection it may be noted that the usual pain in mitral stenosis, which arises in the left auricle, occupies a band on the left side of the chest, extending from the nipple to below the ensiform cartilage; the sensory nerves from the skin of this area pass to the sixth and seventh dorsal segments of the spinal cord. Pain arising in the ventricle and aorta, on the other hand, is felt higher up in the chest, over an area corresponding to the higher dorsal segments, because, in the embryonic cardiac tube, the ventricular part lies anterior to the auricular part, and becomes bent over and downwards later on (**30**). The theory that anginal pain comes from the ventricle is now generally accepted. The fact that pain is sometimes caused by a healthy cardiac muscle need cause no more difficulty than the pain which is often produced by healthy gastric muscle when there is pyloric stenosis. Cardiac pain is due to hard work of the cardiac muscle with an insufficient supply of oxygen, and it seems reasonable to suppose that the muscular fibres must be sufficiently healthy to be able to produce it; they must be capable of hard work. The substernal pain felt by healthy but untrained persons during a hard game of football may be of similar origin. Angina may occur with fibroid heart because, though healthy, the muscle fibres are greatly reduced in number by replacement with fibrous tissue. Angina may occur, while there is no breathlessness on exertion, because the muscle, though overworked, still keeps up the circulation. When the circulation fails angina may disappear, to reappear when the circulation is restored by treatment. However, the commonest condition is, undoubtedly, the simultaneous occurrence of both pain and breathlessness after exertion. On the analogy of experimental pain produced in a limb by muscular work when the circulation is arrested (see intermittent claudication), it has been suggested that arterial spasm is the origin of angina and this liberates a P-substance in the tissue which causes a steady pain not varying in intensity with the heart-beats. The P-substance may be incompletely oxidised metabolites of low molecular weight, which act by the osmotic pressure they produce and disappear fully oxidised, when the oxygen supply returns. Amyl nitrite, which relieves all but the severest type of pain (*i.e.* that due to infarction) in a few seconds, acts by dilating the coronary arteries and in some patients alters the electro-cardiogram, making the T-wave upright (**28**). It also increases the pulse rate, but though it causes a peripheral vaso-dilatation, with marked flushing of the face, this cannot be the cause of the relief, because it often happens that the relief occurs before the blood pressure falls. In a case of mitral stenosis and regurgitation, with pain beneath the nipple, amyl nitrite also caused relief.

Symptoms. The patient is seized quite suddenly with acute pain in the front of the chest, situated beneath the upper or lower part of the sternum, or rather to the left-hand side of it, but not over the heart itself. The pain radiates thence to the left side and back, or through to the scapula ; up to the left shoulder, and down the left arm to the hand ; or less frequently the pain is on the right of the sternum and radiates to the right shoulder, arm, and hand. The pain may occur simultaneously on the right and left side. It may ascend on either side of the neck as high as the scalp, and this is explained by the fact that the trigeminal nerve is the sensory counterpart of the afferent vago-glosso-pharyngeal nerve from the heart and so becomes the seat of " referred pain " (**30**). The pain may be felt in the throat. The pain in the chest is described as " tearing " or " piercing," or " burning as hot as fire," or " constricting." Tingling or numbness may accompany the pain in the arms or fingers. There is considerable variety in the onset of the pain in different cases : thus it may begin in the arm or arms and spread up to the chest ; or it may begin in the upper abdomen (epigastric angina) or lower down in the abdomen (angina abdominis). In one such case the pain was brought on by exertion, was most severe in the umbilical region to which it was at first confined ; but it gradually increased in severity, and spread all over the front and back of the chest. During the attack the patient's expression is anxious or solemn ; he is obliged to stop if he is walking, and he remains quiet ; he becomes covered with clammy perspiration ; the saliva may be increased ; there may be a sense of impending death. The pulse is usually unaltered, but it may be slowed, or irregularities such as extra systoles may be noticed ; it becomes quick towards the end of a fatal attack. There is no characteristic alteration in the blood pressure ; in some cases it is raised by 20 mm. or so. After lasting a few seconds or minutes, the pain quickly passes off, but it may occur again frequently in the course of a few hours, or it may not be experienced again for several months or years. Angina may be fatal in the first and only attack. Between the attacks, and lasting for weeks after the severe attacks have finally ceased, tenderness may be experienced on pressing various spots on the chest wall and arms. These spots vary from day to day. At the same time the patient's attention may be drawn to sensations of fulness or compression inside the chest, which should be regarded as warning signs that the severe pains may come on unless care is taken.

The attack is often accompanied by a feeling of fulness in the stomach, particularly if it is brought on by exercise after a meal, and it may be relieved if wind is successfully eructated. The frequency of this symptom has led to the view (**31**), which, however, few people accept, that the primary cause of the trouble is distension of the stomach or œsophagus with wind. In one observed case (**32**) attempts at eructation regularly relieved the pain, but it was found by X-rays that air had entered the stomach. There is, however, a very close reflex connection between the seat of angina and the upper alimentary tract, since a full meal will precipitate an attack, and some of the pains felt during anginal attacks are produced in the œsophagus, and may be momentarily accentuated or relieved by swallowing. This is to be explained by the peristaltic wave which passes down the œsophagus after swallowing (**32**). John Hunter made a clinical observation on this subject in his own case. The term " pseudo-angina " may perhaps be used for such pains. Angina is sometimes associated with Raynaud's disease.

In angina minor, the patient, as the result of exercise or of exposure to cold, may feel some substernal pain for a few seconds, and be obliged to remain still. These attacks have sometimes incorrectly been called " pseudo-angina " ; but this term should not be used in this connection, as it tends to mask the gravity of the condition.

Diagnosis. The character of the pain, its occurrence as the result of exertion, its relief by amyl nitrite, and the evidence of a cardiac or arterial lesion (valvular disease or arteriosclerosis), are generally conclusive. It must be distinguished from cardiac pain felt over the præcordia, which is so common an

accompaniment of a heart failing from valvular disease or myocardial degeneration. It must be distinguished from neuralgic pains, especially in neurotic women. In this case the pain often occurs during rest, lasts much longer than angina, and may be accompanied by tumultuous action of the heart and palpitation. The milder forms of angina are frequently mistaken for indigestion, or gastritis; and this is partly accounted for by the fact that an attack often occurs when the patient gets about after a meal. Tobacco angina presents rather similar features to angina pectoris. Very severe pain may be caused by thrombosis of a coronary artery as described later. The pain, however, is continuous; the patient is dyspnœic and often restless. The pulse becomes feeble; there is pyrexia and a leucocytosis and sometimes pericardial friction which settles the diagnosis. Finally, acute distension of the stomach has caused similar symptoms, and this has been relieved by passing a tube into the stomach.

Prognosis. Death may occur during, or shortly after, an anginal attack, or during sleep, or suddenly. It may occur from heart failure or independent causes. The outlook depends on how well the case responds to treatment. A patient may have an attack and yet with proper care live for years afterwards. Unfavourable signs are a poor response to exercise, pulsus alternans, and certain alterations in the electro-cardiograms (*see* p. 231), which all help to indicate that the functional power of the heart is below par.

Treatment. The patient must remain quite still during an attack. The most efficacious drug for an attack of angina is nitrite of amyl. From 3 to 5 minims are contained within a small glass capsule, covered with linen: the capsule is crushed between the finger and thumb or forceps, and the vapour is inhaled freely. The face flushes, the cranial vessels throb, and the pain is often relieved at once. The dose may have to be repeated. A good effect is also obtained by placing a tablet of nitro-glycerine gr. $\frac{1}{100}$ to $\frac{1}{12}$ in the mouth and chewing it, when absorption takes place. The first administration of even small doses of nitro-glycerine is often followed by a throbbing headache, but after a time tolerance is established, and the larger doses can be borne. Sodium nitrite ($2\frac{1}{2}$ grains in tabella) and erythrol tetra-nitrate (1 grain in 1 drachm absolute alcohol suitably diluted) are also good vaso-dilators. If these measures fail, the hypodermic injection of morphia may be used; and much collapse will require brandy or ether. Morphia is specially useful when the attacks are precipitated by excitement or mental anxiety. Sal volatile diluted with an equal volume of water may be useful when the attacks are precipitated by a full stomach or are accompanied by flatulence. Repeated attacks have been stopped by the oxygen tent.

When angina has once declared itself in a patient, absolute rest in bed for some weeks and freedom from anxiety and excitement will be required. Food should be given in small amounts at a time. On getting about again the patient's life must be altered so as to avoid those factors—excessive muscular exertion, etc.—that have caused the attack. In regulating his life he will be helped by the premonitory sensations of fulness and compression in the chest which will appear if he is again beginning to do too much. The attacks should be arrested in the first place by drugs; but later on it is probably best not to use nitrites prophylactically, as they may remove the patient's warning signs, so that he may be led to overwork his heart again, and this may lead to circulatory failure. Amyl nitrite or tablets of nitro-glycerine should be carried for an emergency. Smoking in excess must be stopped; some patients are so sensitive to tobacco that one or two cigarettes a day may keep up attacks. In severe cases, where the reserve of the heart is low, such treatment may fail to ward off attacks, and these will still come on whenever the patient gets about at all. In such a case nitro-glycerine will be valuable; the dose may be $\frac{1}{100}$ minim three or four times daily, gradually increased to $\frac{1}{20}$ or $\frac{1}{10}$. Iodide of potassium (5 to 30 grains) is also beneficial in some cases. Syphilis must be treated as already described. In

diabetes mellitus a high carbohydrate diet and insulin should be given. The exposure of the body surface to light from the electric arc has sometimes warded off attacks. Ammonium bromide in doses of 10 to 20 grains is useful as a mental sedative. Surgical treatment, *i.e.* division of the depressor nerve, etc., is not to be recommended in the present state of our knowledge.

The association which has been found between angina and acute engorgement of the heart and lungs from left-sided failure suggests that forcible expiration against a closed glottis may stop an attack by emptying the heart and lungs into the systemic circulation. Personal observation of the writer proves that this is the case, at any rate, for mild left-sided pains. Slow deep respirations are also useful. The reversed process of forcible inspiration *may* have an application for certain right-sided pains. The patient should be taught to carry out these manœuvres ; they can certainly do no harm.

INFECTIVE ARTERITIS

Acute Arteritis. Acute infection may approach the artery from without (*initial peri-arteritis*) or from within (*initial endarteritis*). The former is caused by the direct spread of the infecting agent from some neighbouring suppurative focus or wound. Initial acute endarteritis of the larger arteries may be due to invasion of the wall by organisms carried in a septic embolus which has become impacted in the lumen or to spread of infection from adjacent septic vegetations as in malignant endocarditis affecting the aortic or pulmonary cusps. By whatever route the infecting agent reaches the vessel wall, the whole thickness of the latter may speedily become involved. Histologically, the appearance will be that of acute inflammation, and, depending on the degree of damage, the softened wall may bulge (*mycotic aneurysm*) or may perforate allowing blood to escape.

Polyarteritis Acuta Nodosa. Having used the term acute peri-arteritis, mention may fittingly be made here of a very rare condition (also called peri-arteritis acuta nodosa), the more so as it is also probably due to an acute infection, although the nature of the latter has not been determined. Many of the small arteries in the body may be affected, especially those of the heart and kidneys. The affected vessels are the seat of small nodular swellings, which are really small aneurysms with or without an accompanying thrombosis. The initial lesion appears to be a focal necrosis of the media with a surrounding acute inflammatory reaction which involves all three coats. Thrombosis may occur or the softened wall yields, bulges outwards (aneurysm) and frequently ruptures, allowing blood to escape.

Tuberculous Arteritis. The two commonest causes of chronic infective arteritis are the tubercle bacillus and the Treponema pallidum. In the vicinity of a *tuberculous* focus the wall of an artery may become involved as a result of the direct extension of the caseo-granulation process. The affected wall shows the usual features of a tuberculous lesion, and the lumen may become obliterated by proliferation of intimal or endothelial cells with or without a concomitant thrombus.

Syphilitic Arteritis. In the case of *syphilitic* arteritis two forms are distinguished, one as found in the aorta and the other as it occurs in the small arteries, but the underlying reaction is the same in both. In the former the inflammatory process instigated by the treponema starts in the adventitious coat in relation to the vasa vasorum whose lumen becomes narrowed or obliterated by a proliferation of its lining endothelial cells. The perivascular round-celled infiltration follows the course of the vasa vasorum and so spreads into the middle coat of the aorta. Small areas of muscle cells and elastic tissue undergo necrosis, and with the foci of lymphoid and plasma cells constitute microscopic gummas. The intima in relation to such an area becomes thickened by proliferation of the intimal cells and vascularised by the budding of young capillaries, which grow into the thickened area. Later, as the result partly of absorption of the necrotic

débris and partly because of contraction of the young fibrous tissue which replaces the vanished musculo-elastic tissue, scarring is seen on the inner surface of the aorta. In this way inelastic fibrous tissue replaces the musculo-elastic tissue of the media on which the efficiency of the arterial wall depends, and the latter, where fibrosed, gradually becomes stretched. This is the genesis of an aneurysm. Owing to the fact that the gravity of the lesion depends on the amount of damage to the middle coat, syphilitic disease of the aorta is frequently spoken of as a mesaortitis although it is primarily a lesion of the vasa vasorum.

The affected aorta will show patches of thickening as well as very definite scarring, and it is this latter that serves to differentiate macroscopically a syphilitic lesion from the lesions due to atheroma which, of course, may also happen to be present.

In the case of the small arteries the adventitious coat also shows a small round-celled infiltration. The media is little affected, but the intima shows very definite changes. It becomes greatly thickened as a result of proliferation of the connective tissue cells of the intima. Fibrous laminæ and new elastic tissue are laid down and the lumen becomes greatly narrowed and even obliterated. This process of obliteration may be hastened by thrombus formation. A favourite site for this form of syphilitic disease is the brain-vessels, especially the cortical branches. Syphilitic endarteritis plays an important part in relation to the necrosis which occurs in gummas, and, on the other hand, a gummatous process may, by direct extension, come to involve a small artery in the vicinity hitherto unaffected.

Thus tuberculous and syphilitic endarteritis both tend to bring about obliteration of the lumen and hence they are examples of what is called *endarteritis obliterans* or *proliferans*—a process which may be brought about in other ways than those just mentioned. For example, the term may be applied to the physiological closure of arteries that are no longer necessary. This happens in the case of the umbilical arteries, the ductus arteriosus, many of the uterine vessels after parturition, the ovarian vessels at the menopause, etc. In these cases there is a gradual thickening of the intima, the lumen becomes obliterated and the muscle cells undergo atrophy.

Thrombo-angiitis Obliterans. Another type of endarteritis goes by the name of thrombo-angiitis obliterans. This particular type of arterial disease occurs chiefly among adult Jews of young or early middle age, especially those from Eastern Europe. It is not due to syphilis, but excessive cigarette-smoking may be partly responsible. The blood pressure is not raised. The exact pathogenesis is not clear. There is, however, considerable proliferation of the cells of the intima, which accordingly becomes progressively thicker. Along with this or antecedent to it thrombosis occurs, and later the thrombosis becomes organised. There are no inflammatory changes in the outer coat, and only occasionally does the middle coat show degenerative changes. The nutrition of the part supplied by the diseased artery, though defective, is still possible. Intermittent claudication and erythromelalgia are characteristic symptoms.

Periarteritis nodosa is a rare condition of degeneration of the media, proliferation of the intima, often associated with thrombosis, and granulomatous periarteritis ; the veins are also affected and the condition may be widespread in the body.

CHRONIC ARTERIAL DEGENERATIONS

Senile Degeneration (*Medial Degeneration*). In old age small foci of calcareous material may not uncommonly be found in the middle coat of arteries on the site of degenerated muscle cells. An extreme degree of this type of degeneration, however, is called *Mönckeberg's sclerosis*. It affects chiefly the larger arteries, especially the iliacs and femoral vessels, and occasionally also the lower part of the abdominal aorta, and may cause senile gangrene. The initial change appears to be a hyaline degeneration of the muscle and connective tissue

cells of the media. This degeneration is succeeded by the deposition of lime-salts in the degenerated bands of muscle tissue, so that, in the course of time, the middle coat comes to be replaced by more or less conplete rings of calcareous material. The affected artery becomes, in consequence, more or less rigid and may be slightly dilated. Atheroma may be present in the intima, but there is no inflammatory reaction around the calcareous material.

It is essentially an arterial degeneration of old people, and must not be confused with the calcification that frequently occurs in the intima in relation to atheromatous *débris*.

Atheroma (*Athero-sclerosis, Nodular Sclerosis*). This condition was at one time called endarteritis deformans, but inasmuch as the initial change is primarily and sometimes solely a degenerative one, the term endarteritis is not now heard so often. The degeneration is essentially patchy in its distribution, though, in the smaller arteries, it may be more diffuse.

There is still considerable doubt regarding its pathogenesis, but probably the initial change is a local degeneration characterised by the appearance in the intima of cholesterol, fatty and lipoid substances. Along with this, either as a result of irritation produced by the necrotic *débris* or as a compensatory measure, there frequently occurs a thickening of the intima over the degenerated focus, so that the latter comes to lie in the deepest part of the intima and contiguous to the media. The intimal proliferation and sclerosis may cease and the degenerative process may extend towards the lumen, in which case the intima may finally give way, and what is called an " atheromatous ulcer " forms. Very occasionally the media, where it is adjacent to the degenerated intima, may also undergo fatty degeneration, but it must be emphasised that this is merely an occasional and purely secondary occurrence. The degenerated area in the intima contains, as has been stated, cholesterol, fat, lipoids, etc. Some of these may become converted into soaps, and later calcification occurs, so that occasionally, especially in the lower part of the abdominal aorta, large calcareous plaques may be found. Hence in atheroma of the aorta we may see a variety of lesions.

Thus yellow patches marking the site of fatty deposits in the intima may coexist with opaque whitish cushions, the result of fibrous thickening of the intima obscuring the fatty *débris* below them. Along with these we may see superficial erosions of the fattily degenerated intima (atheromatous ulcers) or calcareous plates frequently pigmented by the remains of broken-down erythrocytes and sometimes covered by a mural thrombus. Occasionally, where the media has been partly involved in the degenerative process the weakened wall may undergo some degree of stretching. Occasionally also a calcareous plate may crack across and so allow blood to force its way between the coats of the artery (dissecting aneurysm). There are, however, no puckered scars unless syphilitic mesaortitis happens also to be present. The difference in the naked-eye characters of the lesions depends on the relative proportions of lipoid degeneration and of intimal sclerosis. In the aorta such patchy nodular thickenings may do relatively little harm, but in the case of the smaller arteries it is quite another matter. These small arteries show much the same type of lesion. It is essentially focal, but may be more diffuse. The nodular thickenings of the intima project into and deform the lumen, which readily becomes obliterated by thrombus formation, so leading to infarction. Where the media is secondarily involved irregular dilatation occurs and the vessel may rupture, especially in places such as the brain, where the vessel is poorly supported. The extent of arterial territory involved varies in different cases. Sometimes only the aorta is affected, sometimes only the smaller arteries or one particular group of such arteries—for example, the coronary, cerebral or renal.

This form of arterial degeneration is best seen in the older age periods, and is frequently a cause of death, but it may occur or begin at an earlier age. Mention may be made here of fatty deposits, often in the form of sheaths, which take place

in the connective tissue beneath the intima as a result of acute fevers. They have been called, probably incorrectly, " early atheroma."

Diffuse Hyperplastic Sclerosis (*Arterio-capillary Fibrosis*). This change, which is associated with increased arterial blood pressure, is usually met with in persons in the third to the fifth decades of life. The vessels affected are chiefly the small arteries and arterioles, and the initial change appears to be a tonic contraction of the media of these small arteries. Both the muscle and the elastic elements in the media undergo hypertrophy, but later they become atrophied and replaced by fibrous tissue laminæ. Along with this there occurs a proliferation of the cellular elements in the intima, which thus becomes more or less uniformly thickened. There is also a new formation of elastic fibres in the thickened intima. In the smallest arterioles the chief change is the intimal one. The lumen of vessels of this calibre becomes much narrowed and may become completely obliterated, with the result that atrophic changes and fibrosis occur in that part of the organ supplied by the affected vessel. The thickened intima in affected arterioles undergoes sooner or later a hyaline change, and fatty degeneration may occur.

Diffuse hyperplastic sclerosis occurs most commonly in the kidneys and next in the spleen and other organs, including the brain, pancreas, liver, suprarenal glands, and less often the stomach and intestines, but not the heart or skeletal muscles. The increased peripheral resistance throws more work on the heart and the left side undergoes very considerable hypertrophy (concentric hypertrophy). This condition may exist without any noteworthy renal change, or the kidneys may show a certain amount of scarring and may even be granular. These renal changes, however, are merely atrophic, depending on the cutting off of the blood supply to areas of kidney tissue (*ischaemic atrophy*). This is a *primary* diffuse hyperplastic sclerosis.

Similar vascular changes, however, may occur *secondarily* in kidneys that are primarily the seat of chronic inflammatory changes, either of a diffuse or focal type, and will add their quota to the inflammatory damage. In these cases also the blood pressure is raised and the left heart hypertrophied. It would thus appear that, owing to a previous inflammatory affection of the kidneys, some substance or substances are retained in the blood and cause a tonic contraction of the small arteries and arterioles, in the kidneys and elsewhere. The same agent or some other irritant may also be responsible for provoking the other changes already described. However, the relations between the primary and secondary disease may be very close, since high blood pressure has been found to result from war nephritis, the nephritis itself having apparently disappeared.

ARTERIOSCLEROSIS

Arteriosclerosis means hardness of arteries. The word is often used in a restricted sense as synonymous with diffuse hyperplastic sclerosis ; but it is convenient to have a term that can be used at the bedside to embrace all the various chronic arterial degenerations just described, since exact differentiation will often be impossible during life, and it is quite likely that they are all types of the same morbid process. It is in this wider sense that the term is used in this book.

Ætiology of Arteriosclerosis. It is possible that the different types are not so much due to different noxious agents as to the different soils in which the bacterial toxins or other agents are implanted. Thus in young people the inflammatory changes result in great internal proliferation (diffuse hyperplastic sclerosis) while in the elderly or cachectic such an intense reaction is impossible, and the blood pressure remains low (senile degeneration) (**32**). Allbutt has pointed out that there is no tendency for primary arterial changes, such as atheroma and senile degeneration, to cause high blood pressures. On the other hand, diffuse hyperplastic sclerosis is associated with a high blood pressure, so that, if all cases with hard arteries are grouped together under the term *arteriosclerosis*, in some the blood pressure will be normal, in others it will be raised. Arterio-

sclerosis, in particular atheroma, is not an uncommon degeneration in the arteries of those whose occupation exposes them to severe muscular strain, and, therefore, intermittent increase in blood pressure may be a pre-disposing factor. The various factors that play a part in the ætiology are over-eating in particular of protein and fatty foods—excess of milk has been incriminated (**57**), and blood pressure is lower in vegetarians (**58**) than meat eaters—gout, alcohol and lead poisoning, malaria and other acute infections, with their bacterial toxins, particularly typhoid, hypothyroidism, Bright's disease (*see* diffuse hyperplastic sclerosis) and possibly intestinal intoxication. Arteriosclerosis may be associated with diabetes in elderly people, owing to the protein and fat diet so commonly taken, but in other cases the diabetes may be secondary, owing to the failure of blood supply to the pancreas, because the vessels are sclerotic.

Pathology. The suggestion has been made that there is primary weakening both of the muscular and elastic elements of the arterial walls; they become stretched and dilated and anatomic alterations with calcification serve the purpose of strengthening the walls and take place particularly at points where there is special strain from the whirl of the blood stream—flexures and the places where arteries branch off. Calcification means healing and rupture never takes place at these points. Elsewhere in the arterial wall the process is diffuse. The rise of blood pressure is secondary (**59**).

Symptoms. In the earlier stages the artery is palpable, and can be rolled under the fingers when all the blood has been squeezed out of it by pressure from the fingers. The artery feels thick. In the later stages the wall may feel hard from calcification. The transverse diameter may be increased, and the vessel may become tortuous, owing to lengthening of the artery. Pulsation is often much diminished, and sometimes is absent altogether; thrombosis may occur. Since the velocity of the pulse wave increases with the rigidity of the artery, the determination of the former by means of the " hot wire " sphygmograph should indicate the amount of arteriosclerosis in a given case.

In arteriosclerosis the coronary arteries are very commonly atheromatous, so that the nutrition of the heart muscle is affected, leading to myocardial degeneration. Consequently symptoms of early cardiac failure may be present—exhaustion, breathlessness, and pain on exertion.

Arteriosclerosis may cause local symptoms from its presence in certain organs. In the brain it may lead to thrombosis or hæmorrhage, and reproduce the characteristic symptoms. Arterial spasm gives rise to a condition that in the presence of albuminuria resembles uræmia and has been called *pseudo-uræmia* (*see* p. 303).

Prevention and Treatment. Prophylaxis consists in treating the causes of the condition. Over-eating must be avoided. Improvement may take place even when the disease is established. Rest in bed for a period should be prescribed, since the horizontal position takes the strain off the circulation. Iodides are commonly given, and these may be beneficial if there is an element of hypothyroidism present, which is not uncommonly the case. Thyroid extract may also be tried. (*See also* Treatment of Arteriosclerotic Kidney.)

HIGH ARTERIAL PRESSURE

(*Hyperpiesia*)

The normal range of blood pressure in young, healthy adults is from 95 to 140 mm. (*see* p. 229). It has frequently been taught that the blood pressure increases with the age of the patient; in fact, formulæ relating age and blood pressure have been constructed. This view arises from faulty weighing of the evidence. There are many elderly people with perfectly normal arteries in whom the blood pressure is normal. On the other hand, arterial disease, which itself often leads to a rise of blood pressure or hyperpiesia, becomes increasingly prevalent as age advances, and this explains the fact that the average blood pressure of a group of

elderly people is found to be increased. In hyperpiesia values from 150 to 300 mm. and more have been recorded. The rise usually begins in middle life, *i.e.* above thirty, and is fully developed by the time old age comes on; so that it is at this period of life that it is most commonly met with; but it has been seen in infants, and even in the new-born. It affects males more than females. The ætiological factors described under arteriosclerosis may be responsible.

Pathology. Arterial pressure is within normal limits influenced by more than one factor; thus the pressure will be increased by over-action of the heart, by increased peripheral resistance, and by an increase in the viscosity (**69**) or volume of blood, though an increased volume is probably always a temporary condition. However, the main cause of hyperpiesia is an increase in the peripheral resistance, at first, perhaps, due to spasmodic contractions of certain arterioles; but later on in the fully established form it is due to swelling of an inflammatory character in the walls of the arterioles, which has already just been described under the heading *diffuse hyperplastic sclerosis* (*q.v.*). The red cells and hæmoglobin of the blood are greatly increased in some cases (polycythæmia), and the high blood pressure in these cases may be partly secondary to the increased viscosity of the blood.

An investigation on a normal man, whose systolic blood pressure was actually below 100 mm., showed a rise of about 10 mm. through the day and a corresponding fall during the night. The rise was chiefly due to taking tea, coffee, and to smoking. Exercise, mental work, worry and excitement increased the rise, and alcohol diminished it. A marked rise was observed during a holiday in the Alps (**34**). This suggests that the lack of oxygen, due to the rarefaction of the air, stimulates the vasomotor centre. Experimentally, hyperpiesia has been induced in dogs by injecting certain colloidal preparations into the ventricular system of the brain; these clog up the Pacchionian bodies through which the C.S.F. is filtered off into the venous sinus; there is a permanent rise of C.S.F. pressure and a secondary rise of blood pressure (**17**). A pressor substance has been found in the urine in a young patient (**68**). The suggestion has been made that the liver is at fault in not destroying a toxin, since when the blood urea and non-protein nitrogen are normal, indicating unimpaired renal function, there is a raised amino acid, uric acid, and cholesterol content in the blood, there is more ammonia nitrogen in the urine compared to the urea nitrogen than normal (ratio under 1 to 30), and there is an increase of urinary indican (**71**).

Symptoms. In the early stages of the disease, at any rate, in some cases, the hyperpiesia is not constant, but occurs spasmodically. Later this condition is permanent. The patient may complain of headaches, insomnia, tinnitus aurium, and giddiness. Pain at the back of the neck near the occiput is very characteristic. The characteristics of high tension are: (1) the records on the instruments employed (*see* Fig. 13B, p. 226); (2) the sensation to the finger of a firm well-filled artery, with long-sustained systole, never completely empty during diastole, capable of being rolled under the finger, but not necessarily palpable as a thick structure when emptied by pressure of the finger; (3) the evidence of enlargement of the heart and forcible apex beat; (4) the modified heart sounds, lengthening and muffling of the first sound at the apex, and accentuation or ringing character of the second sound in the aortic area.

(5) Ophthalmoscopic examination often provides a valuable means of estimating the degree of arterial changes since it is possible to infer from the appearance of the retinal arteries what is the condition of the cerebral arteries. In an early stage the ophthalmoscopic changes are confined to the arteries. In general, the lumen is reduced in size when compared with the veins. The walls of the retinal arteries normally reflect the light to some extent, and this is seen as a bright streak along the middle of the vessel. In arteriosclerosis this reflection is increased owing to the thickness of the walls, and the smaller arteries appear burnished like *copper wire*, and later on, as the opacity of the wall increases,

they look bright like *silver wire*. This bright streak is often irregular and has a dotted appearance. The arteries are tortuous, but owing to extreme variability of the normal artery in this respect this feature is of no value in diagnosis; their lumen is irregular; they are often greatly reduced in size, sometimes looking like fibrous threads. Sometimes they are of normal width, but are sheathed in places by white plaque-like deposits which look like pieces of pipe stem; these may disappear after a time. Characteristic appearances are seen at the arterio-venous crossings. The line of the vein is displaced if it crosses the artery obliquely, so that it lies along the artery for a short distance on each side of the crossing. When the artery crosses in front of the vein, the latter seems to disappear at the crossing, because it becomes hidden behind the thick walls of the artery. The veins are pressed upon, so that there is a swelling of the vein on the distal side of the crossing, but this appearance, called "banking," is by no means very common (*see* Plate 14).

The retinal appearances (*arteriosclerotic retinitis*) are similar to those met with in chronic Bright's disease. Small flame-shaped areas may be seen, due to minute hæmorrhages in the nerve fibre layer; when present in the deeper layers of the retinæ the hæmorrhages are roughly circular. In a later stage there may be small bright spots with sharply defined edges scattered about, very often in the macular region, round which they may form a rough *star*-figure, or they may lie between the macula and the optic disc as a fan-shaped figure. They may be grouped round the radicals of the retinal veins, but more often they are scattered irregularly about. Often a large number are grouped together so closely as to resemble a piece of mosaic. Histologically these patches consist of round or oval masses of hyaline exudate in the internuclear layer of the retina. It is perhaps possible to regard them as of essentially the same nature as white infarcts due to blocking of the smaller branches of the retinal arteries.

Probably, in the majority of cases, the retinal changes persist until the patient's death; but improvement may take place, effused blood being absorbed, and even the spots of degeneration disappearing. In the earlier stages there is no loss of vision. Gradual impairment of vision may be due to degeneration of the nerve elements in the retina from defective blood supply. The fields of vision may become restricted. Optic atrophy may be seen and may be preceded by some slight swelling of the disc. Sudden temporary loss of vision (*amaurosis fugax*) has been attributed to spasm of the thickened retinal arteries (described later). Sudden permanent blindness, quite painless, may result from thrombosis of the central retinal artery. The retina appears pale; the macula shows up in contrast as a cherry-red spot. The blood column in the vessels is broken up into small blocks of red cells with intervening clear spaces of plasma (cattle-truck appearance).

Most of the other conditions found in these cases are not so much evidence of the high tension as the results of the circulatory difficulties which ultimately supervene in the worst instances. They are slight albuminuria, due to secondary renal involvement (*see* arteriosclerotic kidney, p. 532), though in most cases the blood urea is either not at all or only a little raised, and there is usually little or no impairment in the kidney function; hæmorrhages in different parts of the body, as, for instance, epistaxis, hæmoptysis, retinal and vitreous hæmorrhages, and possibly small cerebral hæmorrhages, bleeding from piles, angina pectoris, itching, cramps in the calves of the legs.

The *hypertensive cerebral attack* or *encephalopathy*, also called *pseudo-uræmia*, is rather characteristic. There is a rapid rise of blood pressure before the attack, which may be due to spasm of small cerebral arteries or sometimes to cerebral œdema. The symptoms are transient pareses of muscles, convulsions, aphasia, blindness, hallucinations, delirum, stupor and coma. This symptomatology is still further described under the heading *chronic cerebral softening*.

In many cases of primary hyperpiesia there is a high degree of congestion of

the surface blood vessels. Such persons with advancing years may have the appearance of robust health, from the rich colour of the face, and may seem to be only instances of the somewhat florid colour which so many healthy old persons present. Dieulafoy notes the increased sensibility to cold (*cryœsthesia*, κρύος, cold) which these patients suffer; there may be dead fingers or the cold is felt in the lower extremities, and drives the patient to wear thick clothing, even in the warm seasons. In a patient of the writer's, hyperpiesia led to gangrene of both lower limbs. These cases terminate eventually from an attack of coronary thrombosis or cerebral hæmorrhage, or failing heart, with dropsy and œdema of the lungs, and occasionally from uræmia—cases of so-called "malignant hypertension." In coronary thrombosis and cerebral hæmorrhage death may be sudden.

Treatment. If the cause of the high blood pressure can be recognised, attempts must be made to remove or reduce it. Where there is good reason to believe that the mode of life is contributing to the result, help may be sought by the avoidance of butcher's meat and highly nitrogenised foods or those containing purin bodies, by abstention from alcohol, tea, and tobacco, and from excessive mental or physical strains. It is advisable to give calomel (2 or 3 grains) or blue pill (3 to 5 grains) as an occasional purge, followed by a morning laxative saline. The blood pressure is often reduced promptly when the patient is compelled to take complete rest in bed. Vaso-dilators, like nitro-glycerine, amyl nitrite or sodium nitrite will be useful if angina occurs. Potassium iodide is commonly given; and massage, muscular exercises, high frequency currents, and hydrotherapy will sometimes be beneficial. Since the high blood pressure is probably compensatory to a lesion of the arteries or to chronic toxic nephritis, no attempt should be made to lower it by drugs. Digitalis is not suited for early stages, but may be helpful when the heart has reached an advanced stage of dilatation and there is œdema. The oxygen tent is useful in such cases. In cases of hyperpiesia with high hæmoglobin the question of venesection should be considered, especially if symptoms such as headache are present. Relief may be obtained by removing a pint of blood, and this may be repeated at intervals. Venesection may also be employed when there is failure of the heart. (*See also* Arteriosclerotic Kidney.)

INTERMITTENT CLAUDICATION

In this condition of intermittent limping or *claudication* the patient finds that after walking a certain distance he has weakness in one or other leg, with stiffness, heaviness, numbness, pricking sensations, pains and cramp, so that he necessarily limps in his gait. The painful sensations increase as he progresses, and he is at last obliged to stop. The foot or leg shows signs of circulatory disturbance; it becomes red, often with a cyanotic tinge, mottled, and swollen; and the toes may be white and "dead." After a period of rest the symptoms gradually subside.

The symptoms are due to the affected arteries being unable to carry the increased flow of blood that the limb requires during muscular exercise. In nearly all there is an absence of pulse in the dorsalis pedis artery, or in the posterior tibial of the affected limb (**39**). The blood pressure is sometimes high. In some cases slight muscular wasting and degeneration of the peripheral nerves (peripheral neuritis) have been observed. In many instances the complaint has resulted in dry gangrene of the limb, and it has been associated in a few cases with Raynaud's disease of the upper extremities. The cerebral vessels are sometimes affected with transient hemiplegia and other paralyses, blindness, headaches, and mental symptoms.

Ætiology. In the majority of cases there is evidence of sclerosis of arteries or veins, or of obliterative arteritis or atheroma, or thrombo-angiitis obliterans (*q.v.*) In such cases as do not present any evidence of arteriosclerosis or obliterative arteritis, it is assumed that the condition is due to arterial spasm. It is a disease of adult life; and gout, diabetes, and syphilis, and indulgence in

tobacco or alcohol are often among the antecedents. It is more common in men than in women.

Pathology. It has been shown that if some muscles of a limb are exercised, when the circulation to the limb has been stopped by a tight bandage, pain will be produced in those muscles, and the pain is due to some substance—the P factor—which is liberated from the active muscle into the surrounding tissue spaces and which disappears when the oxygen supply is increased.

Prognosis. Apart from the possible onset of gangrene or other results of arteriosclerosis, the disease is not dangerous. Relief from symptoms depends on the power of the artery to dilate; this may be tested by warming up another part of the body, *e.g.* by a hot-air bath over the trunk or plunging the whole of both upper extremities in a hot bath, when the normal reaction is a rise of the skin's temperature of the legs (**72**). No operative treatment should be undertaken unless this reaction is obtained.

Treatment. The patient must limit his exercise, and avoid quickening the circulation up to the point at which the obstruction in the vessel will begin to operate. Frequent rests in bed may be advisable. Iodide of potassium, sulfarsenol, etc., may be tried in syphilitic cases, and the local remedies used in Raynaud's disease may be employed here, also the constant current, electric baths, warm baths, high frequency currents, and gentle massage. Diathermy applied to the trunk has proved of value. Administration of CO_2, 5 to 7 per cent. with air, in the horizontal position, so as to cause deep breathing for fifteen minutes several times a week has been of benefit.

If gangrene occurs, the pain may be relieved by morphia, and the part should be amputated at a suitable opportunity. The condition of the arteries, *i.e.* the amount of calcification present, may be determined by radiography, and this will help in deciding whether amputation should be performed high up or low down. Gangrene and threatened gangrene have also been treated by removing the sympathetic nerves round the artery, so as to prevent arterial spasm and by injecting alcohol round the artery (**40**). Lumbar sylopathectomy in thromboangiitis obliterans produced good results in nine out of sixteen cases (**65**).

ERYTHROMELALGIA

In this condition, first described by Weir Mitchell, there are attacks of acute pain in the feet and legs associated with, or followed by, dilatation of the blood vessels, the part becoming bright red or deep purple in colour, with shiny surface, prominent veins, and perhaps sweating. The upper limbs and trunk are also sometimes affected. The pain is acute, burning and throbbing. The attacks are brought on and aggravated by heat, exercise, and a dependent position of the limbs; and some relief is obtained by cold and by elevation of the limbs. The attacks last at first a few hours; but with the progress of time they are more persistent, and perhaps at the same time less severe. It occurs in men of early middle age, and rarely in children.

Two of Mitchell's cases subsequently developed spinal symptoms, and other cases have been seen to be associated with tabes, syringo-myelia, and disseminated sclerosis. Some cases of erythromelalgia appear to be due to ergotism and thromboangiitis obliterans. In the latter disease the erythromelalgia has been associated with intermittent claudications, and it has been suggested that it acts as a compensatory mechanism whereby the blood supply to the part is increased by dilatation of capillaries. Erythromelalgia has been observed in the arsenical poisoning of beer-drinkers.

The treatment is mainly symptomatic: by cold, suitable position, and the use of morphia. Faradism and massage have also been of use.

Acroparæsthesia.—In this there are disagreeable or painful sensations, tingling or numbness, or " pins and needles " in the hands and feet. It may be accom-

panied by vasomotor disturbances. It is more common in women than in men. The disagreeable sensations are felt usually in one or both arms when the patient wakes in the morning, and after a time the symptoms subside. Sometimes the hand is paler or redder than normal, or even swollen. In a few cases there appears to be a sufficient cause in much use of the hands in some occupation during the day, or in a faulty position of the arms during sleep; but often no cause can be discovered. The pathology is not clear: it has been attributed to vasomotor spasm, but in many cases there is no evidence of this. It has been seen in general paralysis, tabes dorsalis, and allied disorders; but as a rule it is independent both of these and of hysteria. The treatment consists of rest, tonics, potassium bromide at night, and the constant current.

ANEURYSM

This name (ἀνευρύνω, to widen) is applied to dilatation of an artery for a more or less limited extent of its course. Aneurysms are divided, according to their shape, into *fusiform* and *sacculated*, the fusiform being a more or less uniform dilatation of the whole circumference of the vessel; the sacculated forming a globular projection from one side of the vessel, and connected with it in advanced cases by a constriction or neck. Sometimes, especially in the limbs or the abdomen, a sacculated aneurysm ruptures at a prominent point; blood oozes slowly out into the tissue around and forms a coagulum, bounded by a kind of cyst of inflammatory tissue. This has been called a *diffused* aneurysm. Lastly, a *dissecting* aneurysm is formed when at a part of the artery affected with atheroma the blood penetrates the inner and middle coats, and forces its way between them and the outer coat.

Ætiology. Aneurysms arise from any cause that weakens the vessel at one point. A common cause is atheroma, especially in the large vessels, in which the inner and middle coats are weakened, and the whole wall yields to the pressure of the blood at that point. In smaller vessels, such as those of the brain and lungs, the vessel may be weakened by the local causes of arteritis already mentioned—viz. embolism or the invasion of tubercle. Surgical injuries of the outer coat also lead to aneurysm. Irritation is another predisposing cause, and accounted for the frequency of popliteal aneurysm in the old days, when horse-riding was more common than at present. Of the more general causes disposing to aneurysm syphilis holds an important place, and probably also excessive strain acting through the circulation.

Morbid Anatomy. The following description of results applies chiefly to the sacculated forms. One result is the *coagulation* of the blood in the sac itself. As this is out of the direct current, it moves more slowly, and its coagulation is favoured by the roughness of the aneurysmal sac. The sac thus becomes lined, or nearly filled, with successive layers of pale buff fibrinous deposits; and it is by the complete filling of the sac with these fibrinous layers that aneurysms may be obliterated and cured. The greater the freedom of communication with the main vessel, the less the liability to the formation of fibrin; and in a fusiform aneurysm no deposits take place.

Another result of aneurysm is its *pressure* upon the parts around it. The sac may attain an enormous size; an aneurysm, of which there is a model in the museum of Guy's Hospital, springing from the aortic arch, measured 8 inches in diameter.

A third effect of aneurysm is *hæmorrhage*, which is often the cause of death. Ruptures into hollow viscera and serous cavities are often rapidly fatal. Ruptures into connective tissue or intermuscular spaces are often much slower in their effects, and in the limbs may allow time for successful treatment.

Symptoms. They may be divided into those common to all aneurysms and those determined by the locality.

in twelve months, the average duration being increased by those cases where life is greatly prolonged. This applies to males and females. In the case of single aneurysms the duration of life increases with age; but the reverse is true when the aneurysms are multiple (**65**).

Treatment. The treatment of aneurysm in the chest generally resolves itself into—(1) rest; (2) restricted diet; (3) the use of anodynes and sedatives; (4) iodide of potassium. Absolute rest has been urged by some, the patient being in the recumbent position, and not allowed to sit or stand up for any reason whatever. However, the wisdom of such a course is very doubtful, especially as in many cases the myocardial changes ultimately cause death. However, it is very important to avoid excessive exercise. The diet which was recommended by Tufnell, who strongly advocated absolute rest, consisted per diem of 10 ounces of solid, including 3 of meat, and 8 ounces of fluid, divided into three meals; but it is extremely trying, and few patients will submit to it. It is suggested that a high-protein diet will increase fibrin formation in the sac. Opium or morphia is generally given to ease pain, to produce sleep, or calm restlessness, but other sedatives may also be of use, such as bromide of potassium, chloral, paraldehyde, or sulphonal. Pain may also be relieved by belladonna applications, or by cold, or by venesection to a small amount. Iodide of potassium appears to have a special influence upon the coagulation of blood in aneurysms, as great improvement in diminution of pulsation and of pain has followed its use, even though unassisted by restriction of diet. It may be given in increasing doses, up to 60, 90, or 100 grains daily. Colt has devised a simple method of "wiring" an aneurysm. A trocar and cannula is introduced into the sac after anæsthetising the skin. If there is a free flow of blood a closed set of wires in a container is introduced through the cannula, and, on entering the sac, they open out in the form of an umbrella to induce clotting. A remarkable success has been reported by Theodore Thompson, but in two or three cases the writer has found that no blood issues from the sac in spite of there being well-marked expansile pulsation.

ABDOMINAL ANEURYSM

Pathology. The usual seat is between the diaphragm and the origin of the superior mesenteric artery, and it often involves the origin of the cœliac axis. In its growth it may interfere with adjacent organs, press upon the vena cava, or erode the vertebræ. Aneurysms of the superior mesenteric, or of the iliac arteries, are less common, and will not be specially considered here.

Symptoms. These are pain, the presence of a pulsating tumour with murmur, and sometimes evidences of pressure. The *pain* is situate in the abdomen, is often severe, paroxysmal or neuralgic in character, and may radiate to either side, into the groin or the back. The *tumour* varies with the seat of the lesion; it is more common in the epigastric region, in the middle line or slightly to the left; it is globular or ovoid, pulsatile, and expansile; it is scarcely, if at all, affected by the movements of the diaphragm. A systolic murmur can generally be heard over it. The pressure signs other than pain are not common, since the several organs readily yield to its progress. The average age of onset is thirty-six years in males, and the average duration is eighteen months, the median being thirteen months. Death may result from rupture of the sac into the retro-peritoneal tissue, into the peritoneum, or into one of the hollow viscera.

Diagnosis. It is very common to feel a pulsation of the normal aorta in women on palpating the abdomen, particularly if the muscles of the abdominal wall are weak. This is often mistaken for abdominal aneurysm by the inexperienced. Abdominal aneurysm must also be distinguished from tumours lying in front of the aorta, especially *carcinoma of the stomach*, or less commonly cancer about the *gall bladder*, to which pulsation is communicated from the

healthy aorta. Tumours over the aorta do not expand laterally, and are often irregular or nodulated in shape; the pulsation in some cases ceases when the patient is placed prone, or on his hands and knees, so that the tumour may fall away from the aorta. Carcinoma of the stomach is displaced more than an aneurysm by a deep inspiration.

Treatment. This must follow the lines indicated under the head of Thoracic Aneurysm. But an abdominal aneurysm is sometimes open to treatment by proximal or distal compression by the tourniquet. Colt's wires may be introduced during laparotomy.

CONGENITAL COARCTATION OF THE AORTA

In this condition, which is rare because it is rarely diagnosed, there is stenosis or complete obliteration of the aorta at the point of junction with the ductus arteriosus just beyond the origin of the left subclavian artery. If the child survives, the circulation to the lower limbs is helped by anastomosis between branches of the subclavian and axillary arteries on the one hand and the thoracic arteries and epigastric arteries on the other. The anastomosing arteries become enormously enlarged to carry the necessary amount of blood, and they form large tortuous pulsating vessels which can be felt, especially along the dorsal border and at the angle of the scapula and also elsewhere. There is high blood pressure and hypertrophy of the heart, which forces the blood through the narrow opening; there is no dilatation. X-ray shows depressions along the rib margins from pressure by the dilated arterial anastomoses. There may be systolic murmurs, laterally to the sternum from dilated mammary arteries. The abdominal aorta and iliac and femoral vessels may be devoid of pulsation, or pulsate but feebly, from the diminution of the force of the current by the time the blood reaches them through the narrow aorta; the difference between the blood pressure in the brachials and femorals is a valuable diagnostic point. The condition is compatible with a life of hard muscular work; sudden heart failure is prone to occur. The **diagnosis** depends on palpating the femoral arteries in all young subjects with persistent high blood pressure and feeling for anastomoses round the scapulæ (**61**).

RAYNAUD'S DISEASE

This disorder, first described by M. Raynaud in 1862 as local asphyxia and symmetrical gangrene of the extremities, is due to a spasmodic local contraction of the smaller arteries, commonly the digital arteries, whereby the circulation in the affected parts is retarded or arrested. Up to the present time Raynaud's disease has been thought to be due to vasomotor spasm, and relief in varying degree has been brought about by resection of certain parts of the sympathetic chain. Such spasm is presumably secondary to intestinal stasis, which is almost invariably present, and the symptoms can be removed by lavage of the intestines by an Einhorn's duodenal tube. Further, people with chronic constipation often suffer from cold hands and feet. From recent observations, however, it is claimed that the arteries are directly affected and that the vasomotor system plays only a secondary *rôle* (**16**), though doubt has again been cast on this (**70**).

Ætiology. It is much more frequent in women than in men, and is first noticed commonly between the ages of fifteen and thirty, or even in childhood. Cold and emotional disturbance are exciting causes. Many patients are delicate or anæmic, nervous or hysterical, but some seem to have been in good health until the occurrence of the disease. Associated with Raynaud's disease, hæmoglobinuria, peripheral neuritis, and various skin eruptions, particularly sclerodermia or sclerodactylia, have occurred. In the latter condition the skin of the fingers becomes thick, smooth and glossy, and eventually atrophies.

Symptoms. During the attack, which may be due to cold or emotion or begin spontaneously, one or more fingers turn cold, numb and painful. The colour is either white (*local syncope*) or bluish-white, violet, slate-coloured, or even black (*local asphyxia*). When the fingers are blue, pressure produces a white spot, which only slowly regains the former livid colour. The adjacent part of the extremity is often slightly swollen, and there is a livid marbling of the limb for some distance above it. The condition lasts from a few minutes to several hours. Recovery is accompanied by tingling and pricking, and the livid tint gradually passes through scarlet to the natural pink colour. During the height of the attack the arterial supply is entirely arrested, so that the shade of blue depends on the amount of blood remaining in the capillaries and venules. The "dead fingers" that occur in many normal people after exposure (*e.g.* prolonged bathing) and sometimes lead on to frost bite are not examples of Raynaud's disease

The severest stage is the condition known as *symmetrical gangrene.* During an attack, such as has been described, vesicles or bullæ containing sero-purulent fluid form on the fingers and burst, leaving small ulcers, which heal after the lividity subsides. With a repetition of this process, numerous small cicatrices may form on the affected part, and the fingers acquire a shrivelled, pinched, parchment-like aspect. The skin may desquamate, and the nails may fall off. In other cases, without the formation of bullæ or phlyctenulæ, the fingers and toes become black, shrivelled, and gangrenous; and then a superficial layer of skin, or even some portion of the deeper tissues, separates as a slough in the course of a few weeks. The most marked symptom accompanying these severe cases is intense pain, of paroxysmal character, radiating to other limbs; the pulse may be thin or compressible, but is always perceptible, and the general health of the patient may be remarkably little affected. The toes are attacked as well as the fingers, and sometimes before them; and the nose and ears may be livid, but do not often slough. When the ulcers heal, it is remarkable what slight scarring remains behind.

The attacks occur at intervals of weeks or months, and in some cases, after repeated slight attacks, the fingers remain in a permanently benumbed or shrivelled condition.

Diagnosis. Senile gangrene is distinguished by the age of the patient, by the gangrene affecting a single limb, and generally a lower limb, by its progressive course, and by the diseased condition of the artery of the limb. *Chilblains* present a certain resemblance to local asphyxia, and perhaps may have an allied pathology; they occur from definite exposure to cold.

Prognosis. The disease is not mortal. Much good may be done with treatment.

An efficient **Treatment** of Raynaud's disease consists in irrigating, at periodical intervals, the intestines with 4–6 pints of a 0·85 per cent. solution of sterile saline at body temperature through a duodenal tube, the object being to wash out the contents of the alimentary canal. Alternatively, from 1–2 pints of the solution may be drunk each morning. Intravenous injections of radium emanation in normal saline has also been advocated by Tominek (Prague). Local measures consist in keeping the hands and feet warm; friction, which may be combined with hydrological methods, such as alternative hot and cold douches; high frequency and diathermy. The most valuable drugs are iodine and thyroid. It may be advisable to remove the patient to a warm climate in winter.

PHLEBITIS

Inflammation of the veins, or phlebitis, results in thickening and infiltration of the walls with leucocytes, which may be in such numbers as to constitute a real suppuration of the coats. The terms *endophlebitis* and *periphlebitis* have been

used to indicate inflammation of the intima and the adventitia respectively. Periphlebitis arises from contact with inflammatory foci outside the vein, or from injury. Endophlebitis is most often set up as a result of thrombosis or coagulation of blood in the vein itself. This occurs from a variety of causes (*see* Thrombosis). The clot may then adhere to the vein wall, becoming at the same time organised, and the vein may be completely obliterated. On the other hand, the clot may become channelled, and allow the continuation of the circulation; or in other cases it softens down into a puriform liquid. Periphlebitis extending inwards itself leads to thrombosis; on the other hand, abscesses may form in the tissue around the vein. *Thrombophlebitis migrans* is a condition which has been diagnosed more frequently of recent years, in which veins in various parts of the body are attacked, including the viscera; the lesions probably arise from a septic focus. (For literature see **64.**)

Symptoms. Phlebitis is accompanied by pain and tenderness in the course of the affected vessel, with some reddening of the surface in the case of superficial veins. The vein can be felt as a prominent hard cord, and a varying amount of febrile reaction accompanies the local disease. The formation of abscesses will be indicated by hardening of the surrounding tissue, redness and œdema of the skin, and subsequently fluctuation. The secondary effects which result from breaking down, and transportation of the particles of thrombus, are described below.

The **Treatment** of phlebitis consists in complete rest of the part affected, the application of warm fomentations or of glycerine and belladonna to ease pain, and the administration of opiates, if necessary, for the same purpose. The risk of detachment of a thrombus must always be borne in mind (*see* Thrombosis and Embolism). If abscesses form the pus will have to be evacuated by incision.

THROMBOSIS AND EMBOLISM

Thrombosis is the name applied to the coagulation of blood within living vessels, whether arteries or veins, or in the cavities of the heart; and the clot itself is called a *thrombus*.

Embolism means the transference of a portion of clot or other substance (particles of tumour, parasites, fat globules) from one part of the circulation to another, and its impaction when it arrives at a vessel too narrow for its further progress. Embolism may take place along the arteries to the periphery of the systemic circulation, along the systemic veins and pulmonary artery to the lungs, and along the portal vein to the liver. The transferred particle is called an *embolus*.

Besides the conditions of fibrin formation which usually determine coagulation, two important factors in *thrombosis* are—(1) undue slowness of the current of the blood, whether from diminished cardiac force, from local obstruction in the vessel, or from increased viscosity of the blood, and (2) some lesion of, or irregularity on, the lining membrane of the vessel or cavity concerned; but it must be allowed that there is often an intimate relation with infective disorders in which micro-organisms or toxins may have a share, and with the conditions of health present in gout and in the puerperal state.

Thus we see that blood coagulates in the heart upon its inflamed valves, or in its cavities when dilated or contracting with extreme feebleness. It coagulates in the vessels if their walls are injured, or are in connection with septic or gangrenous processes; in the arteries especially when their walls are the subject of syphilitic or atheromatous lesions, or of aneurysmal dilatations; in the veins when the current of their blood is slowed by pressure, and with the slightest local disturbance in the subjects of various infective, cachectic, and anæmic disorders. The first step in the process seems often to be the accumulation of blood platelets

pain is not relieved by amyl nitrite nor even always by ½ grain of morphia. The former should not be given owing to its stimulating effect on the heart. Later congestive heart failure may occur with œdema of the lungs. While this is a typical history it should be emphasised that the symptomatology is not constant. The attack may begin with fainting; there may be no pain. There may be sudden death. Coagulation of blood commonly takes place on the endocardium internal to the infarcted area and this may break off and cause embolism elsewhere (**35**). The patient may or may not have suffered from angina pectoris at the time, and if he recovers may later begin to suffer from angina, presumably owing to the extra work thrown on the remaining healthy cardiac fibres. The patient may live for hours, days and even years, remaining capable of active work. John Hunter, who probably had a coronary thrombosis at forty-five, lived for twenty years (**36**). Immediate absolute rest and oxygen constitute the treatment. The oxygen tent is most successful, and may relieve pain. The differential diagnosis from angina has been dealt with.

Femoral Thrombosis. Thrombosis of the femoral vein arises in the last stage of phthisis, cancer, and other exhausting diseases, in convalescence from typhoid fever and influenza, and after confinement (" white leg "). The leg becomes swollen, and the vein can be felt to be obstructed; there is generally also some tenderness from co-existing phlebitis. The detachment of a portion of clot, followed by its impaction in a large branch of the pulmonary artery with sudden death, is an occasional accident. To prevent thrombosis in the limbs during convalescence from fevers the movements of the patient must be regulated with care. He must not be allowed to lie so that the veins are compressed. Support can be obtained with soft pillows.

Jugular thrombosis and *thrombosis* of the *lateral sinus* result from the disease of the internal ear, or mastoid cells. From contact with the external ear, septic organisms are frequently present, severe phlebitis is set up, and the clot becomes septic. Particles are then conveyed through the right side of the heart to the lungs, in which pyæmic abscesses are formed. Other cerebral sinuses (longitudinal and cavernous) are sometimes thrombosed as a result of more general conditions, such as marasmus in infants, and chlorosis and anæmia in adults.

Thrombosis of the *pelvic veins* arises from disease of the pelvic viscera in women, or from gonorrhœa in both sexes. (*See also* Thrombo-phlebitis Migrans).

Thrombosis of the inferior vena cava is not incompatible with life. In one case who lived for twenty-five years, the vein was converted into an impervious ribbon from below the entrance of the hepatic veins. Blood was returned from the kidneys by way of the capsule and the lumbar and azygos veins. There is always great varicosity of the veins of the leg and abdominal wall, with a tendency to thrombo-phlebitis, hæmorrhoids, and varicose ulcers. The causes are infection, traumatism and malignant disease (**37**).

Large clots sometimes form in the *heart*, just previous to death, when the circulation is failing, and in recesses of the walls in cases of dilatation. They may hasten death by hampering the action of the organ, or they may supply emboli to the pulmonary or systemic circulation.

Embolism and thrombosis of the *cerebral arteries* are described under Diseases of the Brain.

Embolism of a large *artery* in a *limb* is not a very common event. It causes sudden acute pain, followed at once by numbness, coldness, and loss of power in the limb; the pulse is imperceptible below the seat of embolism, and, as already stated, gangrene may result. In the *spleen* and *kidneys* the occurrence of embolism is not so commonly recognised. Sometimes there is sharp pain in the left side from embolism of the spleen. Embolism of the kidney causes hæmaturia and frequently albuminuria too, and in malignant endocarditis there is often a condition of focal embolic nephritis present. Cases of embolism of the *mesenteric artery* have occurred in which the patient has been seized with severe

abdominal pain and distension, followed by collapse and death in one or two days; and blood has been found in the bowel and in the peritoneal cavity. Very similar results may follow thrombosis of this vein, but the symptoms are more slowly developed.

The effects of embolism and thrombosis of the vessels of the *liver* are described under Pylephlebitis. Pulmonary embolism and thrombosis, and infarction and fat embolism are described on p. 177.

Embolism of particles of *new growth* is the cause of fresh growths in remote parts.

Treatment. The pain of embolism may be relieved by local anodyne applications; if the large artery of a limb is obstructed, the limb should be wrapped in cotton wool or oiled lint. Embolectomy may be carried out during the first few hours or the clot may be manipulated into a smaller arterial branch.

ANGEIO-NEUROTIC ŒDEMA

This is an affection apparently connected with the vasomotor apparatus and closely allied to urticaria; but the lesions are larger. Circumscribed swellings appear in various parts of the body—for instance, on the face, the eyelids, the hands or legs, in the throat or in the tongue. They are not inflammatory, and not dependent upon gravity; they are not painful, but may be accompanied by burning, pricking and itching. They appear suddenly, last from two to six hours or more, and recur frequently, even daily; on the skin they are generally harmless, but œdema of the larynx has frequently proved fatal. Gastro-intestinal symptoms are usually present, such as colic, nausea, and vomiting, and are attributable to an acute œdema of the gastric or intestinal mucous membrane. The disease is often hereditary, occurring in several members of the same family in two or three generations. It is one of the allergic diseases, like asthma (*see* p. 138), and is due to sensitisation to a foreign protein.

Treatment consists in finding out and avoiding the particular protein to which the individual is sensitive; septic foci must be eradicated. Quinine, nitroglycerine and thyroid extract have given relief in a few cases. Laryngeal œdema may require intubation or tracheotomy

Milroy's Disease.—This is a chronic œdema of both legs, often of familial origin, with a tendency to hyperplasia of the skin and subcutaneous tissue, of unknown origin.

REFERENCES

1	Y. Henderson and Johnson ..	1912	*Heart*, **4**, p. 69.
2	H. Sahli	1920	*Schweiz. Med. Wochenschr.*
3	H. Sahli	1923	*Wien, Arch. f. inn. Med.*, **6**, p. 515.
	H. Sahli	1923	*Ergeb. d. inn. Med. u. Kindhkde.*, **24**, p. 73.
4	MacIlwain and Campbell	1923	*Brit. Med. Journ.*, **ii.**, p. 456.
5	E. P. Poulton and H. M. Stewart	1918	*Lancet*, **ii.**, p. 738.
6	Parkinson and Bain	1924	*Lancet*, **ii.**, p. 311.
7	Poulton and Dowling	1921	*Guy's Hosp. Rep.*, **71**, p. 253.
8	C. Dukes	1921	*Brit. Med. Journ.*, **ii.**, p. 987.
	Corney	1922	*Lancet*, **ii.**, p. 863.
9	J. Parkinson and M. Campbell ..	1930	*Quart. Journ. Med.*, **24**, p. 67.
10	J. M. H. Campbell and E. P. Poulton	1928	Quoted in *Lancet*, **ii.**, p. 1281.
11	Emanuel	1923	*Lancet*, **i.**, p. 591.
12	Lewis, Ryffel, Wolf, Cotton and Barcroft	1913	*Heart*, **5.** p. 45.
13	J. A. Calhoun and W. G. Harrison	1934	*Arch. Int. Med.*, **53**, p. 911.
14	Campbell Hunt and Poulton ..	1923	*Journ. Path. & Bact.*, **26**, p. 234.
15	T. Wardrop Griffith	1901	*Brit. Med. Journ.*, Feb. 2.
16	T. Lewis	1929	*Heart*, **15**, p. 7.
17	W. E. Dixon	1929	Communication to Assoc. Phys., Cambridge.

18 T. Wardrop Griffith	1903	*Edin. Med. Journ.*, p. 105.
19 Carey Coombs	1923	*Quart. Journ. Med.*, **16**, p. 309.
20 R. T. Grant	1931–3	*Heart*, **16**, p. 275.
21 Newburgh	1915	*Amer. Journ. Med. Sci.*, May.
22 C. G. Lambie	1926	*Brit. Med. Journ.*, **i.**, p. 80.
23 Sir W. Osler	1908–9	*Quart. Journ. Med.*, **2**, p. 219.
24 Sir T. J. Horder	1908–9	*Quart. Journ. Med.*, **2**, p. 289.
25 Sir Clifford Allbut	1923	*Lancet*, **ii.**, p. 1422.
26 T. Wardrop Griffith	1915	*Lancet*, Jan. 9.
27 W. Evans and C. Hoyle	1933	*Lancet*, **i.**, p. 1109.
28 Sir James Mackenzie (Angina Pectoris)	1923	*London.*
29 Henry Head	1922	*Brit. Med. Journ.*, **i.**, p. 1.
30 W. Verdon (Angina Pectoris) ..	1921	*London.*
31 W. W. Payne and E. P. Poulton ..	1923	*Quart. Journ. Med.*, **17**, p. 53.
32 G. Evans	1923	*Brit. Med. Journ.*, Mar. 17, 24 and 31.
33 Foster Moore	1917	*Quart. Journ. Med.*, **10**, p. 29.
34 W. Edgecombe	1911	*Practitioner*, April, p. 515.
35 A. G. Gibson	1925	*Lancet*, **ii.**, p. 1270.
36 J. A. Ryle	1928	*Lancet*, **i.**, p. 332.
37 Kerr	1921	*Lancet*, **ii.**, p. 1112.
38 Bramwell and Hill	1922	*Lancet*, **i.**, p. 891.
39 Parkes Weber	1916	*Quart. Journ. Med.*, **9**, p. 289.
40 Sampson Handley	1922	*Lancet*, **ii.**, p. 173.
41 F. R. Fraser, C. F. Harris, R. Hilton and G. C. Linder	1928	*Quart. Journ. Med.*, **22**, p. 1.
42 F. Bach and N. Gray Hill	1932	*Lancet*, **i.**, p. 75.
43 W. St. Lawrence	1920	*Journ. Am. Med. Assoc.*, **75**, p. 1035.
44 H. J. Starling	1923	*Guy's Hosp. Rep.*, **73**, p. 388.
45 W. Sheldon	1930	*Lancet*, **ii.**, p. 394.
46 H. F. Swift, Derick and Hitchcock	1928	Bath Conference, *Rheumatic Disease*, p. 157.
47 M. Campbell and E. C. Warner ..	1930	*Lancet*, **i.**, p. 61.
48 E. C. Warner..	1930	*Lancet*, **ii.**, p. 719.
49 W. H. Bradley	1932	*Proc. Roy. Soc. Med.*, **25**, p. 1635.
50 W. R. F. Collis	1932	*Proc. Roy. Soc. Med.*, **25**, p. 1632.
51 E. C. Warner	1930	*Lancet*, **i.**, p. 339.
52 J. F. Carter Braine, W. R. Spurrell, and E. C. Warner	1927	*Guy's Hosp. Rep.*, **79**, p. 473.
53 M. Campbell and S. S. Suzman ..	1934	*Am. Heart Journ.*, **9**, p. 304.
54 C. Bolton	1924	*Heart*, **11**, p. 343.
55 H. A. Treadgold and H. L. Burton	1932	*Lancet*, **i.**, p. 277.
56 M. Campbell and J. W. Shackle ..	1933	*Guy's Hosp. Rep.*, **83**, p. 168.
57 J. Holmes	1929	*Brit. Med. Journ.*, **ii.**, p. 739.
58 F. Saile..	1930	*Med. Klin.*, June 20th.
59 J. Plesch	1932	*Lancet*, **i.**, p. 385.
60 E. J. Wayne	1933	*Clin. Sci.*, **1**, p. 63.
61 T. Lewis	1931–3	*Heart*, **16**, p. 205.
62 D. W. Bennett and W. J. Kerr ..	1931–3	*Heart*, **16**, p. 109.
63 H. A. Treadgold and H. L. Burton	1932	*Lancet*, **i.**, p. 277.
64 S. J. Hartfull and G. Armitage ..	1932	*Guy's Hosp. Rep.*, **82**, p. 424.
65 G. H. Colt	1927	*Quart. J. Med.*, **20**, p. 331.
66 E. D. Telford and J. S. B. Stopford	1933	*Brit. Med. Journ.*, **i.**, p. 173.
67 H. A. Treadgold	1933	*Lancet*, **i.**, p. 733.
68 C. Hoyle	1933	*Lancet*, **ii.**, p. 230.
69 I. Harris and G. McLoughlin ..	1930	*Quart. Journ Med.*, **23**, p. 451.
70 G. Spurling, F. Jelsma and J. B. Rogers	1932	*Surg. Gyn. and Obstet.*, March.
71 R. G. Waller	1930	*Brit. Med. Journ.*, Oct. 11th.
72 T. Lewis	1931	*Heart*, **16**, p. 1.
73 Paul D. White	1935	*Lancet*, **ii.**, pp. 540, 597.

DISEASES OF THE ORGANS OF DIGESTION

EXAMINATION OF THE ABDOMEN

THE abdomen is accessible to the same methods of examination as are employed in the case of the lungs and heart—namely, inspection, palpation, percussion, and auscultation; and in most instances it is desirable that the patient should be in the recumbent position, with the head rested.

For descriptive purposes the abdomen is divided into nine areas by means of two horizontal and two vertical lines. The vertical lines are drawn upwards from the mid-point of Poupart's ligament on each side to the costal margin. The horizontal lines are drawn across from the lowest parts of the costal margin, *i.e.* the tenth costal cartilages on each side, and between the highest points of the iliac crests. The names given to the regions mapped out by these lines are in descending order—(1) in the middle, epigastric, umbilical and hypogastric; (2) at the sides, hypochondriac, lumbar and iliac. As in the chest, accurate localisation of a lesion requires measurement from easily recognised parts, like the umbilicus, xiphisternum, middle line, pubes, anterior superior iliac spine, or tip of the eleventh rib.

Inspection. The first thing to notice is the size of the abdomen. This is extremely variable even within the limits of health. It may be uniformly much enlarged; but it requires the help of other methods of examination to determine whether this is due to a collection of liquid in the peritoneal cavity (*ascites*), to gas in the intestines (*meteorism, tympanites*), to fat in the parietes and omentum, or to some tumour, such as an ovarian cyst. Uniform and symmetrical retraction of the abdomen is seen in starvation, in emaciating diseases, and in death from cerebral diseases, such as tuberculous meningitis and intracranial tumour.

By inspection may be observed various local enlargements or prominences, such as result from tumours or enlargements of different organs, *e.g.* tumours of the liver, dilated stomach, distended intestines in cases of obstruction, infiltrated omentum and adherent intestines in tuberculous peritonitis, enlarged spleen, hydronephrosis, the pregnant uterus, ovarian and other cysts, and a distended bladder. Local enlargements in the upper part of the abdomen may cause asymmetry of the thorax by driving upwards and outwards the lower ribs on one side, thus enlarging the angle between the costal margin and the middle line. This is especially seen in cases of hydatid, carcinoma, and abscess of the liver.

It is important to note the relation of the abdomen to the respiratory movements already referred to in connection with the chest; the descent of the diaphragm is impeded by much distension, and is checked by acute inflammation of the peritoneum, so that in these cases respiration is almost entirely thoracic. In other cases respiration affects materially the position of the organs in immediate contact with the diaphragm, namely, the liver, spleen, stomach, and kidneys, whereas organs or tumours situated lower down, or connected with the posterior wall of the abdomen, are much less influenced by the descent of this muscle. The pulsations of the aorta, or of the right ventricle, or of the enlarged liver in tricuspid regurgitation, or very occasionally of an aneurysm, and the peristaltic movements of a dilated stomach or of the intestines, may sometimes be seen, the latter being visible in proportion to the thinness of the abdominal parietes and the vigour of the peristalsis.

Palpation. For this method of examining the condition of the abdomen,

the abdominal walls should be relaxed as much as possible, and hence the patient should be in the recumbent or semi-recumbent position, and the head should be supported, for if the patient raises his head—*e.g.* to see what is going on—the recti abdominis become tense. The relaxation of the abdominal walls is sometimes assisted by raising the patient's legs a little, but they must be supported in that position by a pillow under the knees. When the abdominal muscles are persistently tense, the patient should be asked to breathe deeply in and out, and should be engaged in conversation while the hand is on the abdomen, or he may be asked to lift up his head from the pillow, and keep it raised for about a minute, when the muscles will become exhausted, and for a moment afterwards the abdomen may be lax enough for the purpose. Another plan which has been recommended is to palpate the abdomen, when the patient is in a warm bath. If these means fail, and an examination is of the first importance, an anæsthetic should be administered.

The examination of the abdomen should be made with great gentleness; the hands should be warm, and should be laid flat upon the surface, and care should be taken not to force the finger tips suddenly into the abdomen, whereby the muscles are made to contract, and trustworthy results are impossible. During the movements of deep breathing enlargements of organs or new growths, especially in the upper part of the abdomen, may be detected, which would otherwise perhaps escape recognition. When examining the sides of the abdomen the observer should never neglect to employ the *bimanual* method—that is, one hand should be placed under the twelfth rib, and another on the abdomen in front; if one hand be pressed towards the other which is still, the slightest enlargement or resistance can generally be appreciated. In particular cases it may be desirable to examine the patient in the knee-elbow position.

In the normal abdomen there is scarcely any resistance to the movement of the hand in all directions. The solid organs, liver, spleen, and kidneys are almost entirely within the bony thorax; the left lobe of the liver, which lies across the epigastrium, is of small bulk, thin, and soft; the hollow viscera yield readily to the hand, and often nothing can be recognised, except, in thin people, pulsation of the aorta or iliac vessels.

By palpation in disease we can recognise changes in shape or size of the organs and the existence of tumours, and can obtain information on the following points: The condition of tenseness or relaxation of the abdominal wall, which may be local or general. The presence of tenderness, general or local; this may be elicited directly the hand touches the abdomen, or only when deep pressure is made. Various kinds of movement may be felt in the abdomen—the pulsations of the normal vessels, or of an aneurysm, or of the liver in heart disease; the peristaltic movement of the bowel; the movements of air in the intestine (borborygmi); the coarser movements or splashing of air and liquid in a dilated stomach when somewhat sudden pressure is made upon it; and the friction of inflamed peritoneal surfaces.

Under palpation also must be included two of the methods by which ascites or liquid in the peritoneal cavity may be recognised—namely, *fluctuation* and *displacement* (*see* Ascites).

Percussion. It is in reference to percussion especially that we must remember that the abdominal cavity extends up into the lower parts of the bony thorax. In health the abdomen is resonant over so much of the combined surfaces as corresponds to the intestines and to the stomach—that is, all the parts below the ribs, and the costal cartilages and lower ends of the ribs on the left side below the heart. It is dull over the parts which correspond to the liver and spleen—that is, for the liver the ribs of the right side below the upper border of the sixth in front, and the eighth at the side, and for the spleen the ninth, tenth, and eleventh ribs on the left side just behind the anterior axillary line. The relative areas of dulness and resonance may be much altered by changes in the amount

of gas in the hollow viscera, and the dull areas of the liver and spleen are moved downwards in inspiration and upwards in expiration. There is, further, much difference in the quality of the percussion note over the stomach and different parts of the intestine.

Alterations in the size of the liver and spleen, or the existence of solid tumours or cysts, will give rise to new areas of dulness, and such dulness will, as a rule, be accompanied by resistance appreciable by palpation. As constant reference to these altered conditions will be made under the diseases of the different organs, it is not necessary to specify them here. In percussion also we have another valuable method of recognising ascites (*q.v.*).

Auscultation. Friction sounds are occasionally heard over the liver and elsewhere in peritonitis; abdominal aneurysms may be accompanied by murmurs. If the region over the cæcum is auscultated, sounds are heard at intervals due to the passage of intestinal contents through the ileo-cæcal valve. In acute inflammation the movements stop, so that auscultation may be of value in suspected acute appendicitis.

Examination by X-rays. The œsophagus, stomach and alimentary canal are examined by giving the patient a meal mixed up with some salt opaque to the X-rays, such as barium sulphate or bismuth carbonate or oxychloride. Full details are given under the respective organs. For the examination of the colon an opaque enema may also be used. Other organs may be examined by taking plates of the abdomen after the alimentary canal has been emptied as far as possible by laxatives. In this way the presence of gall stones may be determined in favourable circumstances. Graham's method of demonstrating the gall bladder is described later.

Cœlioscopy. In this method a small incision is made through the abdominal wall under novocaine anæsthesia; air is passed into the peritoneal cavity and the contents viewed by means of a laparoscope. This method may be used purely for diagnostic purposes when an exploratory laparotomy would be unjustifiable (**1**).

THE ACUTE ABDOMEN

In view of the favourable results obtained from surgical intervention in many acute abdominal conditions the importance of diagnosis cannot be exaggerated. While the distinguishing marks of the various acute conditions are dealt with later under the various diseases, it has been thought advisable to give here some points about the examination of the patient and a list of the conditions that may give rise to the acute abdomen or to symptoms that resemble it.

The previous history will indicate not only whether similar attacks have occurred before, but whether there have been any suggestive symptoms, *e.g.* a history of dyspepsia, which may precede a perforated peptic ulcer or acute appendicitis. The menstrual history and the previous occurrence of jaundice, hæmatemesis, hæmaturia must be inquired into, and whether there has been recent loss of weight. The history of the present condition would include questions as to whether the onset of the attack was acute or gradual; the situation and the character of the pain; whether it has moved or shoots in a particular direction; whether there is any association of the pain with vomiting; the character of the vomit; whether there is nausea; the condition of the bowels. The examination must be complete—not only concerned with the alimentary system—so as to diagnose intrathoracic lesions, such as pleuro-pneumonia, pericarditis, and acute congestive heart failure with coronary thrombosis, the gastric crises of tabes and lesions of the kidneys and urinary tract, *i.e.* pyelo-nephritis, peri-nephritis, acute osteomyelitis and Pott's disease of the spine, and toxic conditions, *i.e.* uræmia, diabetic coma and cyclical vomiting. The colics may produce very acute abdominal symptoms, *i.e.* intestinal colic, lead colic, biliary colic, renal colic including oxaluria. Then there are the organic

intra-abdominal conditions, *i.e.* appendicitis, perforated peptic ulcer, and occasionally perforated intestinal ulcer; acute intestinal obstruction with and without strangulation, acute cholecystitis, diverticulitis, hæmorrhagic pancreatitis, pneumococcal and secondary peritonitis; ectopic gestation, salpingitis, and other gynæcological states; mesenteric embolism and thrombosis, Henoch's purpura and other intra-abdominal hæmorrhages and dissecting aortic aneurysm.

Other possible conditions are abdominal influenza, tuberculosis, especially of the ileo-cæcal glands, the enteric fevers, food poisoning, suppurative pylephlebitis, and, in the tropics, amœbic dysentery, hepatitis and malaria.

STOMATITIS

Inflammation of the mouth, or *stomatitis*, occurs as a general catarrhal condition involving the cheeks, gums, tongue, and lips, and in more localised forms, as aphthous, ulcerative, and gangrenous stomatitis, which are almost certainly due to micro-organisms. At the same time it is clear that some special conditions are required for the operation of micro-organisms, since the mouths of healthy persons contain innumerable micro-organisms, among which are staphylococci, streptococci, torulæ, and sometimes pneumococci, and diphtheria bacilli. The lesions of some diseases of the skin may involve also the buccalmucous membrane, such as those of herpes, pemphigus, and urticaria. *Herpetic stomatitis* is a condition in which numerous small ulcers occur over all the gums and inside of the cheeks; the ulcers are so tender that food must be fluid or semi-solid, as mastication is impossible. Treatment is by frequent application of glyc. boracis.

Stomatitis limited to the gums is called *gingivitis*. Different forms of gingivitis are seen in scurvy and in acute leukæmia, and as local results of dental diseases in the form of *pyorrhœa alveolaris*. For prevention of dental caries, see Vitamin D.

Oral Sepsis. It is necessary to lay especial stress upon the importance of a healthy condition of the teeth in relation, not only to stomatitis, but to conditions of general ill-health. Apart from acute alveolar abscess there are three conditions which are important from the medical point of view: (1) *Apical granuloma*, often incorrectly called abscess, which forms round diseased stumps and the roots of dead teeth and teeth which have become devitalised; these are always infected with streptococci, usually non-hæmolytic in type. As the granuloma has a thick wall and comes away with the tooth in extraction there is not so much danger of dissemination through the body as in rarifying osteitis, described later (2). There may be symptoms of general ill-health with fatigue and anæmia. It is probable that many diseases of obscure origin may in the future be traced to this cause. In particular, angina pectoris, rheumatoid arthritis, infective endocarditis, recurring gastric and duodenal ulcer, ocular inflammations, *i.e.* iritis, keratitis, choroiditis, may result from apical granuloma. Obviously dead teeth must be removed; but this is not enough, as a granuloma may be present when the tooth looks healthy, and there may be no pain and no tenderness on tapping the tooth. The only safe way is to take dental radiograms, when the granuloma is easily identified by the clear space at the root (*see* Plate 16); the root itself may become absorbed. These clear spaces due to infection must be distinguished from certain anatomical features, such as, in the upper jaw, the palatine fossa between the apices of the central incisors, and the nasal fossæ above, the maxillary antrum which is close to the roots of the molars and premolars in the lower jaw, the line of the inferior dental canal below the apices of the molar teeth and the mental foramen below the premolars. (2) *Pyorrhœa alveolaris*, where there is chronic inflammation with absorption of the bone surrounding the roots of the teeth. This begins as a thickening of the periodontal membrane—the clear area immediately surrounding the root—which may be localised at the gum margin or it may be general all round the root. The lamina dura—the opaque line

bordering the periodontal membrane—disappears. Pockets are formed between the teeth; the floor of the pocket is relatively wide between the roots of the teeth, while the opening of the pocket is constricted, so that it becomes filled with food *débris* and pus (*see* Plate 16). In proportion as drainage is restricted, infection by the blood stream is apt to occur; when there is a free discharge of pus, the micro-organisms may be swallowed and produce various alimentary disturbances. However, blood stream infection is probably more dangerous than swallowing the organisms. According to Goodrich and Moseley, pyorrhœa is due primarily to the leptothrix of the mouth; but other organisms, streptococci, etc., are always associated with it, and are responsible for the various diseases secondary to pyorrhœa. There may be rarefying osteitis with absorption of the apices of live teeth, or sclerosing osteitis, which makes the bone of the alveolus denser than usual at the apex of the tooth, which may become bulbous (**3**). Rarefying osteitis is also due to streptococcal infection, mostly non-hæmolytic, and dissemination *viâ* the blood stream takes place more readily than with apical granuloma (**2**).

The *prevention* of oral sepsis consists in keeping the teeth scrupulously clean and free from tartar. At the same time the greatest care should be taken that the gum is not injured habitually by too hard brushing. The diet should contain enough vitamins. The treatment of apical granuloma usually consists in the removal of the tooth, and the same applies to well-advanced pyorrhœa, as there is no cure for this condition. It is advisable to scale and otherwise clean up all the teeth on two separate occasions some days beforehand, as this will tend to prevent septic absorption. Then it is best to remove as far as possible all the condemned teeth at one time (**4**). Palliative treatment consisting in cleaning out the pockets periodically is also adopted.

A solution of thymol in water is a valuable mouth wash, as it is a particularly powerful antiseptic. Thymol is very slightly soluble in water, so that it is only necessary to put two or three crystals into a bottle of water and leave it to stand for some time. If the external temperature is high, the solution becomes stronger, and causes a stinging sensation in the mouth, and so it must be diluted before use.

CATARRHAL STOMATITIS

Ætiology. Catarrhal stomatitis may be set up firstly by chemical or mechanical irritation, such as contact with acids or alkalies, excessive drinking, or the presence of broken or carious teeth; secondly, by inflammation spreading from adjacent parts, such as the nose or naso-pharynx; thirdly, by the action of some poisons, viz. mercury, lead, and arsenic; and fourthly, in consequence of some general and mostly infectious conditions, such as measles, variola, syphilis, scurvy, leukæmia, and others.

Symptoms. These are swelling and increased redness of the mucous membranes of the gums, lips, and cheeks, swelling of the tongue, salivation and increased secretion of buccal mucus, which adheres as a coating to the surface, and swelling of the neighbouring lymphatic glands. Mastication and deglutition are painful, and the breath may be offensive. In later stages abrasion and superficial ulceration take place.

Treatment. All causes of irritation should be as far as possible removed; and antiseptic washes should be employed, such as boric acid (2 to 5 per cent.); potassium chlorate (3 per cent.): in later stages much more astringent solutions such as alum (5 grains to the ounce) or glycerine of tannin.

APHTHOUS STOMATITIS

This occurs in children, especially about the time of the first dentition, and less frequently in adults: it consists in the formation of circular grey patches, or

aphthæ, on the gums, tongue, and the inside of the lips and cheeks. They are from 3 to 5 mm. in diameter, slightly raised above the surface, and, though looking like vesicles, are really caused by a fibrinous exudation beneath the epithelium. After a time the epithelium is shed, and small ash-grey ulcers with narrow red margins are left. Children thus affected are restless and feverish, there is slight salivation, and sucking or mastication is painful. The ulcers commonly heal in a few days, but may recur frequently in some patients. In adults the aphthæ are rarely so numerous as in children.

Treatment. Antiseptic washes and glycerinum boracis may be used. The application of nitrate of silver in adults at once relieves pain and often quickly cures.

GANGRENOUS STOMATITIS

This disease, also called *cancrum oris* and *noma*, occurs in debilitated children, or those subject to bad hygienic conditions, or those who are recovering from infectious disease, of which measles and enteric fever are most common. It is due to bacterial infection. The changes are very rapid; a small spot of induration appears on the inner side of the cheek, and soon the whole thickness of the cheek is hardened, black in the centre, and reddened around, or, in other words, a slough has formed. If it goes on, the cheek will be perforated, or if it is on the lips, the gum will be invaded, and the teeth will fall out. There is very little pain or fever, but the child rapidly becomes exhausted and dies.

Treatment. The only means of saving the child is the prompt destruction of the part by nitric acid, or its removal by the knife. In addition, the child must be supported by food and stimulants.

THRUSH

Thrush is seen in weak and badly nourished infants, especially in those who are being fed by hand, or are suffering from diarrhœa, and also in adults in the last stages of exhausting diseases, such as phthisis, carcinoma, and enteric fever. Upon the mucous membrane of the lips, cheeks, gums, palate, and tongue, milk-white patches occur, which are irregular in shape, scattered or confluent, slightly raised above the surface, and surrounded by a thin red line. If the patch is stripped off, the mucous membrane beneath is bright red, or even bleeds slightly, and the patch may form again in a short time. It consists of epithelial scales, fat globules, and the spores and mycelium of a fungus, *Oïdium albicans*. According to Castellani thrush in the tropics may be due to many different varieties of fungi. The fungus develops first in the middle layers of the epithelium, and spreads thence in both directions to the more superficial and the deeper layers. It is probable that the growth of the fungus is the cause of the stomatitis which accompanies it; but it is stated by Vogel that the deposit is favoured by the secretions of the mouth, which are acid before any white patches appear. Children who have thrush and diarrhœa frequently have excoriations about the anus, which lead to the popular notion that the thrush has "gone through" the child; but though in severe cases thrush may extend to the pharynx and œsophagus, it does not occur on parts covered with cylindrical epithelium. The anal rash is either erythema intertrigo or a congenital syphilide. A certain amount of local discomfort, with pain on swallowing or sucking, results from thrush, but symptoms beyond these are chiefly due to the condition of health preceding it.

Treatment. The general condition of the patient must be improved. In infants the food must be rendered suitable, and the diarrhœa checked. After every meal the mouth should be carefully wiped out with a fresh piece of soft linen, and the patches should be touched with a solution of borax (10 grains to ℥j), or a little glycerine of borax should be left in the mouth.

OBSTRUCTION OF THE ŒSOPHAGUS

This is the most important pathological condition of this part of the alimentary tube. The causes are—impaction of foreign bodies, such as false teeth; compression from outside by mediastinal growths and very occasionally by thoracic aneurysms; the growth of carcinomatous or other tumours in the walls of the tube itself; constriction by the contraction of ulcers following injury by corrosive poisons; functional spasm of the muscular walls; and achalasia of the cardia or cardio-spasm; diverticula. The last four conditions will be separately considered.

CARCINOMA OF THE ŒSOPHAGUS

This generally occurs in advanced life, and in males more often than in females. The growth occupies the middle and lower thirds of the œsophagus more often than the upper third; but it is especially frequent opposite the bifurcation of the trachea, and at the cardiac extremity of the œsophagus. It is always primary. In course of time it forms an irregular ulcerated surface on the inside. The tumour partially or completely encircles the tube, extending vertically from 1 to 4 inches; moreover, it often involves the trachea or the root of the lung, or compresses the recurrent laryngeal nerves. The mediastinal lymph glands are enlarged, and not infrequently quite early the cervical glands.

Symptoms. The first and prominent symptom is dysphagia. The patient finds he has difficulty in swallowing solids when he may get fluids down with comfort. The difficulty increases gradually, and at length solid food has to be given up; liquids alone can be taken, and if more than a mouthful is attempted at a time, it is regurgitated, and the patient may choke. Pain is usually absent. After a few weeks the patient begins to waste, and loses strength and energy. The symptoms are generally progressive, but occasionally temporary improvement takes place from crumbling away of portions of growth from the surface, so as to enlarge again the calibre of the œsophagus. If no relief be afforded, death takes place from simple exhaustion, or from complications. Thus in some cases a communication with the trachea is produced by the spread of the growth; food particles are inhaled, and a septic broncho-pneumonia is set up. In others the lung is directly invaded by the new growth, and gangrene or broncho-pneumonia, with which pleurisy or empyema may be associated, carries off the patient. In others, again, compression of the recurrent laryngeal nerves when the growth is at the upper end leads to paralysis of the abductors of the glottis, which may produce asphyxia. Rarely a growth has eaten into the aorta and caused fatal hæmorrhage. Lastly, there may be deposits in other organs, especially in the liver and lungs. Occasionally these are the cause of death, when the growth in the œsophagus has been too slight to produce any difficulty in swallowing.

Diagnosis. Gradually increasing dysphagia in a person over fifty years of age is, in the great majority of cases, due to carcinoma of the œsophagus. Sometimes the fact of dysphagia may be overlooked: food may be retained sufficiently long in the œsophagus above the stricture for its regurgitation to be mistaken for vomiting, both by the patient and by a careless inquirer; and so a gastric lesion may be diagnosed. The patient can often tell the exact level at which obstruction occurs.

The presence of an obstruction can be most readily confirmed by the use of X-rays after a bismuth meal, when the exact position and extent of the obstruction may be demonstrated. The rays will also show whether the lesion is within the œsophagus or is due to pressure from without (*see* Plate 17). When the obstruction is situated in the œsophagus it is still necessary to distinguish between carcinoma, cicatricial or spasmodic stricture, diverticula, and achalasia of the cardia. Direct inspection by the *œsophagoscope* may be employed. In achalasia the œsophagus is greatly dilated, but there is usually not much

dilatation with growth, because in the latter case the obstruction comes on more acutely. A closed hollow tube containing mercury, to make it heavy, may be passed down the œsophagus (Hurst). It will not pass in the case of growth, but will usually pass in the case of achalasia. The presence of enlarged and hard cervical glands is also in favour of growth.

Prognosis. This is uniformly bad. Even if the obstruction is overcome, the malignant growth must be fatal by its further extension within a short time. The duration is generally from six to twelve months.

Treatment. If a bougie, even of small size, can be passed, the passage may be kept open for a time by its use every two or three days. But the maintenance of a channel for the food is best secured by some modification of the method of intubation introduced by Krishaber. A tube is passed through the stricture and retained *in situ* for several days or permanently, and the patient is supplied by that means with fluid nourishment. If these measures are inapplicable, the stomach may be opened by the operation of *gastrostomy*. A diminution of the constriction is sometimes obtained by the use of radium applied locally to the growth of the œsophagus. The application of deep X-rays has given good results.

CICATRICIAL STRICTURE

In this, again, dysphagia is the main symptom ; but it differs from carcinoma in this, that it may not advance beyond a certain point, and that it does not lead to any secondary effects, except dilatation of the tube above it. In consequence of this dilatation food often accumulates above the stricture, and is regurgitated after a time.

The **Diagnosis** is determined by œsophagoscopy.

Treatment offers a fair chance of success if the sound or mercury tube can be passed through the stricture into the stomach. It should be used regularly once or twice daily, and attempts should be made to pass larger and larger instruments. Liquid food may be required always. In unfavourable cases gastrostomy may be advisable.

SPASMODIC STRICTURE

This is really quite a common condition, although it is not generally realised. There is difficulty in swallowing, accompanied by a painful sense of constriction in the throat and chest (heart-burn). The spasm can be recognised by X-rays (*see* Plate 18, B). It may be a feature of the dyspeptic symptom complex (*see* p. 333), and so may be associated with aerophagy. The pain is probably due to the associated œsophageal distension. As the radiogram shows, the spasm is not absolute ; some of the opaque meal manages to get through.

Plummer-Vinson Syndrome. This is a dysphagia occurring in patients with secondary anæmia and sometimes spleno-megale ; the nails are often spoon shaped. It occurs almost exclusively in women, and most patients have had total extraction of the teeth. The tongue is bald and red and the pharyngeal wall is glazed. The condition was originally recognised by Paterson and Brown Kelly in 1919 (**5**). The obstruction occurs at the junction of pharynx and œsophagus, and may be due to weakness of the pharyngeal muscles concerned in swallowing or to inability of the crico-pharyngeus muscle to relax. Treatment should be directed to the cure of the anæmia and the dysphagia by the passage of bougies (**6**).

ACHALASIA OF THE CARDIA

(Cardio-spasm, Œsophagectasia, Idiopathic Dilatation of the Œsophagus)

The lower 2 or 3 inches of the œsophageal wall, which may often be seen at autopsy in a relaxed condition a little thicker than the wall above, is the cardiac sphincter. In life the cardia is closed by contraction of both its

longitudinal and circular muscle fibres; it relaxes in front of each peristaltic wave and subsequently contracts firmly again, probably becoming invaginated a little way into the stomach during the process (7). Peristalsis travels rather slowly from the upper end of the œsophagus after swallowing, while a fluid meal is projected straight down. Consequently the bulk of the fluid remains some seconds above the sphincter, before the latter relaxes.

Pathology. In achalasia of the cardia (**15, 16**) (α priv. and χάλασις, loosening, slackening) or cardio-spasm, the cardia remains closed; but the tightness of the closure varies in different cases and at different times. It may offer no resistance to the passage of a sound, or the resistance may be insuperable (**8**). It has been found that Auerbach's plexus, which lies between the circular and longitudinal muscles, is inflamed, and in long standing cases has been destroyed (**9**). In the early stages the muscular coat hypertrophies above the paralysed portion of the œsophagus, so that food is passed through the cardia successfully, and there are no symptoms. Later, dilatation with hypertrophy in varying degrees takes place and there may be some chronic inflammation of the œsophageal mucosa.

Auerbach's plexus is probably a relay station for the vagus nerve, and it is to be noted that stimulating the vagus in the rabbit relaxes the cardia, so that achalasia may be regarded as a vago-paralysis of the lower end of the œsophagus, with the result that the sphincter does not open in front of peristaltic waves. Since the sympathetic nerve fibres that pass to the muscle fibres are probably intact, and probably cause contraction of the sphincter, it is not surprising that a real cardio-spasm is commonly met with.

Achalasia of the cardia may be due to syphilis, and has occurred in mitral stenosis, where presumably the vagus has been pressed on by the dilated left auricle. It has occurred with gastric ulcer and carcinoma. Usually there is no obvious cause.

Symptoms. The patients suffer sometimes for years from a sense of the food sticking in the throat after it has been swallowed, from actual pain in the epigastrium, from regurgitation of the food, or what is described as vomiting. The condition often comes on gradually, and at first may be spasmodic, recurring from time to time. An X-ray examination after a bismuth meal shows that the œsophagus is dilated into a fusiform body wider at the lower part (*see* Plates 19 and 20). The dilatation may also be seen with the œsophagoscope. In fatal cases the internal circumference at its widest part has reached a measurement of from 10 to 16 cm. (4 to 6 inches).

Treatment. Some cases have been fatal. In others the patients have got over the difficulty by liquid food, or by extremely careful mastication of solid food. It is often found that a column of fluid the length of the œsophagus forces its way through the sphincter by hydrostatic pressure, until the level has fallen by a certain amount, and this fact enables some food to be taken. Cases have been more promptly dealt with by the passage into the stomach before each meal of a rubber tube filled with mercury or by feeding the patient for four days by means of an œsophageal tube introduced into the stomach and left *in situ* all the time. In refractory cases the stomach is opened through the abdomen and the sphincter dilated with the fingers.

DIVERTICULA

These are pouches in the walls of the œsophagus; they have been divided into (1) pressure diverticula and (2) traction diverticula.

1. *Pressure diverticula* arise from the impaction of foreign bodies, or from other local injury. As a consequence, apparently the muscular coat is weakened, and the mucous and submucous coats are bulged out between the muscular fibres, which do not share in the coverings of the diverticulum. When once this has taken place food accumulates in the sac, which gradually enlarges, so that it may

attain a diameter of 3 or 4 inches. 2. *Traction diverticula*, which usually produce no symptoms, are caused by adhesion of the œsophagus to surrounding parts, *e.g.* through the suppurating or tuberculous bronchial glands, whereby the coats are pulled out in a funnel-shaped manner. Diverticula are usually hemispherical in shape; they are most common posteriorly, at the junction between pharynx and œsophagus, and may project on both sides of the neck, sometimes on the left side only. The next commonest place is near the lower end of the œsophagus (**1**) (Plate 23, A.)

The **Symptoms** are dysphagia, regurgitation of food, often accompanied by choking or coughing, and foul breath from the decomposition of food in the sac. So much food may accumulate as completely to obstruct the œsophagus. Diverticula are diagnosed by means of X-rays after swallowing some barium (*see* Plates 18, A and 23, A), and by the œsophagoscope.

Treatment.—The pouch may be removed by operation. In slight cases it is possible to wash it out regularly by mouthfuls of water with subsequent regurgitation.

EXAMINATION OF THE STOMACH

The position of the stomach varies with the position of the patient. In the erect position the cardiac end lies within the bony thorax, while the body and pylorus lie within the abdomen. In the horizontal position the stomach sinks further back beneath the ribs, and only the pyloric part of the stomach lies in the epigastrium. The stomach always contains some air, and this can be recognised by the full tympanitic note which is yielded on percussion of the lower part of the left thorax in front. This area is limited above by the præcordial dulness, and posteriorly by the splenic dulness and pulmonary resonance. It is impossible to separate the note obtained by percussion of the stomach from the note due to air in the intestines, so that this method is of no value in outlining the stomach. The stomach is remarkable for the great alterations in size and position it may undergo, so as to accommodate variable quantities of food. Like other organs it possesses a system of longitudinal and circular muscle fibres, but it has, in addition, an inner system of oblique fibres which pass down from the circular fibres of the œsophagus along the lesser curvature, spreading out like a fan on the anterior and posterior surfaces. It seems likely that this system is concerned with the downward movement of the greater curvature, which takes place as the stomach fills up.

EXAMINATION OF STOMACH BY X-RAYS

This gives valuable information about the shape, size, and motility of the stomach. The patient swallows a meal of porridge or bread and milk containing 2 ounces of a solid salt of bismuth, preferably the oxychloride, or 4 ounces of barium sulphate. The rays are then used, and the position and size of the stomach are indicated by the shadow cast on the screen by the contained metallic salt. The X-rays show that the stomach consists of a vertical part and a horizontal part, separated by the *incisura angularis* on the lesser curvature. The vertical part is divided into two by an imaginary horizontal line at the level of the cardiac orifice. The part above, which usually contains air, is called the *fundus*, the part below the *body*. The horizontal part consists of the *pyloric vestibule* and the *pyloric canal*. The first part of the duodenum during the action of the stomach receives and retains for a time the chyme, so that under the X-rays it shows a dark shadow like the stomach, which often has a triangular shape with its base towards the pylorus, the *duodenal cap*. It is separated from the stomach by the transparent line of the pylorus, in the middle of which the pyloric canal may be seen from time to time, wider or narrower according to the amount of chyme going through. Peristaltic waves of muscular contraction from

the body to the pylorus are recognised by the X-rays with accompanying changes in the shapes of the body and pyloric vestibule. The average position of the normal stomach in the vertical position is such that the greater curvature lies just below the iliac crests (or umbilicus), while the lesser curvature is above it. However, there are wide variations in the position of the stomach quite compatible with health. It may be elongated, reaching low down, and this is sometimes known as the *dropped* stomach which is usually also *hypotonic* (*see* Plate 21 and also Fig. 48 on p. 340), or may be entirely above the iliac crests, the *hypertonic* stomach (*see* Plate 22). In the horizontal position, with the patient lying on his back, the stomach falls back beneath the diaphragm, and so lies higher than in the vertical position; it is often divided into two by the vertebral column. It has been observed that a stomach may drop several inches, when viewed in the vertical position, as the result of emotion, or just before a fainting attack, or after a nauseating smell, such as asafœtida. Conversely the stomach tends to be hypertonic when the appetite of the subject is aroused (**11**). The mean position of the stomach depends on the physical build of the individual. It is high when the body is broad and short, *i.e.* when the circumference of the chest is 3 cms. greater than the body length (*see* p. 472) and, conversely, low when the circumference of the chest is 7 cms. less than the stem length. The high stomach is usually associated with a high acidity of the gastric juice (**12**). Members of a family tend to resemble one another in the emptying time of the stomach and in the type of their test-meal curve.

No X-ray examination of the stomach is complete without determining the rate of emptying. The patient is examined two hours, four hours, and eight hours after taking the meal to see if there is any shadow still remaining in the stomach. Normally the stomach is empty in four hours. The small hypertonic stomach is often empty in two hours. Pyloric stenosis is suggested if most of the contents are still present after eight hours. It will be noticed that these times are rather greater than are obtained with the fractional test-meal method.

EXAMINATION OF THE CONTENTS OF THE STOMACH

By the examination of the vomit, and of liquids artificially withdrawn from the stomach during the process of digestion, we may try to ascertain the share which a deficiency of the acids, of the pepsin, or of the motor powers of the stomach may have in different forms of disease, especially in the chronic disorders of digestion.

Vomit. If the patient vomits, the quantity, odour, colour, and consistence of the liquid should be noted. The smell may be modified by substances recently taken, such as volatile oils or alcohol. The liquid may be colourless, or different shades of brown, or stained yellow or green by bile pigment, or pink or red by blood. Often blood is altered by contact with the gastric juice, and a dark brown, opaque fluid is the result, resembling *coffee grounds*. In consistence vomit may be watery, or more or less viscid from mucus, or frothy. The presence of half-digested or undigested food should be noted.

Microscopically animal and vegetable tissues may be detected, such as muscle fibres, cellulose, starch granules, oil drops, red blood corpuscles, leucocytes, and numerous micro-organisms, especially *torulæ*, *sarcinæ*, and sometimes Oppler-Boas bacilli. For chemical examination the vomited fluid must be strained through fine muslin, and the filtrate may be submitted to the tests presently to be mentioned.

Test Meal. The functions of the stomach can be more accurately determined by the use of a test-meal than by examining vomit. Two methods are used: (1) *Ewald's Test Breakfast.* The stomach is first washed out, or the meal, consisting of 2 or 2½ ounces of bread or toast and 20 ounces of weak tea, is given in

CHRONIC DYSPEPSIA

Sufficient has already been said to indicate that chronic dyspepsia is not a disease, but rather a series of symptoms resulting from disturbance of function in the upper alimentary tract.

Pathology. In considering the problem two questions must be kept distinct: (1) What is the organ the functions of which are disturbed in dyspepsia and how does the disturbance produce symptoms? (2) What is the lesion that causes the disturbance?

(1) It is at the present time a relatively easy matter to determine in what organ the symptoms are being produced. Pain is the symptom which has been most fully investigated (**7**). When it is felt high up in the epigastrium by the xiphisternum, or behind the sternum, it is caused by the œsophagus (*see* Plate 18, B, p. 325). Substernal œsophageal pain may be distinguished from cardiac pain by getting the patient to make a swallowing movement. The resulting peristaltic wave that travels down the œsophagus at about the rate of 1 inch a second momentarily relieves the pain, but may intensify it if the pain is very slight. Swallowing does not make a difference to cardiac pain; but it must be remembered that the two kinds of pain are quite commonly associated. Pain in the stomach is felt in the epigastrium, probably rather lower than the œsophageal pain, and sometimes along the left costal margin, and very commonly round the umbilicus. Pain in the duodenum is felt at about the same level but rather to the right of the middle line. Pain in the jejunum is probably felt below the umbilicus.

Visceral pain may be produced experimentally by blowing up an airbag placed inside a viscus and it is due to the stretching of the pain nerve endings in the wall (**21, 22**). The presence of such a foreign body in the œsophagus, the organ which has been investigated most completely, causes a series of peristaltic waves to pass down it. Each time the wave passes over the bag and compresses it the pain diminishes or disappears, because the muscle by contracting and lessening its diameter takes the strain from off the nervous structures, even though a high "systolic" pressure is produced by the contraction. The pain reappears as soon as the wave has passed and the wall becomes stretched again during "diastole." In this case the pain is discontinuous or "griping." The tone of plain muscle has been defined as "tension during diastole," and pain produced experimentally is associated with increased tone. If an incompressible water bag is used the pain becomes continuous and exceedingly severe because the peristaltic wave is held up in its course. The pain is partly due to the continuous stretch, but it is also due to a strain in the nervous structures at the zone between the muscle contracted in systole above the bag and the muscle contracted isometrically and so still stretched by the bag itself just below. Thus the pain is made worse with each peristalsis. This experiment represents the painful spasm associated with the presence of gallstones or renal calculus in the duct. Hollow viscera have a great power of enlarging, *i.e.* altering their "posture," using Sherrington's term, and a foreign body that causes symptoms in the first place ceases to do so when the organ has become big enough by the lengthening or rearrangement of its fibres, so that it can hold it without being stretched. But this process can only take place rather gradually. Hence the postural lengthening of a fibre must be distinguished from its stretching, which causes pain. Counter irritation acts chiefly by causing reflexly increase in posture.

The sensation of sinking or emptiness is produced in the stomach; the sensation of globus or of a ball of wind in the chest is produced in the œsophagus; while the sensation of nausea, which is felt at the back and lower part of the throat, is due to reflex disturbances in the upper part of the œsophagus. It is suggested that these sensations are due to specific end organs which react to a lower degree of tension than the pain nerve endings, but as the tension increases these sensa-

tions become replaced, as elsewhere in the body, by the over-riding sensation of pain. The sensation of fulness may be due to extension of the abdominal wall.

Observations carried out by means of a small water bag on patients, while they were experiencing pain, showed the presence of a series of contractions. These have been observed in the œsophagus, stomach, duodenum, or jejunum. Further, the diastolic pressure inside the viscus was increased, though the extent of the increase varied in different cases. The contractions tended to diminish the pain, which was in one case experienced during the subsequent muscular relaxation, during which stretching of the pain endings occurred from the increased diastolic pressure in the viscus. Thus, there was very great similarity between the artificially produced pain and that which occurred naturally. Further, a very close connection was observed between the different viscera. Distending the stomach with air produced peristaltic waves down the œsophagus (the gastro-œsophageal anti-regurgitation reflex). Contractions in the stomach in a patient with hunger pains were followed about one second later by similar waves in the duodenum.

Dyspeptic pain is due to stretching of the pain nerve endings in the wall, and this agrees with other observations that dyspepsia is often the result of unsuccessful attempts at emptying the stomach (**24**). It is quite possible that in some conditions the muscle may be unduly extensible from fatigue, so that stretching of the pain endings occurs under a relatively low diastolic pressure; but where the pressure is high there must be simultaneous closure of the sphincters, or otherwise the contents would be driven out, and it is quite likely that the dyspeptic syndrome depends primarily on one of these two factors: undue extensibility of the muscular wall; or closure, possibly achalasia, of the sphincters. Localised contractions (spasms) may occur at other places than at the sphincters—in the œsophagus, or duodenum, or on the greater curvature of the stomach. Pain in the stomach is usually of two kinds. It may come on shortly after a meal, or after some hours, when the viscus is empty of food, the so-called *Hunger Pain*. The view is held out that there are two important factors associated with these types of pain, both of which would tend to cause stretching of the wall. These are (1) aerophagy, which may be quite involuntary, and (2) prolonged secretion from the gastric mucous membrane. In fact, these factors have been regarded as compensatory, the aerophagy leading to a rise of pressure and so to the emptying of the organ, and the prolonged secretion acting as a diluent of any noxious substance, in the same way that irritation in the mouth leads to a copious salivary secretion (**24**).

So far, no account has been taken of hydrochloric acid as a possible pain producer in dyspepsia. Gastric ulcer responded to the administration by stomach tube of 200 c.c. of 0·5 per cent. HCl, in 35 cases with pain, in 24 cases without pain; the figures for duodenal ulcer were 41 and 64. Further, pain was produced in cases where the lesion was distant from the stomach (**17**), but gastritis cannot be excluded in these cases. Possibly the acid causes pain by increasing the tone of the stomach.

The nausea, sense of fulness or pain of dyspepsia, may lead reflexly to vomiting, or retching, which is the quickest and safest way for the upper part of the alimentary tract to rid itself of its contents. It is due to strong contractions of various skeletal muscles, by which the contents of the stomach are forced out along the œsophagus and through the mouth. In adults vomiting is usually an extremely painful process; but the pain is possibly due to the stomach contents being pressed out through a closed cardia. Vomiting itself is painless, as the writer himself observed when once attempting to push a bag tied on to the end of a stiff catheter down his own œsophagus. It was simply pushed out again by abdominal contractions. The vomiting of babies and hysterical vomiting are painless, and the same is often the case when vomiting is due to intracranial disease. Stimulation of the lower part of the lesser curvature leads to vomiting

movements. The abdominal muscles contract, while the stomach is motionless (**11**).

(2) *Lesions responsible for Chronic Dyspepsia ;*

(*a*) The stomach itself may be the primary cause, owing to deficiency in the tone of the muscle, which is often accompanied by dropping of the organ (*see* p. 339), or to gross organic disease, such as gastric ulcer and carcinoma, and pyloric stenosis, or to chronic gastritis.

(*b*) Dyspepsia may be caused reflexly by organic lesions situated at a distance, by duodenal ulcer, chronic appendicitis, gall stones, and other lesions of the gall bladder, chronic pancreatitis, lesions of the kidney, particularly movable kidney and calculus. It may be secondary to constipation. In the gastric crises of tabes the primary lesion is in the posterior nerve roots. Angina pectoris may cause a secondary indigestion—*heartburn* in particular. That the origin of the dyspepsia in these cases is reflex, is shown by the following observations. Manipulation over the appendix area in chronic appendicitis has produced a localised spasm of the greater curvature of the stomach. The latter has also been produced by stimulating electrically the peritoneal surface of a duodenal ulcer at operation (**11**). In a case of jaundice from gallstones, the epigastric pain was found to be associated with the gastric movements. Reflex subternal pain has been noted when manipulating a chronically inflamed appendix (**25**).

(*c*) Dyspepsia may be due to more general agencies : pregnancy, sensitiveness to foreign proteins (*see* p. 138), mental anxiety, overwork, and other debilitating influences, such as prolonged illness, fever, anæmia, Bright's disease, which may act by causing hypotonus of the stomach wall or by interfering with the secretion. Hypoglycæmia may cause a feeling of hunger with pain. The fact that some people may suffer from indigestion all their lives without any obvious cause has led to the suggestion in times past that there is a dyspepsia "sine materia." It is, however, probable that careful examination in such cases will always disclose, apart from well-marked organic disease, some lesion, whether this takes the form of weakness of the stomach wall which has been called atonic dyspepsia, or hæmorrhagic erosions in the mucous membrane (**24**). The present writer has been much impressed with the frequency of slight hæmorrhage in chronic dyspepsia. The majority of his dyspeptic patients show no obvious abnormality in the X-ray appearances of the stomach and duodenum ; but the stools contain occult blood and give a hæmatoporphyrin spectrum ; this is now looked on as due to chronic gastritis. The term *acid dyspepsia* only refers to one symptom of variable occurrence, viz. acid regurgitations, which may or may not be accompanied by hyperchlorhydria. The term *nervous dyspepsia* may be used to describe the dyspepsia of organic nervous disease or disturbed mental states, such as the uneasiness and sinking felt in the epigastrium associated with anorexia and nausea, which are characteristic of certain psycho-neurotic conditions.

Anorexia nervosa. In this disease of mental origin, described by Gull, the patient, usually a young woman, refuses food or takes very little and becomes emaciated. She states she is not ill and may even show exceptional energy. The condition begins in many instances with an attempt to maintain an elegant figure ; the patient overdoes the reduction of weight, and the family become anxious and even nag, which only makes the patient more determined. The under-nutrition may lead to tuberculosis. The treatment must be firm, with rest in bed, a prescribed diet and a special nurse to ensure that the diet is take In refractory cases nasal feeding may be required.

Dyspeptic symptoms may persist for some time after the cause has been removed. This is illustrated by an experiment, in which the œsophagus was distended by a bag so as to produce pain. The skin over the sternum was tender and there was pain in the back ; both these symptoms continued for some hours after the experiment was ended, and a severe attack of ordinary dyspepsia

occurred the next day. The œsophageal muscle fibres were probably slightly injured and produced reflex gastric disturbances.

Symptoms. These vary much in different cases.

Pain. Dyspepsia is shown frequently by pain in the epigastric region, which comes on after taking food, and lasts a certain time, gradually subsiding. It is commonly situated around, and particularly just above, the umbilicus or at the level of the xiphisternum or along the left costal margin. It may be felt behind the sternum; this pain is called *cardialgia* or *heartburn*. Often it is felt between the shoulders, going "through to the back." Gastric pains may be referred to the head, producing a brow ache. In other cases pain begins when the stomach is empty, and is relieved by ingestion of food. Instead of pain there may be only a sense of discomfort, tightness, or fulness, or a sinking feeling. Severe pain may be accompanied or followed by superficial tenderness of the overlying skin, or deep tenderness on pressing the abdomen.

Flatulence. This is a common occurrence in all types of indigestion. There is distension of the stomach with corresponding discomfort in the upper abdomen and pain relieved by eructation. Flatulence is usually regarded as due entirely to aerophagy (*see* p. 338), but it is sometimes partly due to CO_2, which is probably given off when the alkaline duodenal contents regurgitate and meet the acid gastric contents in the stomach. Thus the gas in the stomach has sometimes been found to contain 10 per cent. CO_2.

Nausea is a common symptom of dyspepsia, and *vomiting* less frequent, except in alcoholic dyspepsia. The vomited matter is either the ingested food or merely mucus. With repeated emesis bile may be rejected, and a few streaks of blood. *Pyrosis*, or *water brash*, is a name given to a condition in which a quantity of liquid is brought up into the mouth. The liquid is sometimes neutral or alkaline in reaction, and is then commonly believed to consist chiefly of saliva; but it is often acid. There is an accompanying burning sensation felt in the throat and behind the sternum. This is not due to burning by the acid, because acid of this strength does not cause any sensation in the œsophagus.

General Symptoms. The tongue is variable; it is sometimes furred. The fur may be thin and white, or thick and yellow or brown. The furring so often met with may be due to a slop diet, with absence of mastication, or to a deficient flow of saliva, so that the surface scales are not rubbed off. It is accompanied by offensive breath. Constipation is frequent, but may be interrupted by occasional diarrhœa. The appetite is variable; there may be thirst, especially with vomiting. The skin eruptions, erythema, rosacea, urticaria, and acne vulgaris, are often associated with indigestion. The effect upon the body generally, or more correctly upon the nervous system, is seen in malaise, indisposition for exertion, giddiness, subjective sensations of sight, drowsiness, irritability, and mental depression; while slight anæmia or sallowness, some loss of nutrition, and in chronic cases a settled expression of discomfort or anxiety upon the face, are not uncommon. But in other instances there is no general indication whatever of the gastric fault.

Diagnosis. The symptoms of indigestion, and their association with food or hunger, are so characteristic that there is no difficulty in diagnosis. However, diagnosis of the cause of the condition is quite another matter, and in long-standing cases, in addition to a thorough general clinical examination, X-ray examination of the alimentary tract, examination of the stools for occult blood, a test-meal and analysis of the duodenal contents, may all yield valuable information. Even when gross disease of the stomach has been excluded, the presence of occult blood may indicate a hæmorrhagic lesion in the mucous membrane, which may be due to chronic gastritis.

Treatment. It is necessary to treat any disease or faulty habits of life which may be responsible for the dyspepsia. In particular oral sepsis must be attended to. The actual treatment of the dyspepsia may be classified as follows:

(1) *Diet.* All foods containing indigestible residues in the form of pips and skins should be avoided, and solid food must be thoroughly masticated, or minced in the absence of teeth, before it is swallowed. Highly flavoured or spiced sauces, fried food, made-up dishes, condiments, acid fruits, and uncooked substances such as radishes, salad, etc., are not allowed. Food must be simple; but it is impossible to give a hard and fast list of what is allowable. So much depends on the patient's own experience. The following principles should be borne in mind: Flesh foods stimulate the stomach to produce a highly acid juice with much pepsin, and are best digested in such a medium. Starchy foods are digested by the enzyme of the saliva, which requires a slightly alkaline medium, while fats diminish the secretion of HCl and delay the emptying of the stomach. Under ordinary circumstances, and especially if the gastric juice is rather deficient, meat should be given at the beginning of a meal so as to stimulate its production, and the meal may be continued with starchy foods and fats in the form of vegetables, cereals, or fruit, with butter or cream. On the other hand, if the secretion of gastric juice is very abundant, the best results may be obtained by giving fats to begin with, in the form of olive oil, ½ ounce, or sardines in oil, with butter, to be followed by meat and cereals, etc., later. It is probably better practice to lessen the secretion by means of fat than to neutralise the HCl in the stomach after it is formed by drugs. Fat should not be given with flesh foods, and the presence of much fat in pork may be the reason that this is usually tolerated badly. Fish, of which many kinds contain no fat, is usually tolerated best of all.

In more severe cases meals of ordinary size cannot be taken at all, and it is certainly the case that the stomach works best when it contains only a small quantity of food, while pain or discomfort are noticed both when the stomach is full up and when it is quite empty. Hence it is advisable to give food in small quantities at a time and at frequent intervals. Besides a light breakfast, lunch and dinner, something should be taken on waking in the morning, in the middle of the morning, at 4 p.m., and before going to bed at night.

The liquid part of the diet may be regarded from two points of view. There is the volume of fluid that, mixed with the solid part of the meal, produces the optimum concentration for digestion. This should be taken during, or immediately after the meal, and may amount to a pint in the twenty-four hours. There is the additional fluid, amounting to 1 or 2 pints, that is required in the general metabolism of the body. This should be taken a quarter or half an hour before meals. Solids and liquids should always be taken warm. The most suitable fluids are water, *weak* tea or cocoa, and, of course, milk, which is also an important food. Alcohol must not be taken.

Some dyspeptic patients are greatly wasted because they refuse to take food owing to the fear of unpleasant consequences. For such patients rest in bed is essential, and they should be compelled to take food in excess of their basal requirement (*see* Plate 37) until they regain their weight. It is a good plan to allow a varied breakfast, lunch and dinner, the amount of food being equivalent to the basal requirement, and to prescribe, in addition, 3 pints of milk to be taken on waking, 11 a.m., 4 p.m., and last thing at night.

Drugs. These should only be prescribed when symptoms are complained of in spite of careful regulation of the diet. One of the most valuable is CO_2, which may be liberated in the stomach and acts by inhibiting gastric contractions, or by causing eructations which relieve the intra-gastric pressure. Two mixtures are made: (1) ℞ Sod. Bicarb. gr. xxx.; Infus. Gent. Co. ad ℥i. (2). ℞ Citric acid, gr. xxx.; aq. chloroformi, ad ℥i. To get a maximal effect with eructations the first mixture is followed immediately by the second. A milder effect is obtained by taking repeatedly a teaspoonful of No. 1, followed by a teaspoonful of No. 2, until the pain or discomfort disappears. Instead of the sod. bicarb., a teaspoonful of equal parts of prepared chalk and mag. carb. may be mixed up in a little water

and used similarly. The mag. carb. will act beneficially in relieving the constipation so often present. The beneficial effect of sodium bicarbonate in relieving pain when given by itself is almost certainly due to this liberation of CO_2 by the acid in the stomach, and not to its alkaline nature. The advantage of giving citric acid is that it makes the action more certain, and it is probably bad practice in most cases to neutralise the HCl of the gastric juice suddenly during digestion. If it is desired to prescribe an alkali independently of the CO_2 effect, magnesium oxide may be used. Where it is suspected that there are lesions in the mucous membrane, bismuth or kaolin may be prescribed with the idea of covering the lesions with a plaster and so protecting them ; but they must be given in fairly large doses, *i.e.* 2 to 4 drachms, suspended in water with mucilage. In some cases of indigestion acid hydrochlor. dil. in doses up to a drachm, well diluted with water, taken during and after the meal, is of great benefit, especially when the HCl of the gastric juice is low, and there is much flatulence accompanied by flushing of the face, as in cases of rosacea. Other drugs called carminatives have been taken from time immemorial, and are of subsidiary importance. They are sal volatile, tr. nucis vomicæ, strychnine, ipecacuanha, the vegetable bitters such as calumba root, and the volatile oils, such as oil of peppermint.

Physical Methods. Heat externally applied to the upper part of the abdomen is a powerful help to digestion and probably acts, like counter irritation, by causing reflexly effective visceral movements. Heat may be applied after meals by means of Gamgee tissue, tied round the abdomen, a small portable hot-water bottle, electric or ordinary poultices, or plasters including antiphlogistin or thermogene wool. Other methods applicable to cases of gastroptosis with deficient motor functions on the part of the stomach are described on p. 340. In cases of very severe acute intractable gastric pain, a tube should be passed into the stomach to relieve the pressure. This is preferable to giving morphia, which may, however, be sometimes necessary.

AEROPHAGY

The condition of *aerophagy* or excessive air-swallowing gives rise to one form of flatulent dyspepsia. In the past the accumulation of gas in the stomach was considered to be due to fermentation ; but normally this does not occur to any appreciable extent, because the stomach contents are too acid and stay there too short a time. Carcinoma of the stomach, producing pyloric stenosis, is the condition chiefly predisposing to fermentation, because here there are both low acidity and stasis of food. Normally some air is swallowed with food, and is observed in the stomach by X-rays as a clear area just below the left diaphragm giving rise to the tympanitic note obtained on percussing over the upper part of the stomach. It is only when excessive quantities of air are swallowed, and particularly if the process continues between meals, that the condition is known as aerophagy.

Ætiology. There are three groups of cases :—

1. *Dyspeptic.* This is to be regarded (*see* p. 335) as an exaggeration of the normal mechanism by which air enters the stomach (**24**).

2. *Bad Habits.* This is closely related to the dyspeptic variety and may result from it. The patient feels some discomfort, such as a feeling of tightness or fulness in the epigastrium, which he feels can be relieved by a successful eructation. This feeling may arise spontaneously, or may result from an attack of acute indigestion or an acute gastric ulcer, or some other illness. It persists after the original cause has disappeared. It is not due to excess of gas in the stomach, as the latter is often nearly empty. The patient tries to relieve himself by eructation, but the only effect is to force air into the stomach, so that the discomfort increases ; this is repeated once or twice until a considerable amount of air has

walk on hands and feet, which will facilitate the passage of food through the pylorus.

HYSTERICAL VOMITING

Like other hysterical manifestations, hysterical vomiting usually arises from some complaint of which vomiting is one of the symptoms, and is continued owing to "suggestion" after the original complaint has been cured. The vomiting which is a natural accompaniment of pregnancy may be continued in this way in suggestible individuals. Vomiting of this kind may continue after an attack of appendicitis, even when the appendix has been removed surgically. In the war vomiting was one of the symptoms of "gassing," and in many cases hysterical vomiting resulted.

Treatment. As in other hysterical conditions, psychotherapy must be employed. The exact state of affairs must be explained to the patient. All special drugs and diets which were originally prescribed on account of the vomiting, but which may keep up the condition by suggestion, must be removed, and the patient must be encouraged to take ordinary food. In resistant cases the patient may be fed by a thin rubber tube passed through the stomach into the duodenum.

CYCLICAL VOMITING

This is a relatively common complaint among children of three to thirteen years of age both in private and hospital practice, though it is apt to be dismissed under the diagnosis of "bilious attacks" which are attributed to some indiscretion in diet. The attacks occur at varying intervals, and are brought on by mental excitement such as attending parties or doing examinations, by infection such as coryza or tonsillitis, by muscular over-exertion as in competitive games, and by shaking as in a motor drive. There is often a family history; and the subjects of the complaint are sometimes, but by no means always, below par, suffering from constipation listnessness, pallor, "nervousness," nocturnal enuresis, backwardness, ketonuria, etc.

Symptoms. The attack begins suddenly. The symptoms, which last for two or three days, are lassitude, drowsiness, headache, vomiting and prostration. Pyrexia, which may reach 103° F., is invariably present on the first day. There is abdominal pain often in the right iliac fossa and sometimes accompanied by tenderness and rigidity, so that appendicitis is simulated. In a case of the writer's the stools were offensive at the beginning of the attack and unusually copious after it was over. Constipation is the rule during the attack. The vomit as well as the breath of the patient smells of acetone, and the acetone bodies—acetone, aceto-acetic acid, and β-oxybutyric acid—are found in the urine. This ketosis may be present at the beginning of the attack, before the vomiting begins. If the vomiting continues, the child rapidly emaciates, the abdomen is retracted, the face is drawn, and the eyes are sunken. Occasionally the attack is fatal, with headache, delirium, restlessness, convulsions, and collapse or coma from ketosis (*see* p. 466); and in fatal cases the liver has generally been found to be in a state of fatty degeneration.

Pathology. Hypoglycæmia has been found in some cases; in others the blood sugar is normal. The suggestion has been made that through sympathetic stimulation there is an increased outpouring of adrenalin, which increases glycogenesis (*see* p. 479) and ultimately leads to the dissipation of the liver glycogen in the form of glucose, which is rapidly burnt up in the body.

Prevention and Treatment. The attacks may be prevented and treated by giving plenty of sugar. If the child is unconscious 5 per cent. dextrose may be administered through a nasal tube passed as far as the pylorus or duodenum (*see* p. 479), and *per rectum*. The ketosis should be treated by giving plenty of fluids, sodium bicarbonate, etc., but insulin must not be given.

ACUTE DILATATION OF THE STOMACH AND DUODENUM

(*Gastric and Duodenal Ileus*)

Stomach. Cases of this kind are comparatively rare, though many have now been recorded. Their occurrence is not easily explained; in the majority of cases there is no obvious cause of obstruction, but some have come on after overloading the stomach, especially with vegetables. Excess of gas is rapidly produced, and the stomach becomes distended like the rumen in sheep after eating green wheat. A few cases have occurred after injury, because, presumably, the gastric muscle is paralysed, and more than one-fourth after surgical operations. Here the anæsthetic is supposed to be responsible, especially if it is ether, because patients are apt to swallow air with this anæsthetic.

The onset is generally very sudden; the patient is seized with vomiting, and brings up frequently large quantities of green, brown, or grey fluid. With this are gastric discomfort, pain, and tenderness. The abdomen is generally found to be considerably swollen in its left and lower portions, while the epigastrium is relatively flat. Visible peristalsis is quite exceptional (once in forty-four cases collected by C. Thompson); but varying amounts of resonance, fluctuation, and splashing may be obtained. The patient becomes collapsed, suffers from thirst, the urine is scanty, and the bowels are confined. The symptoms may last a few days.

After death the stomach is found to be enormously distended, stretching down towards the pubes, and there bent on itself with a portion returning up towards the duodenum. The distension sometimes extends some way along the duodenum.

From observations by Box and Wallace it appears that when once the dilatation has begun the distended stomach falling in the abdomen causes a kink in the duodenum, and thereby an obstruction by which the escape of gases from the stomach is prevented, and so the condition is aggravated; and the more the gases accumulate, the more certainly are they prevented from escaping.

Treatment. A tube should be passed so as to remove the contents from the stomach, which are under great pressure. The patient should lie face downwards, and the bottom of the bed should be raised so as to straighten out any kinks.

Duodenum. In this condition there is obstruction due to kinking, possibly by the mesenteric vessels, with or without spasm near the duodeno-jejunal flexure. A chronic condition of dilatation of the duodenum is probably not very uncommon, accompanied by dyspeptic symptoms, distension of the abdomen and bilious vomiting (**28**).

INFLAMMATION OF THE STOMACH

ACUTE GASTRITIS

Ætiology. Acute inflammation of the stomach, or acute gastric catarrh, may be set up by various forms of irritants. The most intense form of gastritis occurs in poisoning by the strong mineral acids, or other corrosives. The more common cases arise in consequence of the use of indigestible food, such as lobster, crab, or shell-fish, or of unripe fruit, or of flesh, fish, fruit, vegetables, or other food which is in a state of commencing decomposition (*see* p. 367). It is thus common in hot weather. Infants frequently suffer from gastritis associated with enteritis (*see* p. 365). Multiple gastric erosions, described under the heading *acute gastric ulcer*, form one variety of acute gastritis.

Morbid Anatomy. In the well-known case of Alexis St. Martin it was shown that changes quickly followed irritation of the mucous membrane. Red pimples appeared, which were sometimes filled with purulent matter, or there were red patches, or aphthous crusts, or abrasions. The gastric juice was secreted in less

quantity, and mucus was poured out freely. Slight hæmorrhage also occurred sometimes.

Symptoms. In corrosive poisoning the symptoms are acute pain and tenderness in the epigastrium, vomiting of blood and mucus, and collapse; death is a frequent result. These cases are described in works on toxicology.

In the more familiar case of acute gastritis the symptoms are those of acute dyspepsia. The acute gastro-enteritis of infants is described later.

It must be remembered that diseases such as typhoid fever and influenza and appendicitis may begin as an acute gastritis.

Treatment. Food should be stopped altogether for a time. Later a diet should be given as laid down under peptic ulcer. For the pain, hot fomentations or poultices may be used, or, in very severe cases, morphia injected. The same drug will sometimes allay continued vomiting; bismuth and an effervescing draught (*see* p. 337), or 2 or 3 minims of tincture of iodine in a teaspoonful of water given every half-hour, are also useful. Washing out the stomach by syphonage may often be useful at the beginning of an attack.

Acute Suppurative or Phlegmonous Gastritis. Suppuration of the walls of the stomach is a very rare event, and occurs either in the form of a circumscribed abscess or as a purulent infiltration. The symptoms usually resemble those of acute intestinal obstruction, with severe pain in the epigastrium (**30**).

CHRONIC GASTRITIS

This disease has been a fruitful field of controversy, because of the rapid changes that the stomach undergoes after death from post-mortem digestion. Good fixation, however, can be obtained by injecting 10 per cent. formalin into the abdomen immediately after death. Chronic gastritis arises in two ways: (1) *by the blood stream* from toxic or infective agents which tend to cause involvement of the whole gastric surface; (2) *directly from* the effect on the mucous membrane of injurious agents in the lumen of the stomach; these tend to produce, in the first place, pyloric gastritis (affecting the pyloric part of the stomach), because the contents are more firmly pressed against this part of the stomach than elsewhere (**31**).

In the earlier stages there may be excessive secretion of hydrochloric acid with a continuing secretion after the meal has left the stomach. Achlorhydria is a final result of chronic gastritis. The term "achylia gastrica" was introduced with the idea that certain people were constitutionally unable to secrete HCl, and it has even been suggested from fractional test-meal figures that 4 per cent. of healthy students may be affected in this way; but it is inconceivable that healthy oxyntic cells could be present in the stomach without a function. Further, even when the free HCl is absent, pepsin and chloride are found to some degree (*see* Fig. 47), and there is probably a little "active HCl." In some cases, at any rate, the achlorhydria is due to excessive duodenal regurgitation (**14**); or it may require a test-meal consisting of 5 per cent. alcohol or an injection of 0·5 mgm. histamine to elicit the secretion. A persistent achlorhydria or achylia is not a functional condition; in the absence of carcinoma ventriculi it indicates chronic gastritis; it is not uncommon in diabetes and Graves' disease.

Ætiology. There is a familial tendency to chronic gastritis. In children chronic hæmatogenous gastritis may result from acute infectious diseases, and especially acute gastro-enteritis; and in adults it may result from various acute intestinal infections, such as dysentery, the enteric fevers, appendicitis, and also from pulmonary tuberculosis, Graves' disease, pellagra, rheumatoid arthritis and the toxæmias of pregnancy. The pyloric form of gastritis results from poorly prepared food, from drugs, and especially alcohol. These agents act, in the first place, by stimulating the HCl secretions, which may be excessive; it is only later when the gastritis spreads all over the stomach that an achlorhydria

results. Statistically it is found that the frequency of achlorhydria increases with age.

Morbid Anatomy. In the hæmatogenous forms early inflammation shows itself by a round cell infiltration between the gastric glands. Later the glands become atrophied and replaced by granulation tissue, or in some places they are cystic; sometimes intestinal epithelium with goblet cell and even Lieberkühn's glands appears. In follicular gastritis there is a formation of typical lymphoid follicles. Similar changes may occur in the pyloric form, but, in addition, a mammillated condition of the mucous membrane, and even a regular polyposis, may be obvious, and superficial erosions are characteristic.

Symptoms. In the hæmatogenous form the commonest symptoms are flatulence, constipation or diarrhœa, or both alternately, a sore tongue with atrophied papillæ or ulceration as in pernicious anæmia, fatigue, depression, sleeplessness and migraine. There may be no dyspeptic symptoms; the presence of these would appear to depend on the activity of the inflammation. There is occult blood in the stools. Pyloric gastritis, on the other hand, may produce exactly similar symptoms to those of juxta-pyloric ulcer (*q.v.*), with hypersecretion of HCl, hunger pains and even hæmatemesis. Further, it has been found, on examining microscopically the pyloric part of the stomach which has been removed at operation for peptic ulcer, that a pyloric gastritis is frequently present and also a duodenitis, which suggests that peptic ulcer is frequently merely an advanced form of this condition. Chronic gastritis, in the later stages when achlorhydria has developed, is associated with a microcytic anæmia (simple achlorhydric anæmia), pernicious anæmia and subacute degeneration of the spinal cord; it predisposes to carcinoma ventriculi; but there is difficulty here, as achlorhydria is much commoner in women, but carcinoma of the stomach is much commoner in men.

Diagnosis. The significance of achlorhydria has already been dealt with. A dyspepsia associated with hypersecretion may be attributed to gastritis, especially the pyloric form, if other causes have been excluded.

Treatment. For achlorhydria 1 drachm of acid hydrochlor. dil. in 4 ounces of water should be supplied with meals, while other fluids must be taken half an hour before meals. The treatment of dyspepsia has already been considered.

PEPTIC ULCER

(*Ulcer of the Stomach and Duodenum*)

Ulceration is very apt to occur on mucous membranes that habitually come into contact with the acid gastric juice. Such ulcers are conveniently called *peptic*, and there are several varieties. The *acute* ulcer, most commonly multiple, varies in size from a tiny superficial erosion of the mucous membrane up to an inch in diameter. *Chronic* ulcers, usually single, are best classified according to their positions: (1) in the body of the stomach, usually on the lesser curvature, and on the posterior rather than the anterior surface; (2) in the pyloric part of the stomach, also usually on the lesser curvature and posteriorly, but not extending nearer to the pyloric ring than ¼ inch; (3) in the first part of the duodenum, usually posteriorly. In this connection it must be remembered that the first part of the duodenum has a completely different function from the other parts, but resembles more closely the pyloric part of the stomach. Thus the acid chyme is pushed through the pylorus into the first part of the duodenum, and remains there until the next peristaltic wave pushes some more chyme forward to take its place. Ulcers situated actually at the pyloric ring are uncommon. Ulcers in the body of the stomach often have distinct characteristics, and much confusion has arisen from grouping the pyloric ulcers and these ulcers together under the heading *gastric*, merely because they both happen to be in the stomach, whereas the pyloric ulcers have a much closer affinity with those in the duodenum.

Pyloric and duodenal ulcers should be considered together as *juxta-pyloric;* ulcers both of the stomach and duodenum may be present simultaneously.

Ætiology. Acute peptic ulcers occur scattered about irregularly, and are probably quite common in both sexes; but they are commoner in women and tend especially to affect the body of the stomach. Some ulcers in this situation become chronic, though most of them heal readily enough. However, they may come again later and again heal. A continuation of this process, viz. acute relapsing ulceration, tends to the formation of an hour-glass stomach, which is much commoner in women than in men (**32**). While peptic ulceration in women occurs most commonly in the body of the stomach, in men it occurs most commonly in the juxta-pyloric region and does not heal so well. Consequently we find (1) that chronic duodenal ulcer is four to six times commoner in men than in women, whereas (2) chronic gastric ulcer is about equally common in both sexes, since the preponderance of the male ulceration in the pyloric region about neutralises the female preponderance in the body of the stomach, and (3) ulcer scars are more commonly met with in the body of the stomach (**33**). It has recently been claimed that in women duodenal ulcer is commoner than gastric ulcer, but that the symptomatology of cholecystitis is imitated (**29**). Peptic ulcer has a tendency to run in families. Very occasionally gastric ulcer is due to syphilis. Painless hæmatemesis, so common in young women, which has been called *gastrostaxis*, is due to acute ulceration. The lesions are often so small that they are called hæmorrhagic erosions, and so widespread that the mucous membrane may present the appearance of "weeping blood." Such a condition is an exacerbation of chronic gastritis. The relation of peptic ulcer and pyloric gastritis has been considered. Duodenal ulcer has been described in infants.

Morbid Anatomy. *Acute Ulcer.* In the earliest stage there may be a superficial necrotic lesion with reddened margins situated on a slightly raised and thickened patch of mucosa. Then excavation occurs and tiny vessels are exposed in the floor, which is often covered with a thin black layer of altered blood. This layer separates, leaving a smooth clean floor before healing. The ulcers have a punched-out appearance; the smaller ones are quite shallow, affecting only the mucosa; the larger ones penetrate the muscular coat and have a "terraced" appearance, because the ulcer becomes narrower the more deeply it penetrates. The *chronic ulcer* is generally much larger, and may reach a diameter of 5 or 6 inches. It extends deeply into the wall of the stomach; the edges are thickened and raised, from infiltration with inflammatory fibroid material, and overhang the ulcerated surface; and the thickening extends some little way into the surrounding mucous membrane. When *active*, the chronic ulcer has a narrow zone of sloughing inflammatory exudation in the floor. When *healing*, the floor becomes clean by separation of the slough, the margins become flatter, and epithelium grows inwards over the floor. In a *callous* ulcer the process of healing remains stationary.

When the ulceration reaches the peritoneum this may rupture so that perforation takes place. This is commoner on the anterior than the posterior wall of both stomach and duodenum. The visceral contents escape into the peritoneal cavity and set up intense general peritonitis, or a more localised abscess, *perigastric abscess*, or *subphrenic abscess* (*see* p. 416). This abscess may perforate the diaphragm and set up pneumonia, pleurisy or pericarditis, or it may perforate the colon or duodenum, or open again into the general peritoneal cavity. The term *chronic perforation* is used for an ulcer which leaks into the peritoneal cavity a little at a time over a long period, so that adhesions form and shut off the main peritoneal cavity. These may be so dense as to suggest carcinoma. The stomach becomes connected through the ulcer with a large cavity outside the stomach, sometimes involving the greater part of the lesser sac. More often the inflammatory process, extending to the serous surface, causes the stomach to

adhere to one of the adjacent parts before perforation can occur. This is most frequently the pancreas or the left lobe of the liver, but adhesion also takes place occasionally to the diaphragm, spleen, colon, anterior abdominal wall and even the suprarenal capsule. The ulcerative process then extends into the newly attached organ, and cavities may be formed in the liver and pancreas. Very rarely fistulæ may be produced into the colon or through the skin. Hæmorrhage is a common accident, mostly from gastric vessels in the wall of the ulcer, but sometimes from the splenic artery after adhesion to, and ulceration of, the pancreas.

But many ulcers recover completely, and small scars are often found. They are often very difficult to see, and are frequently missed at post-mortem. Larger scars, which are thick and puckered, may themselves give rise to considerable trouble. Thus at and near the pylorus they may by their contraction cause *stenosis*, and consequent *dilatation of the stomach*; if near the cardiac extremity, the stomach may be contracted. Sometimes an *hour-glass contraction* is due to ulcer. *Perigastric adhesions* sometimes give rise to pain and dragging sensations. The relation of gastric ulcer to carcinoma is considered on p. 353.

Pathology. Bolton produced ulcers experimentally in animals by preparing a special gastrotoxic serum and injecting it beneath the peritoneal surface of the organ. The cells were devitalised, and the HCl of the stomach took part in the digestion of these cells with the formation of an *acute ulcer*. No ulcer was formed if the stomach contents were kept alkaline. The naturally occurring acute ulcer in man can be explained along these lines. There may be several different factors that play the part of Bolton's gastrotoxic serum, such as embolism, from septic foci elsewhere, a chronically inflamed appendix, or gall-bladder, septic teeth, extensive and infected burns; or venous thrombosis of small vessels or hæmorrhage, sometimes due to portal obstruction. The stomach may on rare occasions be injured directly by a blow, or there may be a primary pyloric gastritis. The HCl and pepsin digest away the necrotic tissue forming the ulcer. Bolton's ulcers, experimentally produced, healed readily in a few weeks. The rate of healing was very little altered by trying to infect the ulcers with bacterial cultures, or by bleeding the animal so as to make it anæmic. Healing was, however, definitely delayed by feeding the animals (cats) with meat instead of milk, and by producing some occlusion of the pylorus, so that there was delayed emptying of the stomach. In monkeys administration of HCl caused some delay in healing, and this was greatly accentuated by partially occluding the pylorus. There is no doubt that in man many ulcers heal readily enough, but there is a proportion of them that persist and gradually change into the chronic ulcer for two possible reasons: (1) The hydrochloric acid may play a part in this change; but observations that gastrojejunostomy, in the case of juxta-pyloric ulcer, produces very little alteration in the HCl of the gastric juice suggest that this factor is not of great importance (**39**). (2) Increased tension of the stomach wall leading to feelings of pain or discomfort are also common, and these movements, which are probably associated with the closure of sphincters or spasms in various parts of the upper alimentary tract or chronic duodenal ileus (**40**), may be an even more important factor, since relatively high pressures have been recorded (**7**). It is possible that a vicious circle becomes established, the ulcer causing the high tension in the first place, which tends to prevent it from healing. The hydrochloric acid may perhaps act by producing reflex closure of the pylorus and so increasing the mechanical factor. Finally, mention must be made of the fact that strains of streptococci of low virulence have been isolated from tonsils and from various sources, which produce peptic ulcer in animals on intravenous injections, and the same micro-organisms have been found naturally occurring in the ulcers of man, so that they appear to have a specific affinity for the stomach and duodenum, in the same way that typhoid bacilli attack the gut. This phenomenon has been

called "elective localisation" (**41**). Simultaneously with peptic ulcer there may be appendicitis and cholecystitis—the abdominal triad—and the same streptococcus has been isolated from all three lesions (**29**).

Symptoms. *Acute Ulcer.* In a number of cases the first symptom is due to hæmorrhage from the ulcer. In cases of *gastric ulcer* this often leads to *hæmatemesis*, or vomiting of blood, which may be pure or mixed with gastric contents. The patient feels faint, has a sense of oppression in the epigastrium, and in a few minutes vomits the blood, which may amount to 1 or 2 pints. Some of the blood discharged into the stomach finds its way into the intestine; the hæmoglobin is converted into hæmatin and hæmatoporphyrin, and the motions subsequently passed are black, treacly, or tarry, constituting *melæna;* these may appear some hours after the hæmatemesis has ceased. The vomiting of pure blood is rarely fatal; it usually ceases entirely, and may not be repeated. High degrees of anæmia and weakness result from the loss of blood. In *duodenal ulcer* hæmatemesis may also occur; but the tendency is for most of the blood to be discharged *per rectum* as melæna. Apart from hæmorrhage, peptic ulcer may produce dyspeptic symptoms of acute onset, associated perhaps with prolongation of the gastric secretion, as already described (on p. 335). *Perforation* of the ulcer rarely gives the first indication of its presence.

Chronic ulcer of the body of the stomach is characterised by *pain* which is felt deeply in the epigastrium, just below the ensiform cartilage, sometimes nearer the umbilicus, or to the right or left of the middle line, the right more often than the left. It is brought on by the ingestion of food, appearing from half an hour to two hours after a meal; it may continue intense until vomiting takes place, by which it is generally relieved, or it subsides as the food leaves the stomach. In character it is piercing, boring, tearing, or burning, and more severe than in any other gastric disorder. Sometimes there is pain in the back, between the eighth dorsal and the second lumbar vertebræ, and even over the forehead. Associated with the pain, and often noticed for some little time after the pain has disappeared, there is cutaneous hyperæsthesia or soreness experienced when the skin is lightly pinched. Heartburn (*see* p. 336) is rather common, but hunger pains are only found in one quarter of the cases; but complete emptying of the stomach is often delayed, though the food passes out readily to begin with (**33**). The secretion of HCl is found to be normal (**39**).

Chronic Juxta-pyloric Ulcer. The pain resembles in its character that already described; but it is sometimes felt to the right of the umbilicus, and it comes on two, three or four hours after food, or wakes up the patient in the early morning. The pain is relieved by taking some food, and so has been called *hunger pain.* There are two types of cases: (1) When the pylorus opens freely, the stomach readily empties itself of food. There is marked hyperchlorhydria of the resting juice, perhaps most marked in duodenal ulcer, and there is a prolonged secretion of highly acid juice after the stomach is empty; (2) When the pylorus opens freely to begin with, but later there is spasm; this constitutes the early stage of a pyloric stenosis. The hydrochloric acid of the gastric juice shows the climbing curve also with prolonged secretion and hyperchlorhydria; but there is delay in emptying and vomiting is common. Hæmorrhage may be severe or fatal when a large artery is eroded. In this case the vomited blood retains its arterial brightness. There may be remission of symptoms, but the history of the disease is not so long as in ulcer of the body of the stomach, because, owing to the beginning pyloric stenosis, the symptoms are usually more severe and radical treatment more necessary.

In chronic peptic ulcer other symptoms described under chronic dyspepsia, such as flatulence and distension, are commonly present, the continued pain, the defective assimilation of food from vomiting, and the loss of blood, naturally impair the general condition of the patient sooner or later and cause anæmia; but there is no fever, the tongue is clean, and the appetite is often very good and

nausea absent. Constipation, however, is frequent. Examination of the abdomen generally reveals nothing; there may be some hardness or tenseness of the abdominal walls. Only in the case of old ulcers with much thickening, or adhesion to other organs, can anything like a tumour be felt; and if pyloric stenosis results, the dilated stomach may be recognised (*see* Plate 26), and there may be visible peristalsis.

Diagnosis. In a case of hæmatemesis where hæmorrhage is the only symptom cirrhosis of the liver and splenic anæmia must be thought of before the diagnosis of acute ulcer of infective origin is made. Hæmatemesis must not be confounded with hæmoptysis or with vomiting of blood after epistaxis. The complaints likely to be confounded with chronic peptic ulcer are the various forms of dyspepsia already described, carcinoma and chronic appendicitis (appendix dyspepsia), or the dyspepsia associated with gall stones.

A test meal which shows a high concentration of "free" or "active" HCl will favour juxta-pyloric ulcer. The presence of a trace of blood in the meal is suggestive, but it may be produced by slight trauma of the mucous membrane caused by the tube. The presence of occult blood in the stools and of a hæmatoporphyrin spectrum in the fæcal extract is, however, valuable evidence in favour of gastric or duodenal ulcer.

The most valuable evidence in favour of chronic gastric ulcer is obtained by X-rays after an opaque meal. A small projection in the shape of a funnel or sac (*nitch* or *diverticulum*) is seen on the edge of the stomach near the lesser curvature (*see* Plate 23, B). The projection depends on the presence of the stomach contents in the cavity of the ulcer, and will not be seen if the cavity is closing up in the process of healing. An ulcer cavity on the posterior surface of the stomach will not be seen when the stomach is full. In order to diagnose it, it is necessary, after the patient has taken the first mouthful, to manipulate the abdominal wall so as to spread the opaque material over the stomach wall. Some of it will stick in the ulcer cavity, and show it up. In some, but not in all, cases the projection is associated with a deep indentation of the greater curvature or *notch* or *incisura* at the same level or slightly above or below it, due to spasm, and there may be localised painful spots. The indentation may be seen alone without the projection, and may remain constant in position when from the symptoms it would be judged that the ulcer had healed. In such a case the deformity may become permanent owing to the deposition of fibrous tissue, and a cicatricial *hour-glass stomach* is produced. The indentation may occur with duodenal ulcer or appendicitis, and so by itself it is not diagnostic of gastric ulcer. It is also important to see how long it takes for the stomach to empty, so as to detect pyloric spasm as well as cicatricial pyloric stenosis. A positive Wassermann reaction will suggest that a gastric ulcer is syphilitic, and anti-syphilitic measures should be instituted in addition to other appropriate medical treatment (**38**).

Chronic duodenal ulcer may be diagnosed by the X-ray appearance of the duodenal cap. The latter is shown up best if sodium bicarbonate is given with the opaque meal. The appearances are very variable, depending partly on the cavity of the ulcer and partly on spasm of the muscular coat (*see* Plates 24, 25).

Diverticula of the duodenum are shown up by X-rays and are comparatively common; they may be indistinguishable from ulcer and doubtless in some cases are healed ulcers; but the symptoms are often like those of ulcer. The pocket is usually the size of a finger tip and is situated at the junction of the first and second parts, but may be in the second and third parts and in the small intestine, but here they do not so often give rise to symptoms. Adhesion about the gall bladder and twisting at the junction of the second and third parts give appearances resembling diverticula (**34**).

Prognosis. Analysis of the cause of death in 150 cases of chronic gastric ulcer and 200 cases of chronic duodenal ulcer considered together showed that in

51 per cent. it was perforation, which was commoner in duodenal than gastric ulcer, 9 per cent. hæmorrhage, 5 per cent. the effects of long obstruction, carcinoma, etc., 17 per cent. the result of operation, particularly pulmonary complications, and in 18 per cent. the cause was not related to the ulcer (**37**). In *acute* ulcer hæmorrhage, though common, is rarely fatal, and perforation is also rare. In *chronic* ulcer hæmorrhage may be fatal and perforation is not uncommon, but these complications will nearly always be preceded by severe pains of some duration, which indicates that efficient treatment is essential. The absence of pain suggests that the ulcer is healing and these complications are then unlikely. Chronic ulcers of the largest size will heal under conditions favouring the absence of symptoms, especially pain, though the process may take months.

Treatment. The most important indication is to give the stomach as much rest as possible. The patient must go to bed and not smoke, and for some weeks afterwards should take but little exercise. The old method of trying to "rest" the stomach by not allowing the patient to take food by the mouth for weeks at a time, but feeding him rectally instead, has now been given up; the well-known "hunger contractions" of the empty stomach show that this treatment was based on a fallacy. Rest can best be obtained by taking food a little at a time and at frequent intervals.

The patient is fed at hourly or two-hourly intervals during the day, but complete rest is given during the night. Milk will form the chief article of diet, and raw eggs may be mixed with it, if the patient can tolerate them. Junket and cream, arrowroot, custard, potato or artichoke purée, Benger's food, red currant jelly and the juice of fresh fruit can also be given from the beginning of the treatment. Later on, weak tea, thin bread and butter and toast, pounded fish, minced chicken, minced meat can be added. Half an ounce of olive oil may be given before the more substantial meal. Alcohol and smoking are not allowed. At no time should the patient ever feel hungry; *e.g.* on waking in the night an extra feed *may* be required. Treatment in bed should be carried out for fourteen days after pain, rigidity, occult blood in the stools and X-ray evidence of ulcer have disappeared.

Alkalies, and in particular sodium bicarbonate, are much used in treating peptic ulcer, and in Sippy's method the attempt is made by frequent doses to keep the gastric contents always alkaline; in fact, in some cases enough alkali has been given to cause nephritis and uræmia (**42**). A doubt has already been expressed as to whether the acid of the gastric juice is really responsible for keeping up a chronic ulcer, and in any case it would seem more rational to counteract a hyperchlorhydria by means of giving fat in the form of cream or olive oil, etc. The writer's plan is to use two powders alone—prepared chalk and a mixture of magnesium carbonate and prepared chalk—a teaspoon of either to be taken after each feed in water or milk, with a double dose the last thing at night. The bowels are regulated by increasing the number of administrations of the second powder. These substances act beneficially by relieving pain, including heartburn; but this may be because CO_2 is liberated; and very successful results may be obtained by prescribing a little citric acid at the same time when there is hypochlorhydria (*see* p. 338). The aim should be to keep the patient for a prolonged period free from pain or discomfort, and so the ulcer will slowly heal. Other drugs for treating pain are tinct. belladonnæ ℥ v—x. and atropine injections gr. $\frac{1}{100}$, opium in small doses of the extract or tincture, or the liquor morphinæ hydrochloridi in 10 or 15-minim doses. In severe cases the hypodermic injection may be used, but the opiate treatment must always be discontinued as soon as relief is obtained. Local applications to the epigastrium may be used (*see* p. 338). In cases where the pain and discomfort does not rapidly disappear with the medical treatment described above, recourse may be had to feeding through a duodenal tube kept in position for a week at a time, and this is applicable especially to chronic gastric ulcer.

If a profuse hæmorrhage occurs, the patient must be kept at rest under morphia, and calcium chloride gr. i in 100 minims of water may be injected intramuscularly (*see also* p. 175). A stomach tube should be passed and the contents removed with a Senoran's evacuator and the stomach washed out with small amounts either of ice-cold water or water at 130° F., so as to stimulate it to contract down. Adrenaline (20 to 30 drops of a 1 in 1000 solution) may be left in the stomach. No food must be taken for twenty-four hours after the hæmorrhage has stopped, but water may be drunk in amounts not exceeding 5 ounces at a time. Ice should be applied to the epigastrium. When death is threatened, blood transfusion may be carried out. This does not tend to keep up the hæmorrhage, as might be expected owing to the rise of blood pressure. Surgical measures, such as suturing the bleeding vessel, have also been successful in stopping hæmorrhage from a chronic ulcer.

If a patient known to suffer from gastric ulcer is seized with the symptoms of perforation (*see* Peritonitis), the abdomen should be opened as soon as possible—*i.e.* within five or six hours—the peritoneal cavity washed out, and the ulcer sutured.

In ulceration of old standing, with frequent recurrence of pain and vomiting, or of severe hæmorrhages, or with evidence of much thickening about the ulcer, operation will naturally be considered. This has been most successful in cases where the ulcer is accompanied by stenosis of the pylorus or cicatricial hour-glass stomach. The operations practised for chronic gastric ulcer are gastro-jejunostomy, sometimes with excision of the ulcer, or its destruction by the cautery or with jejunostomy, gastro-gastrostomy, partial gastrectomy (removal of pyloric part of stomach), and the median "sleeve" resection of the stomach. For chronic duodenal ulcer the operations are excision of the ulcer, gastro-duodeno-pyloroplasty and gastro-jejunostomy.

Prevention. When an ulcer is healed, care must be taken to prevent a relapse, which readily occurs. Septic foci in the teeth, tonsils, appendix, gall-bladder, etc., must be dealt with, if necessary by operation. Meals must be light and taken at frequent regular intervals, and the rules of diet on pp. 337, 349, should be followed. Alcohol is best avoided, though light wine and very weak whisky may perhaps be allowed at meals. He must eat slowly and masticate thoroughly and only smoke a little. The teeth must be looked after. The patient must be prepared to go to bed on a diet principally of milk at the onset of pain, and olive oil may be taken before meals.

Sequelæ of Gastro-jejunostomy. Statistics show that a cure is by no means invariable after gastro-jejunostomy. Out of 108 cases operated on at Guy's Hospital between 1910 and 1915, 65 per cent. were cured or much improved seven years later, while 35 per cent. were unsatisfactory. The best results were in pyloric stenosis (**43**). In a series of fifty-one cases complaining of symptoms subsequent to gastro-jejunostomy, examination showed a variety of conditions: Gastro-jejunal or jejunal ulcer (*20*), delay in stomach (*18*), recurrent duodenal ulcer (*10*), regurgitation of bile (*8*), dyspepsia due to operation (*24*), etc. The symptoms complained of were pain (*50*), flatulence or distension (*40*), vomiting (*40*), weakness (*38*), constipation (*38*), diarrhœa (*22*), and headaches (*22*). Patients may show glycosuria and there may be deficient assimilation of fat (**45**).

Gastro-jejunal and Jejunal Ulcers. The gastro-jejunal ulcer occurs at the actual site of the anastomosis, and in most cases it is due to the use of unabsorbable suture material or hæmatoma or bruising by clamps at the operation (**44**). Jejunal ulceration occurs just beyond the junction, and is evidently due to the presence of the same factors as cause a duodenal ulcer, such as infection from focal sepsis that has not been eradicated, hyperchlorhydria which has persisted in spite of operation, and spasms round the stoma or in the descending loop and altered motility. The symptoms are the same as in duodenal ulcer, except that the site of the pain is now rather lower and on the left side of the abdomen.

When the ulcer has burrowed down on to the colon, there may be epigastric pain on defæcation. Sometimes jejuno-colic fistulæ occur, with vomiting of fæculent material. These are usually not seen by X-ray examination after an opaque meal.

Treatment. Secondary ulceration must be treated on the same lines as peptic ulcer. Operation may be required and if the pylorus is acting well, the gastro-jejunostomy may be undone. The treatment of the other conditions depends on the X-ray findings. If the stomach empties too rapidly, liquids should not be taken at meals. Massage and gastric lavage may be beneficial. Usually these patients do not tolerate fat well.[1]

DILATATION OF THE STOMACH

Dilatation of the stomach may take place very gradually (chronic dilatation), or may occur quite suddenly (acute dilatation). The latter has been already described.

CHRONIC DILATATION

This results (1) from the various conditions which produce obstruction of the pylorus, so that the stomach wall is also hypertrophied, and (2) from conditions which alter the contractile power of the muscular walls (*see* Gastroptosis). The causes of obstruction are cicatrices of ulcers of the pylorus or duodenum; spasm of the pylorus secondary to neighbouring ulceration; carcinoma of the pyloric part of the stomach; hypertrophic stenosis of the pylorus; pressure from without, binding down by adhesions, or dragging of a prolapsed kidney; and, quite exceptionally, cicatrices from corrosive substances, which, however, generally involve the œsophageal aperture.

Physical Signs of Dilatation following Pyloric Stenosis. In marked cases, when the abdomen is exposed, it is seen to be asymmetrical, presenting a rounded *prominence* in its left half. This prominence extends below the level of the umbilicus, its lower margin having a curve convex downwards and outwards, from the lower part of the costal margin to the right of the middle line. From time to time a wave of peristaltic movement passes from left to right and downwards across the prominent part. A portion at the extreme left, about the size of the palm of the hand, quickly forms a convex prominence, with a decided amount of resistance to pressure; in a few seconds the swelling subsides, and another part, more to the right, swells up for a similar length of time. After each successive portion of the stomach wall has become hard and prominent the whole subsides. This phenomenon occurs spontaneously, or may be set up by manipulating the abdominal wall, or flicking it with the finger sharply, or sometimes on mere exposure of the abdomen. It is called *visible peristalsis*. By sharp movements of the abdomen, as when the patient is shaken, the liquid contents are set in motion, and *splashing* can be heard and felt. This, however, has no significance unless it can be recognised over an abnormal area, as, for instance, as low as an inch from the umbilicus, or at a time when normally the stomach should be empty, namely, six or seven hours after a meal.

A striking feature of many cases of chronic dilatation is the manner in which vomiting takes place. The food is retained for three or four days, and then 2 or 3 pints of fluid are vomited at once. It is generally of a greyish-brown colour, frothing on the surface; and on microscopic examination it shows numerous yeast spores, sarcinæ, and long rod-shaped bacilli, the *Oppler-Boas bacilli*. In other cases the vomiting is more frequent, and the quantity ejected is less at a time.

In addition to the vomiting, the patient suffers from discomfort or actual pain,

[1] The numbers in *italics* refer to percentages.

which is increased as the contents accumulate, and is temporarily relieved after they are evacuated. Great thirst, loss of strength, emaciation, pallor, and constipation are also observed. Much mental depression, and sometimes tetany and convulsions, may also occur. The urine is scanty, and there may be ketosis.

Diagnosis. This depends ultimately on an X-ray examination after an opaque meal (*see* Plate 26). The stomach is enlarged downwards and to the right. At first there may be over-active peristalsis with rapid emptying. Peristalsis then becomes intermittent and the waves of variable depth, so that there is a residue of about half the meal in six hours. In the later stages peristalsis may only be seen occasionally and it may travel in the reverse direction, and the stomach may remain full after twenty-four hours. A fractional test meal (*see* Fig. 46, p. 331) also shows delay in emptying and a steadily rising free HCl curve.

Prognosis. Dilatation from narrowing of the pylorus must persist as long as the disease which causes obstruction, and treatment other than surgical can only be palliative.

Treatment. The treatment is surgical and a gastro-jejunostomy is most often performed. As a palliative measure the operation of washing out the stomach with normal saline (*lavage*) is often of great value. The over-distended organ is thus relieved of the accumulation of liquid and undigested food, and any catarrh which may co-exist is at the same time benefited. A rubber tube attached to a funnel is introduced into the stomach; the stomach is filled by raising the funnel above the level of the mouth and pouring in water; it is emptied again by depressing the funnel and inverting it into a suitable vessel, or better by means of a Senoran's evacuator. The object of using saline is to counteract tetany. The washing should be done once daily, half an hour before the largest meal.

HOUR-GLASS CONTRACTION OF THE STOMACH

This condition is practically always due to cicatrisation of a chronic gastric ulcer, although occasionally perigastric adhesions may fasten the stomach to the liver, and produce a similar appearance by kinking. Carcinoma may produce narrowing of the stomach, and in gastroptosis the stomach is divided into an upper and lower compartment with a narrow neck intervening; but there is no difficulty in differentiating these conditions from true hour-glass contraction.

The symptoms are those of the associated gastric ulcer; but when the latter has completely healed and the constriction is considerable, the patient will complain of being only able to take small quantities of food at a time, larger quantities being immediately regurgitated, so that œsophageal obstruction may be suspected.

Diagnosis. This is carried out by means of X-rays after an opaque meal. The stomach is divided into two compartments connected together by a narrow neck, which joins the upper compartment on the right side and not at its most dependent part. This is quite characteristic, and serves to distinguish the condition from the sagging of the stomach in gastroptosis. If the ulcer is not completely healed, there may be some spasm of the musculature in addition to the cicatrisation; this makes the obstruction still greater, so that only the narrowest streak of barium joins the two compartments. When spasm is present it may relax somewhat on cautious manipulation or after a dose of belladonna. An active ulcer may or may not be present, and is shown as a projection to the right of the neck (*see* Plate 27).

In carcinoma the growth will be seen projecting into the stomach, as a clear area (*see* p. 355); but if it arises from the ulcer, the X-ray appearance may be the same as in hour-glass contraction.

Treatment. The only efficient treatment is surgical; the constriction can

be widened, or the proximal cavity can be united to the distal cavity, or to the jejunum.

CONGENITAL HYPERTROPHIC STENOSIS

This is a form of pyloric obstruction of which the symptoms appear as a rule from a few days to six or seven weeks after birth, most commonly during the first four weeks of life (47). The disease is about five times as common in boys as girls. The symptoms consist of vomiting and constipation owing to the smallness of the amount of food that reaches the intestine, and emaciation; and the vomited matters are often abundant and thrown up with much force. At first they consist of food, but later there is mucus, and altered blood, as gastritis becomes established; but very occasionally bile. The peristaltic movement from left to right, so characteristic of pyloric stenosis, will be seen; and in nearly all cases—a careful and prolonged examination may be necessary during and after a feed—a tumour or thickening, $\frac{1}{2}$ or $\frac{3}{4}$ inch in diameter, will be found to the right of the middle line, a little below the costal margin, varying in hardness from time to time with the contraction of the pylorus, and so distinguishable from scybala. Visible peristalsis may occur apart from organic disease, so that the presence of a tumour is necessary for certain diagnosis. X-rays may also be helpful.

The thickening is a hyperplasia of the muscular fibres of the pylorus, chiefly of the circular coat, and is probably developed during fœtal life; within the thickened mass the mucous membrane is thrown into folds.

Treatment. Medical treatment consists of gastric lavage followed by thickened feeds. After lavage, in which the use of alkalies must be avoided owing to the risk of alkalosis, small doses of atropine may be left in the stomach. Good results have been recorded by the use of luminal in doses sufficient to keep the infant drowsy.

In this country the best results have been obtained by Rammstedt's operation: this consists in cutting through the tumour longitudinally from the peritoneal surface as far as the mucous membrane, so that the obstruction is relieved. After operation food should be very gradually increased. Sudden increases usually lead to diarrhœa owing to the fact that during the preceding starvation the absence of the stimulus of food has led to poor secretion of digestive enzymes. Similar intolerance is found in most under-fed babies when the diet is increased too rapidly. The operation has sometimes been followed by diarrhœa with fatty stools (48), which suggests that biliary and possibly pancreatic insufficiency play a part in the disease.

CARCINOMA OF THE STOMACH

Ætiology. Carcinoma of the stomach is rarely seen before the age of thirty, and 60 per cent. of the cases occur between forty and sixty; it is about twice as common in males as females; heredity is not a prominent feature of carcinoma of the stomach. It is equally frequent among the rich and the poor, and is not related to any particular occupation. Much controversy has arisen as to whether carcinoma arises commonly from gastric ulcer; against this view is the fact that duodenal ulcer is very common and yet carcinoma of the duodenum is very rare. In a series of fifty cases of gastric carcinoma, 56 per cent. had a history extending back for a year, but no longer; in 70 per cent. the history was up to two years (57). Hence in most cases, say roughly two thirds, a carcinoma starts *sui generis* (46), though chronic gastritis, and especially polyposis of the stomach, are likely predisposing causes. In the remainder it results from gastric ulcer.

Pathological Anatomy. Carcinoma affects all parts of the stomach, but

in the majority of cases the pylorus is involved, and the disease extends thence to the adjacent parts of the organs, especially along the lesser curvature. If it affects the cardiac end, the œsophagus is generally also invaded. Sometimes the wall of the stomach is uniformly infiltrated and thickened, and the organ, as a whole, is contracted to a small size (*leather-bottle stomach*). With few exceptions, carcinoma of the stomach is in the form of spheroidal carcinoma or cylindrical carcinoma; and the former is much more common. Either variety may be scirrhous from excess of fibrous tissue, or medullary from deficiency of it; and colloid degeneration may take place in either, but is more common in the spheroidal variety. The scirrhous change is the most common. Sarcoma is rare.

Carcinoma begins as an overgrowth of the epithelial cells of the glands of the mucous membrane; the growths project into the submucous tissue, proliferate further, and gradually involve all the coats. The wall of the stomach is thickened and the growth projects so as to narrow considerably the lumen of the stomach. The growth does not invade the duodenum. In later stages it often ulcerates upon the inner surface. The adjacent mucous membrane may show nodular growths of villous processes due to chronic gastritis.

The ulcerative process may erode vessels and lead to hæmorrhage; this is much less often profuse than it is in simple ulcer. Dilatation of the stomach is frequent as a result of *stenosis* caused by a pyloric growth; but a leather-bottle stomach is small. *Adhesion* of the stomach to other organs commonly takes place, as the growth reaches the peritoneal surface, and invasion of the organ with carcinoma may follow. The liver and pancreas are thus frequently attacked, occasionally the spleen or colon. In the last case a *gastro-colic fistula* may result. Carcinoma of the cardiac extremity frequently invades and obstructs the œsophagus.

Secondary deposits occur in various organs, in the peritoneum, in the liver, pancreas, lungs, and adjacent lymph glands. These are the mesenteric, retroperitoneal, and portal glands; but, as occurs also in œsophageal carcinoma, the cervical lymph glands are sometimes affected quite early.

Symptoms. Clinically there are two groups of cases according to whether the pyloric function is disturbed with undue retention of gastric contents or not.

(1) In the earlier stages of this group the symptoms are chiefly those of dyspepsia. There are loss of appetite and nausea, in the first place, and then sinking, pain after food, and flatulence. The *pain* may be at the epigastrium, or in the position of heartburn. Vomiting is likely to occur earlier in the case when the carcinoma is situate at the pylorus than if it is remote from that point. The vomit consists of food in different stages of digestion, mixed with more or less mucus or streaks of blood. Often the blood mixed with the vomit has the appearance of coffee grounds.

Pain then becomes a more prominent symptom, and if the growth invades neighbouring organs, such as the pancreas, it becomes constant, or arises independently of a meal; it is felt between the shoulders, or in the lumbar region. It is often stabbing and lancinating, but may be boring, burning, gnawing, or tearing. Indications of severe constitutional disturbance set in comparatively early in this type of carcinoma of the stomach. The patient loses flesh, strength, and colour; and in advanced conditions *emaciation* and *anæmia* are extreme. The bowels are mostly constipated. Melæna is rare as an early sign, but *occult blood* (*see* p. 330) is common.

(2) When the function of the pylorus is not interfered with, the growth is usually, but not always, in the body of the stomach. There may be no symptoms until the growth is far advanced. Pain may then be felt in the back from infiltration of neighbouring structures. But such a growth may bleed continuously, the altered blood being passed in the motions, and the resulting anæmia may arouse suspicion of pernicious anæmia, when the tumour is impalpable. At the same time there may be progressive cachexia.

In general, it may be said that in the majority of cases of carcinoma a *tumour* is discovered at some time or other, but rarely in the first three or four months, and according to some statistics in only 33 per cent. of the cases within the first six months. The position of course varies with the part of the stomach affected. A pyloric tumour is commonly situated in the middle line, or a little to the right, midway between the xiphisternum and the umbilicus. When the stomach is much dilated the tumour is even below the umbilicus. It varies in size from that of a walnut to that of a small orange, and is generally very hard. It is at first freely movable, and descends on inspiration, but in later stages it may contract adhesions and become more fixed. It frequently receives an impulse from the underlying aorta. On percussion it is dull or imperfectly resonant; handling it causes pain.

Occasionally perforation into the peritoneal cavity takes place, and is followed by peritonitis; but the symptoms of this event are often obscure or not distinctive. Carcinoma of the retroperitoneal glands causes œdema of the feet, or the same is brought about by thrombosis of the large veins. Gastro-colic fistula, which is mostly the result of carcinoma spreading from the stomach to the colon, is marked either by undigested contents of the stomach passing directly into the colon, and hence *per rectum*, or by fæcal vomiting, the contents of the colon passing into the stomach and hence being vomited.

Death commonly takes place from exhaustion as a result of deficient assimilation of nutriment, or of a rapid spread of secondary growths in the peritoneum with ascites, or in the liver with continued pyrexia. A profuse hæmorrhage or peritonitis, bronchitis, or pneumonia may terminate the scene.

Duration. The illness commonly lasts from six months to two years; two-thirds of the cases last less than eighteen months, and a very small proportion more than two years.

Diagnosis. Carcinoma in its later stages is distinguished from the majority of the diseases of the stomach by the presence of a tumour. Occasionally the diagnosis has been suggested by the discovery of a hard enlarged cervical gland, especially on the left side. If no tumour is discoverable, carcinoma may be confounded with pernicious anæmia, as already indicated, or chronic dyspepsia, including gastritis or peptic ulcer, or purely neuralgic pains may be thought to be due to carcinoma. Exceptionally the tumour of carcinoma may be simulated by the matting and adhesion of parts caused by ulcer. The age of the patient and the relatively short duration of the disease are also important elements in its diagnosis, since carcinoma in most cases is not the result of a previous gastric ulcer.

The X-rays show characteristic appearances. There is an interruption of the shadow due to a bismuth meal by a more or less extensive clear area, or "filling defect," which encroaches upon the shadow by two or more curved or scalloped outlines; this represents the fungating growth projecting into the lumen of the stomach (*see* Plate 28, A). It is tender on pressure, and is constant in shape, taking no part in the peristaltic movements which may be seen elsewhere in the stomach. This interrupted peristalsis may be the earliest sign, before any filling defect is visible. In the case of leather-bottle stomach, the food is seen to fall rapidly through a comparatively narrow tube straight into the duodenum without any peristalsis being visible at all (*see* Plate 28, B). A normal X-ray report was made in 16 per cent. of cases (**57**).

Examination of the stomach contents in the early morning should be undertaken, after the patient has taken two teaspoonfuls of charcoal in milk the night before (**49**). The presence of visible blood, either fresh or altered, is suggestive of carcinoma, especially if it is found on more than one occasion, while the presence of charcoal indicates delay in emptying. In 47 per cent. of cases blood was present in the resting juice, and in 87 per cent. there was no free HCl (**57**). A persistent oozing of blood is characteristic of carcinoma, while an occasional

profuse hæmorrhage is more probably the result of ulcer. Coffee-ground vomit is seen in both.

After washing out the stomach a test meal may then be given. The presence of lactic acid in the test meal suggests carcinoma of the stomach. There was achlorhydria in 64 per cent. of cases; so that free HCl in varying amount is commonly met with. There may even be hyperchlorhydria (57). But usually there is great diminution in the "active HCl" and in the amount of "free HCl." In some cases the mineral chloride is low, due to an associated chronic gastritis. In other cases the mineral chloride is high, which suggests that the HCl has been neutralised by the serum exuding from the growth. Only 46 per cent. of cases showed delayed emptying of the stomach. Blood was present at some time in 64 per cent., and in the remaining 36 per cent. it was present in varying amounts in the stools when examined for occult blood. Hence the absence of blood, both in the test meal and stools, will nearly always exclude gastric carcinoma, but the present writer had a case in a woman of forty, proved by operation, with no blood in the test meal and stools, though there was achlorhydria and a large filling defect by X-rays.

Prognosis. This is very unfavourable, as death is inevitable unless the growth and all infected glands can be entirely removed.

Treatment. In suspected early cases laparotomy should be advised, as removal of the growth is almost the only possible method of cure. It is usually too late to do this by the time a lump can be felt, owing to spreading of the growth and involvement of the lymphatic glands. Gastro-jejunostomy may be performed as a palliative measure. Deep X-ray therapy may be tried.

If dilatation is a prominent symptom, and large quantities of food are vomited every few days, relief may be temporarily afforded by washing out the stomach daily (*see* p. 352), or the patient may be instructed to pass a tube when pain is felt, relief sometimes being obtained by this simple measure alone. Otherwise the measures described under chronic dyspepsia may be used.

Benign Tumours of the Stomach.—These include *adenoma*, *myoma*, *accessory pancreas*, *lipoma*, *fibro-lipoma*, *lymph-adenoma*, and *cysts*. They are quite infrequent. The first three are the least uncommon, and they occasionally cause symptoms by obstructing the pylorus. In other cases the symptoms will depend on the size and position of the growth.

CONSTIPATION

The healthy action of the bowels depends on a sufficient supply of food, the waste of which forms the material for the fæces; a natural secretion of intestinal juices; and an intestinal muscular system readily stimulated and strong enough to force on the fæces from point to point. This action, however, varies in different individuals, who may still all be healthy. Most persons have an action of the bowels once a day, but others twice a day, and some only every other day. Constipation is the retention of fæces for longer than the normal period of twenty-four hours, or in some persons two days; and is due to delay (1) in the general movement along the large intestine (*colonic stasis*), or (2) in the evacuation of the pelvic colon and rectum (*dyschezia*), or in both the processes together.

1. The general movement of fæces along the intestinal canal is purely involuntary, and is dependent upon the adequate muscular power of the intestinal wall, properly stimulated to action by suitable food. A weak musculature may be a hereditary failing, or it may supervene in later life as a cause of senile constipation. A temporary weakness occurs in fevers and acute illnesses, and may result from anæmia, chlorosis, rickets, and diseases involving nervous depression, such as melancholia, neurasthenia, etc. Locally it may be due to flatulent distension, and to catarrh of the mucous membrane.

The stimulus to the bowel comes chiefly from the food; and this may be insufficient in quantity, or too dry, or deficient in mechanical stimuli, of which the cellulose of vegetable substances is the most important. It appears also that in some individuals unusual powers of digestion and absorption on the part of the intestines may leave so little residue that evacuations must be infrequent; a condition that is known as "greedy colon." In many gastric disorders, especially where vomiting is frequent, constipation occurs. Further, the reflex action of the bowel may be directly inhibited by painful local affections of an inflammatory or traumatic nature in the pelvis or abdomen.

Colonic stasis can only be diagnosed by examining the intestines after an opaque meal has been given. Under ordinary circumstances, at the end of four hours the stomach is empty and the food is collecting at the end of the ileum. The taking of a second meal causes special activity at the end of the ileum and in the colon, so that the intestinal contents move forward rapidly (*gastro-ileal and gastro-colic reflexes*) (**50**). The opaque meal has usually left the ileum four hours after it has completely disappeared from the stomach; but ileal stasis can only be diagnosed with safety if no trace of the meal has entered the cæcum six hours after taking it, or if the bulk of the meal is still at the end of the ileum nine hours after the meal is taken if the stomach is known to have emptied itself in three or four hours. Normally the opaque meal reaches the rectum in twenty-four hours. *Colonic stasis* will exist if at the end of this time it is still entirely in the cæcum and ascending colon, or if the splenic flexure is first reached in twenty-four hours, but the opaque meal still remains in the transverse colon forty-eight hours after the meal. If colonic stasis is severe, there will also be delay in the passage of the intestinal contents through the ileo-cæcal valve (*ileal stasis*). Ileal stasis may occur without colonic stasis, especially in cases of sub-acute appendicitis (*controlling appendix*).

2. The desire to defæcate is caused by the entry into the rectum of the fæces which have accumulated in the pelvic colon during twenty-four hours, and this is brought about reflexly by the stimulus of eating breakfast, or of getting up, or of some other daily recurring function.

The defect in the final process of defæcation, that is, in the passage of fæces into the rectum, and the final evacuation, is a common cause of so-called habitual constipation. It is called by Hurst *dyschezia* (χέζω, I ease myself). The performance of this function is dependent upon a stimulus conveyed from the rectum, and the response upon the part of the pelvic colon. In well-regulated persons the stimulus arises at a given time every day, and if allowed to operate an evacuation is the result. If the stimulus is disregarded and the desire to go to stool is repressed, the reflex is likely to be less active on a subsequent occasion, and in course of time the stimulus may fail to be felt. Thus the repression of the desire and the disregard of the sensation are common causes of constipation. Want of time in the case of persons hurrying to business, false modesty in large houses, or in girls' schools, inadequate supply of accommodation in large establishments, mere laziness in many people, contribute to this, and lead to a postponement of the process until the regular habit is entirely given up, the fæces are retained for two or three days or even a week, and then evacuation can only be secured by the use of aperient drugs or an enema.

Another cause of dyschezia is weakness of the voluntary muscles which compress the abdominal contents, and thus assist in the passage of fæces from the colon into the rectum, and from the rectum through the anal passage. These are the abdominal expiratory muscles, the diaphragm, and the levator ani and other muscles of the pelvic floor.

Dyschezia can be diagnosed if the greater part of the opaque meal has reached the pelvic colon and rectum twenty-four hours after it has been taken, and if, in spite of this, there is no desire to defæcate.

In any part of the large intestine delay may be caused by mechanical obstacles

to the passage of the fæces, such as compression or kinking of the colon, hard fæcal masses, stricture by growth, a retroverted uterus, spasm of the sphincter ani, and spasm of the colon, a condition described as *enterospasm*. Some of these conditions in a higher degree lead to complete obstruction.

Symptoms. If left to themselves the bowels only act at intervals of two, three, four, or more days; the colon or rectum becomes loaded with hard, round masses of fæcal matter (*scybala*), generally rather pale, which are welded together into masses. The desire to go to stool perhaps at first only results in ineffectual straining efforts; but finally some scybala are passed, and the same may be repeated two or three times within a few hours, till the lower bowel is emptied. After this the bowel is inactive for another period of several days. During the retention the patient may suffer various inconveniences. Locally there may be a sense of fulness in the perineum, or pruritus ani; and the hæmorrhoidal veins may swell, and possibly hæmorrhoids may be caused. Sometimes there is pain down the thigh from pressure of the fæcal masses on the nerves in the pelvis; moderate distension of the abdomen often occurs, with perhaps flatulence and eructations; the tongue is often furred, whitish or dirty brown, and the breath may be foul. Some patients feel languid, confused, wanting in vigour or freshness, and have actual headache, or even a great deal of mental depression. These and many other symptoms are attributed by some to the retarded progress of the bowel contents or *intestinal stasis* (*see* p. 360). But it must be noted that often the more habitual the constipation, the less is the general disturbance; and many are not conscious of having anything the matter with them though their last evacuation was many days before.

Where the fæces are retained in the rectum the latter becomes enormously dilated to accommodate them. The scybalous condition of the fæces is explained by their retention in the colon, during which there is time for the absorption of most of the liquid contained in them. Even when the rectum is distended with scybalous masses, some fæcal fluid may escape from the anus, or a secretion of mucus may be excited, and the discharge of these liquids may stimulate a diarrhœa. A more extensive catarrhal colitis, and stercoral ulcers, may also result from constipation.

The accumulation of fæcal matter in the pelvic colon may be such that it forms a large tumour in the lower part of the abdomen, of which the distinguishing feature is the fact that it can be indented by firm pressure with the finger.

Treatment. In general it may be said that colonic stasis requires treatment by means of diet, and in severer degrees by massage, abdominal exercises and drugs, and dyschezia by persuasion and exercises, and in severer degrees by graduated enemas. It must be remembered that some patients do well with an evacuation every second or third day.

The patient should make a regular and not a hurried daily visit to the closet whether he feels any desire or not at the time; and this should be continued as a habit for the rest of life, but it may take months before its good effects come into full operation. In dyschezia the squatting position should be adopted.

The diet should be modified so as to include a sufficiency of vegetables, fruit, fresh or preserved, or salad with salad oil; brown bread, wholemeal bread, or oatmeal porridge sometimes supplies the desired stimulus to the bowel. The diet also should be liquid enough, and with some a daily evacuation is ensured by drinking a tumblerful of cold water or eating an apple before breakfast. A teaspoonful or two of the non-absorbable powdered agar-agar added to porridge, potatoes or stewed fruit is valuable in cases of greedy colon.

To those of sedentary habits walking exercise, fencing, horse-riding, or driving is often of benefit, or the abdominal muscles may be specially exercised by Swedish exercises and massage carried out along the line of the colon as indicated by X-rays after an opaque meal. The pelvic floor in women may be exercised by

getting the patient to draw in the anus thirty times morning and evening, as if to prevent the escape of flatus.

But with all this it may be still necessary to have recourse to drugs, and a careful selection is requisite. As a rule, very active or drastic purgatives must be avoided; they produce abundant liquid motions, from the effect of which the intestinal muscle is completely exhausted, and consequently no further evacuation takes place for days afterwards. But it has already been shown that constipation depends on deficiency of peristaltic action, and hence over-stimulation and exhaustion are especially to be avoided. From this point of view much advantage is gained by combining with the ordinary laxatives such drugs as have a tonic effect upon the intestinal muscle. These are especially nux vomica and iron. Senna pods, soaked some hours in cold water and drunk at night, are a valuable laxative. Cascara sagrada may be given every night in doses of 30 or 40 minims of the liquid extract combined with syrup of ginger, or 2 or 3 grains of the solid extract in pill. Pure liquid paraffin may be given in doses of ½ ounce to 1 ounce once or twice daily according to the necessities of the case. An efficient combination is that of aloin with extract of nux vomica, 1 grain or 1½ grains of the former with ¼ or ½ grain of the latter, given in the morning before breakfast; ¼ grain of extract of belladonna or ½ grain of ipecacuanha is sometimes usefully added. Sulphate of iron (1 grain) with aloin and nux vomica is also very useful. If a daily pill is insufficient, two or even three pills may be taken; but in either case the essence of the treatment is that active purgation should be avoided, and directly this seems likely to be produced the three pills each day must be reduced to two, or the two to one; and ultimately the bowels will act without any assistance whatever. In some acute abdominal conditions and after abdominal operations eserine salicylate or pituitrin may be injected subcutaneously. The natural saline waters, when procurable, are of value, such as Rubinat, Püllna, Hunyàdi Janos (containing the sulphates of magnesium and sodium), and Carlsbad (mainly sulphate of sodium); the patient may take from a wineglassful to half a tumblerful before breakfast. Carlsbad salts extracted from the water of the different springs, or sulphate of sodium itself, may also be given—a teaspoonful is dissolved in half a tumblerful of hot water, and drunk before breakfast. Enemas of cold water are often necessary at the beginning of treatment when there is accumulation of fæces in the bowel, and particularly in the rectum, which is below the point of direct operation of aperients. When a large accumulation of fæces has taken place, the enema may have to be assisted by the use of the finger; for some days after this the enema may be used to supply the stimulus until a more natural method is established. In dyschezia not curable by persuasion and exercises graduated glycerine enemas should be tried, beginning with 1 ounce and gradually replacing more and more of the glycerine by water on successive days.

ALIMENTARY TOXÆMIA

By alimentary toxæmia is meant the absorption into the blood of toxins or poisons derived from the alimentary canal. The belief has been gaining ground that a great many symptoms, pathological conditions, and even definite diseases are due to this toxæmia. But many difficulties will have to be overcome before this theory can be put on a thoroughly scientific basis. At present one cannot say much more than that treatment based upon the hypothesis has often been successful. The steps between the cause and the result are not always easy to trace.

Firstly, the origins of the toxins may be organisms introduced from without, as in the case of oral sepsis already referred to (*see* p. 321), in which disease may be produced either by streptococci entering the blood stream or by the constant swallowing of these micro-organisms which come from infected dental

sockets. These may settle down in various parts of the alimentary tract, and produce infections there. Recently some cases of rheumatoid arthritis and osteo-arthritis have been ascribed to this cause. Secondly, food may actually contain poisons, or an excessive proportion of proteins which may decompose, or carbohydrates which may undergo fermentation; and, thirdly, food, or rather fæcal matter, may be retained, as the result of habitual constipation, sufficiently long to undergo bacterial or chemical changes with the production of toxins, or poisonous chemical substances (*enterostasis*).

The complicated processes of digestion which take place in the alimentary canal from stomach to rectum inclusive, and the chances of delay and disturbance offered by such an elongated cavity, seem to provide abundant opportunity for the formation of chemical poisons, or toxins, and their passage into the circulation. But at the outset it is possible that it is not only a question of the occurrence of new poisons or toxins, but of the breaking down of the mechanisms by which normally poisons in the alimentary canal or elsewhere are prevented from reaching the blood. These are the digestive secretions, the mucous membranes and their mucus, the antitoxic action of the liver, and possibly the action of the thyroid gland.

But it appears to be uncertain whether at all, or in what circumstances, the bacteria usually found in the intestine do any material harm; and with regard to chemical substances there is still much to be learned, some attaching importance to the formation of indol, skatol, and phenol, and of ethereal sulphates in excess, while others, as Mellanby, see more danger in the amines produced by the splitting off of CO_2 from the proteolytic amino-acids by intestinal bacteria.

Cases of food-poisoning, in which decomposing food containing specific bacilli is ingested and symptoms result therefrom, need no comment.

Gout and allied conditions are attributed to the prolonged use of food containing a high proportion of proteins, but it is still open to question whether this is because the proteins decompose readily; whether micro-organisms have any relation to them; or whether bacterial toxins, or other chemical compounds, such as purins, cause the mischief. Similarly an excess of carbohydrates may, in infants, cause a toxic condition in which fever, sickness, diarrhœa with acid green stools, and abdominal distension are present. Some cutaneous eruptions appear to depend upon gastro-intestinal irregularities—for instance, acute urticaria after shell-fish, whether this is due to direct poisoning or is an instance of anaphylaxis, as some believe.

Interest has also centred around the third factor, namely, chronic constipation or enterostasis, causing fæcal retention, to which Sir Arbuthnot Lane has attributed so many evil results. His contention is that from improper feeding in early life and from the maintenance of the erect posture the intestines tend to fall, that peritoneal adhesions are formed in various parts to support them, that subsequently with continued retention, and excessive weight of the retained fæcal matter, kinks are formed at the end of the ileum and in the duodenum, which increase retention and lead to dilatation of the parts above, while there is a general proptosis of all the organs. From the fæcal matter thus retained in consequence of this intestinal stasis toxins are formed which act prejudicially both locally and generally. Among the local results are said to be the following: appendicitis, duodenal ulcer, spasm of the pylorus, gastric dilatation, gastric ulcer, gastric carcinoma, and pyorrhœa alveolaris.

In the general condition of the patient the toxæmia caused by this intestinal stasis is recognised by him in every tissue of the body: cold hands, defective circulation, dusky hue of face, pigmentation of the face and body, dull sclerotic and œdema of the conjunctiva, mental dulness, depression, headache, insomnia, incapacity for physical or mental exertion, neuralgia. In the female especially, he states, the effects are pernicious: loss of fat occurs, the kidneys

fall, the uterus is retroflexed, cystic disease and carcinoma of the breast occur, and infection of the genito-urinary tract readily takes place.

It must, however, be admitted that other observers do not believe that chronic intestinal stasis does produce such evil results; they believe that the symptoms complained of by such patients are really due to neurasthenia, which has developed from the habit of introspection, and in particular of constantly paying too much attention to the movements of their bowels.

Prof. Arthur Keith holds different views from those of Sir Arbuthnot Lane with regard to the origin of stasis in the bowel. As the result of observations with X-rays on the movements of the stomach and intestine, and of microscopical researches on Auerbach's plexus and associated structures in the bowel, he puts forward the theory that the peristaltic movements start from separate points in the intestinal canal, which are, in relation to such movements, divisible into the following sections:—duodenal, jejuno-ileal, proximal colic, and distal colic. In each of these sections peristalsis has been observed to be more active at the upper end, and less active as it proceeds downwards, so that at the lower end a condition allied to sphincter action is assumed. Keith recognises in the upper end of each of these sections neuro-muscular tissue analogous to the sino-auricular node of the heart, which he therefore calls *nodal tissue;* and he looks upon the mesenteric (Auerbach's) plexus as the analogue of the auriculo-ventricular bundle. He thinks that an alteration in the orderly transmission of impulses along either of the sections from its upper nodal tissue downwards will account for the enterostasis in the section concerned without the necessity for the adhesions, bands and kinks described by Lane. He is disposed to believe that similar neuro-muscular tissue in the œsophagus and stomach respectively may function in the same way.

A very thorough treatment on medical lines by diet, purgatives, and other measures, as described under "Constipation," should be carried out.

DIARRHŒA

By diarrhœa is meant the passage of motions more often and of looser consistence than is normal. It is the result of excessive peristaltic action, and of excessive intestinal secretion or deficient absorption. Its causes may be classified as follows: (1) *Gastrogenous.* There is often hypochlorhydria, and the administration of 20 or 30 minims acid. hydrochlor. dil. three times a day may check it. Diarrhœa may follow gastro-jejunostomy. (2) Infection of the *small intestine,* such as occurs in catarrhal enteritis, typhoid fever and tuberculosis, may be responsible. In tuberculosis the looseness and undigested character of the motions may be due to deficient absorption. There is also the diarrhœa of cœliac disease, chronic pancreatitis, sprue and lardaceous disease. (3) In the *colon and rectum* the causes of diarrhœa are numerous, including the dysenteries, ulcerative colitis, acute colitis often associated with septicæmias, *e.g.* pneumococcal, the colitis of chronic nephritis, malignant disease, the irritation which follows the abuse of purgatives and enemas. (4) *Reflex diarrhœas* result from cholecystitis and appendicitis. (5) The *nervous system* may cause diarrhœa through emotion or hysteria, and there is a rare form of diarrhœa due to tabes. (6) There is a *mixed* group, which includes the diarrhœa of Graves' disease and excess of insulin.

It must be remembered that the frequent discharge of liquids in small quantities does not of itself show that the canal of the bowel is free. Thus intussusception which partly obstructs the gut is accompanied by the passage of mucus and blood; fæcal fluid mixed with mucus may find a way past very large masses of impacted fæces; and, lastly, even a distinctly contracted intestine may allow some of the thin liquid which collects above the obstruction to pass through and simulate a diarrhœa. These are called *spurious diarrhœas.*

Varieties. Diarrhœa has received different names according to the nature of the matters passed. Thus we have *choleraic* diarrhœa, in which the stools are profuse and watery, or like the rice-water stools of cholera; *dysenteric* diarrhœa, in which mucus is largely present, and perhaps blood; *lienteric* diarrhœa, where taking food into the stomach produces a motion: this is probably due to an increase in the normal gastro-colic reflex (**50**); and *bilious* diarrhœa, when the discharges are deeply stained with a brown or greenish-brown colour, which is due not so much to any increase in the quantity of bile secreted as to the fact that the contents of the duodenum and jejunum stained with bile have been hurried through the alimentary canal without giving time for the natural reabsorption of the altered bile pigment (urobilin). *Colliquative* diarrhœa is a term applied to the profuse, exhausting, and intractable discharges which occur in the last stages of phthisis. A *critical diarrhœa* is an old term for a diarrhœa that accompanies the termination of a pneumonia by crisis; it is probably due to an associated entero-colitis.

Treatment. This must depend upon the cause, or the associated condition. In most cases not of a specific nature, the treatment described under Enteritis may be employed. Lienteric diarrhœa, which depends upon an exaggerated intestinal reflex, may be treated with full doses of potassium bromide.

HÆMORRHAGE FROM THE BOWEL

The passage of blood *per rectum* has already been noticed as occurring in enteric fever, and in ulcer of the stomach and of the duodenum. It also results from other ulcerations, as dysentery and ulcerative colitis, from intussusception, from carcinoma of the sigmoid or rectum, from conditions of intense congestion, from embolism or thrombosis of mesenteric vessels, and from purpura and other conditions of blood disease. The way in which the blood is passed may give a clue as to the point whence it comes. In bleeding from gastric or duodenal ulcers the blood is considerably altered by the secretions, and forms a black, tarry, semi-liquid or treacly mass (*melæna*); in hæmorrhage from typhoid ulcers the blood is equally unmixed with fæces, but brighter red and more fluid than in the former case, from the action of the alkaline contents; the blood in dysentery is in streaks or small clots mixed up with mucus or pus, or thin fæcal matter, though from time to time small quantities of pure blood may be passed. Large quantities of blood may be lost from piles, or from an ulcer of the rectum. Here the bleeding is generally caused by the act of defæcation, the blood either streaking one side of the solid fæcal mass, or coming more or less pure in drops or streams after the motion is evacuated. In scorbutic, purpuric, and hæmorrhagic conditions (scurvy, purpura hæmorrhagica, acute yellow atrophy of the liver, malignant variola) blood comes from the rectum more or less mixed with fæces, or pure, according to the part of the intestine yielding it, or the freedom with which it escapes. The diagnosis of small quantities of blood has already been considered (*see* p. 330). The **Treatment** of hæmorrhage is described with the various diseases which may cause it.

COLIC

The term *colic*, though derived from the word *colon*, means a spasmodic abdominal pain of visceral origin. It is due to a violent peristaltic contraction which is held up by some obstruction during its course down the alimentary canal. Colic may occur in the ureter (renal colic), the bile ducts (biliary or hepatic colic), or the intestines (intestinal colic).

Ætiology. A common cause of intestinal colic is irritating and unsuitable ingesta, such as pork, cheese, high game, shell-fish, ices, etc. In children, colic is a common result of indigestible food, or even simple excess. With these may

be classed the more active purgatives. On the other hand, constipation is often associated with colic, and this is markedly so in the colic due to lead poisoning, whether acute or chronic (*see* Lead Poisoning). Some cases may perhaps be referred to a purely nervous source—for instance, the severe pain of gastric crisis in tabes dorsalis. Lastly, mechanical and acute inflammatory lesions of the bowel, such as strangulation and intussusception, lead to severe pains, which are partly or wholly due to muscular contraction. The term *colic* is, however, generally reserved for conditions in which there is no structural or inflammatory change.

Symptoms. The important symptom is pain, which is situate about the umbilicus, but may move about other parts of the abdomen. This pain is often relieved by pressure, but sometimes there is tenderness. The abdomen is either drawn in, and the abdominal muscles are contracted, or the belly is distended from the presence of flatus. When flatus is present borborygmi are produced by its movements, as it is driven on by the varying intestinal spasm.

The pain may be so severe as to cause much collapse, with profuse clammy sweat and small feeble pulse. Sometimes there is vomiting; often there is constipation; on the other hand, some ingesta, which cause colic, set up active diarrhœa with brown watery stools, and mucus after a time. Here the colic is associated with a definite, though slight, enteritis. The more active purgatives also produce griping and " colicky " pains, which are commonly diminished after each evacuation.

Diagnosis. Any of the colics may be confounded with the pains of any acute inflammation in the abdomen or acute intestinal obstruction. The characteristics are the restlessness of the patient, who may throw his arms about; his flexed position, since pressure on the abdomen usually relieves the pain; while rigidity is usual during the pain, there is flaccidity between whiles; the pain may shoot in a characteristic direction, especially in renal and biliary colic.

Treatment. Obviously, cases of severe abdominal pain must be treated with much caution. If the pain is certainly due to irritating ingesta, relief generally follows the exhibition of purgatives, such as an ounce of castor oil with 15 minims of tr. opii, or ½ ounce of magnesium sulphate with ½ drachm of tr. hyoscyami, or 5 grains of calomel; and a similar line of treatment is used in lead colic (*see* Lead Poisoning). A warm water or castor oil enema may also help, and hot fomentations or a hot-water bottle should be applied to the abdomen. Papaverine hydrochloride ½ to 1½ grain by mouth may also be tried as an antispasmodic. If there is any likelihood that appendicitis, peritonitis or obstruction may be present, purgatives should be avoided; and the question of treatment by operation must be considered.

ENTERITIS

There are several conditions, affecting different parts of the alimentary canal, which may properly be termed enteritis, or inflammation of the intestine. For instance, the catarrhal process, of which some forms of diarrhœa are the result; tuberculous and typhoid ulcerations in the ileum; the ulcerative inflammation of the colon, known as dysentery; and the acute changes set up by intussusception and strangulations, are all, in fact, enteritis. But a large number of these have already received distinctive names; others are only secondary conditions, which produce few symptoms beyond those of the primary disorder; and in others, again, inflammation of the coats of the intestine involves a peritonitis, which throws the symptoms due to the mucous inflammation completely into the shade. Thus the number of cases which require separate description as enteritis is but a small one, though it is probable that a fair consideration of the pathological side of many of our intestinal cases, such as diarrhœa, would show that the name might be justly used more often.

The following forms of enteritis will be here described: *catarrhal enteritis*,

infantile enteritis, food poisoning, sprue, diphtheritic enteritis, and *phlegmonous enteritis.*

CATARRHAL ENTERITIS

(*Intestinal Catarrh*)

Anything which irritates the mucous membrane of the intestine may set up catarrh, such as unsuitable food, certain poisons, and purgative drugs. Catarrh is also ascribed sometimes to chill; but a much more potent factor in its production is excessive heat, and it is always more prevalent in the hot weather of summer and autumn than in the remaining part of the year. This frequency in the summer concerns people of all ages, but infants are especially attacked, as described later. Passive congestion in cardiac and hepatic disease may lead to catarrh of the intestines.

Morbid Anatomy. The changes in the mucous membrane of the intestine are similar to those in other mucous surfaces of the body. The tissues are more vascular, and become swollen. The epithelial cells, including those of Lieberkühn's glands, are swollen, cloudy, and become detached, forming mucus, which is present in large quantity, and cellular infiltration takes place in the intertubular tissue. In more advanced cases the solitary follicles are enlarged, and they may become eroded and produce small ulcers (*follicular enteritis*). In some cases also ulcerations occur in other parts of the mucous membrane, and the secretions may consist of muco-pus, or even pus. As a rule, the inflammation subsides, but it may lapse into a *chronic* condition, with more prominent changes in the mucous membrane. Sometimes there is considerable thickening, with slaty discoloration of the surface; often—especially in the chronic catarrh of infants—there is atrophy of the mucous membrane, involving the glandular layer, but leaving the muscular layer of the mucous membrane, and the submucous tissue, intact.

Symptoms. The chief symptom of enteritis is diarrhœa, or the frequent passage of motions loose or liquid in consistence. This symptom is due not only to the alteration in the secretions poured into the intestinal canal, but also, and largely, to the increased peristaltic movements which the irritation of the mucous membrane calls forth. The condition of the fæces varies much: they are generally at first abundant, liquid, and brownish in colour, with flakes or lumps of more solid matter; but they soon become paler, or, it may be, yellowish or sometimes green. In consistence they are often quite watery, or perhaps slimy, or they contain lumps of stained mucus. Under the microscope there are particles of undigested food, meat fibre, starch granules, and fat, with crystals of ammonium magnesium phosphate, epithelial and pus cells, and bacteria. The bowels may be moved from two or three times a day to ten, twelve, or more.

Colicky pain is often present, which precedes the passage of the motions. Actual tenderness is sometimes present. Borborygmi from time to time accompany the more active intestinal movements. The temperature is variable. Frequently the appetite is lost, the patient complains of thirst, the mouth is dry, the tongue is slightly furred, and a considerable degree of bodily weakness results when the diarrhœa is excessive. A very sudden and acute attack may begin with vomiting.

In most cases the symptoms pass off in the course of a few days; the diarrhœa may cease suddenly, leaving a long interval before the bowels are again opened, or the motions may gradually become less frequent, gaining a firmer and firmer consistence. If the complaint becomes chronic, the patient is troubled with three or four evacuations daily of watery mucus, with occasional griping pains. The imperfect digestion and absorption of food may lead to considerable loss of nutrition.

The disturbances of enteritis frequently extend to the large intestine, so that strictly an *entero-colitis* results. When they can be discriminated catarrh of the *small* intestine is more likely to be present if the stomach is at the same time involved; it is less likely to be accompanied by diarrhœa, which must depend finally upon the action of the large intestine. The evacuations often contain bile and undigested food; and mucus, if present, is more intimately mixed with the fæces. In catarrh of the *large* intestine the mucus occurs in separate masses; muco-pus or pus itself may be recognised. As catarrh approaches the *rectum* tenesmus is more likely to be a symptom.

Treatment. The patient should remain in bed and be kept warm. In severe cases it will be advisable to keep the patient without food for the first twenty-four hours; but as much water should be given as the patient wishes to drink. Later gruel, arrowroot, beef tea, or mutton broth, with rusk or toast, milk and soda water, or milk and lime water in small quantities at a time, should take the place of the ordinary meals. They should not be given too hot. It is a good plan to begin treatment with a purgative. For this purpose a single dose of castor oil may suffice, or one of compound rhubarb powder or of calomel. But generally, by the time the case comes under treatment, there has been a free evacuation, and it is desirable to check the excessive peristalsis and abundant discharge as well as to relieve pain. The tincture of opium may be given in doses of 5 minims every four hours, combined with an astringent such as hæmatoxylum, catechu, tannigen (5 grains in cachet), the aromatic chalk powder, or dilute sulphuric acid. Bismuth carbonate and bismuth salicylate are also of value, and may be given with opium. If the griping is very severe, morphia may be injected subcutaneously. If the diarrhœa is obstinate and exhausting, an enema of 2 ounces of starch containing 15 minims of laudanum may often be used with success.

INFANTILE ENTERITIS

Infants are subject to diarrhœa from a number of causes. (1) In the neuropathic infant, abnormally irritable to all stimuli, increased peristalsis is readily produced, with resulting diarrhœa, often aggravated by excessive feeding given in an attempt to appease his cries. (2) Apart from such children, overfeeding leads to dyspepsia, associated with wind and colic. Loss of appetite and restlessness precede an attack of acute diarrhœa. Such overfeeding is especially likely to occur in hot weather when milk is given to quench the child's thirst. (3) In artificially fed babies, excess of sugar or fat in the food leads to fermentation in the bowel and an explosive diarrhœa. The attack is often preceded by an abnormally rapid gain in weight. Composition of the food is less likely to be important in the case of breast-fed babies; though immediately after birth, diarrhœa, with acid green stools, is not seldom encountered and is cured by giving extra protein. (4) Diarrhœa is often a symptom of a general infection. (5) Stale and contaminated milk may cause fermentation in the intestines, with resulting diarrhœa. Infection of the alimentary tract with specific organisms is probably a rare cause, though small epidemics undoubtedly occur from time to time.

(6) The incidence of so-called *summer diarrhœa* (epidemic infantile diarrhœa) shows a close relationship to the atmospheric temperature. Tolerance to food is diminished in most infants under conditions of prolonged rise of temperature, and alimentary reflexes are exaggerated. The intake of milk is often mistakenly increased in order to meet the demands of thirst, instead of reduced at a time when the body needs less food. Food tends to be more contaminated by organisms which thrive at a higher temperature and which are more readily conveyed to it by flies. Fermentation, already begun before administration, continues in the alimentary tract, unless the organisms are killed by careful sterilization of the food. Restlessness and broken sleep decrease the infant's

resistance. A number of breast-fed babies are usually affected, but in artificially-fed infants, the incidence is very much higher, and the affection tends to be much more severe ; this will readily be understood from what has already been said. Many of the babies on artificial foods have already been suffering from dyspepsia ; tolerance in these infants is already low, and resistance to original infections or to super-added ones is further decreased.

Symptoms range from those of a mild dyspepsia to those of intoxication—a state closely resembling that of the late stages of tuberculous meningitis, except that if the child is disturbed, for a time its reactions appear to be almost normal. A high temperature is the rule at the onset ; later, it often falls. Often there is air-hunger associated with the ketosis. Loss of fluid causes a depressed anterior fontanelle, and dry, inelastic, wrinkled skin, especially over the abdomen. Broncho-pneumonia is common.

Prevention. Avoidance of over-feeding and too frequent feeding is of great importance. In artificially-fed babies, too rapid a gain in weight is often associated with excessive intake of carbohydrate and fat, which should be avoided. In hot weather, the total intake of food should be reduced, boiled water being given to quench thirst. Milk should be as fresh as possible and sterilised or pasteurised before use. If a refrigerator is available, the day's supply of milk should be placed in it and warmed only immediately before use. When there is reason to doubt the quality of the milk, one of the preparations of dried milk should be used. All bottles, containers and teats should be scrupulously clean, kept covered to prevent the access of flies and scalded before use. Ventilation and temperature of the room and the provision of suitable clothing for the infant require constant supervision (*see also* Infant Feeding).

Treatment. If the diarrhœa is not severe, a dose of castor oil may be of advantage in eliminating the fermenting contents of the bowel. Food should be withheld for twelve to twenty-four hours, boiled water being given freely. After this interval, if accompanying vomiting has ceased, food may be gradually resumed, several days being taken before full diet is allowed, any previous errors in diet being corrected. When diarrhœa is a symptom of parenteral infection, the amount of food should be reduced, milk being peptonised and water given freely. Improvement in the diarrhœa is only to be expected with improvement in the infective process. In neuropathic infants, small doses of chloral combined with one or two minims of the tincture of belladonna may be of considerable help. The temperature of the child's environment should be kept as constant as possible. Every care must be taken to minimise the risk of cross-infection from parents and nurses and from other sick infants. In mild cases, no other treatment may be required, but if the diarrhœa continues gentle washing of the stomach and bowel with warm Ringer's solution may be of great value. If the stomach is washed gently and pressures of over one foot are avoided, the process is not greatly distressing, and after a time it will usually be found that the fluid passes freely through the pylorus. Half a pint may be allowed to run through in this manner. The child should then be given a dose of chloral and allowed to sleep ; a diluted feed may then be retained. In more severe cases and in intoxication, if the above measures fail it is probably best to resort to feeding by a continuous intravenous drip of 5 per cent. glucose in 0·45 per cent. solution of sodium chloride. It is usually well to initiate this treatment with a transfusion which can be given through the same cannula. The rate of flow should average about 130 c.c. per kilo of body weight in the twenty-four hours. The appearance of œdema usually means that the flow has been too rapid. Expert supervision is absolutely essential and the treatment should not be attempted except under such conditions. If treatment must be given in the home, loss of fluid may be met by subcutaneous or intra-peritoneal injections. Symptoms of collapse may be met by brandy (℥. x.), diluted and given by mouth, or by injections of strychnine (gr. 1/200).

FOOD POISONING

By far the commonest cause of acute food poisoning in England is infection by the *Salmonella* group of bacilli, and of these *B. ærtryche* (four types) accounted for three-quarters of the cases; this bacillus causes a low death rate, *e.g.* about 1 per cent., probably because it has but low invasive powers. Next in frequency comes *B. enteritidis* of Gaertner, which causes a more serious infection. *B. suipestifer* has a low virulence for man and is a rare cause, though it is commonly met with in pigs. These living bacilli gain access in warm weather to food such as " made up " meat, cheese, fish, crabs, mussels and milk products, and even potatoes and duck's eggs (**54**). However the salmonella toxins are also poisonous, and they may be present in tinned foods, even when the bacilli themselves have been destroyed; these toxins or *ptomaines* accounted for 17 per cent. of cases. Paratyphoid bacilli are probably not a cause of food poisoning; but dysentery bacilli were found in 4 per cent. of cases; an epidemic of dysentery (Sonne) recently occurred (**55**). The *B. botulinus*, which does not produce symptoms of enteritis, has been found chiefly in sausages made from liver and blood in Germany, and in tinned fruit and vegetables in the United States. Its spores are widely diffused in nature and the bacillus grows anaerobically, producing a toxin which is a very powerful poison, but which is easily destroyed by a temperature of 80° C. (**53**).

Symptoms. The symptoms of " Gaertner " and " ærtryche " come on as a rule within from six to twelve hours after eating the food, and consist of vomiting, diarrhœa, colicky pains, numbness, and weakness, with perhaps albuminuria, catarrhal pneumonia, and cutaneous lesions, such as herpes, erythema, urticaria, and petechial hæmorrhages. In the less acute and more prolonged cases there may be a close resemblance to typhoid, or paratyphoid, fever. The cases are sometimes fatal, and the autopsies have shown acute gastro-enteritis, sometimes with hæmorrhages, swelling of Peyer's patches, enlarged spleen, and congestion of the liver and kidneys. The bacilli may be isolated from the blood, bowels, or solid organs. Food poisoning by these organisms must be distinguished from typhoid and paratyphoid infections, the usual method being to test the agglutinating power of the patient's serum towards these various organisms.

The symptoms caused by *B. botulinus*, known as *botulism*, concern the nervous system, and consist of paralysis of accommodation, diplopia, ptosis, dysphagia, aphonia, and diminished salivary secretion. Death occurs with great suffering, since the patient retains full consciousness, while he cannot see, speak, or swallow, and his respiratory movements become gradually paralysed (**56**).

Treatment. In cases of gastro-enteritis the stomach should be washed out to prevent further infection; and, except in cases of great collapse, a laxative should be given to clear out the intestines. Stimulants are often required, such as brandy, ether, and ammonia, and if the diarrhœa is a prominent symptom opium in small doses, 5 to 10 minims of the tincture. In cases of great collapse, normal saline solution should be injected into the subcutaneous tissue.

CŒLIAC DISEASE

This is the name given by Gee to an uncommon disease of children, which presents some similarity to sprue. The child, generally between the ages of one and five, passes abundant pale or almost colourless semi-fluid stools, like gruel or porridge, with a very offensive odour. These stools contain an excess of fat, and with the fatty acid there is a loss of calcium. The abdomen is full, but not tense; there is flatulence, but no vomiting. Wasting of the buttocks is a characteristic feature. The child grows pale, thin, and apathetic; irregular pyrexia may occur; there is marked delay in the growth of the child, although the mental characters are normal: in fact, the disease is sometimes called *cœliac infantilism*.

The condition is occasionally encountered in adults and is called idiopathic steatorrhœa; usually the history can be traced back to childhood. The other characteristics are dilatation of the colon, tetany, osteomalacia, anaemia, skin lesions. The serum, phosphorus and calcium are low, hence the tetany, and there is increased output in the stools (**51**).

Owing to deficient absorption of fats symptoms of deficiency of vitamins A and D are constantly found, though rachitic manifestations may only be revealed during a period of growth. Another suggestion is that fat is excreted into the intestine, because the same oil when given by mouth does not appear in the fæces, indicating that absorption is satisfactory (Snapper). Other deficiency symptoms may occur from feeding difficulties. Severe anæmia is common. In the earlier stages this is usually microcytic; later it may be erythroblastic.

Treatment. Fats should be avoided, vitamins being provided in concentrated form. Many patients improve on a diet consisting largely of ripe bananas. Malted rusks, jellies, chicken, broth, rice boiled in water, potato, and revalenta prepared from lentils are usually well tolerated. In view of the very limited number of articles which can be given, changes should be as frequent as possible to prevent the establishment of strong dislikes, which so often add to the difficulties of feeding these patients. Liver extract and Marmite are necessary when the anæmia is megalocytic, and iron should be given in all cases in which anæmia is present. The prognosis is fairly good with suitable treatment.

PHLEGMONOUS ENTERITIS

In this form all the coats of the bowel are involved, including the serous coat or peritoneum. There is generally intense redness and vascularity, the mucous and submucous coats are thickened, softer, and more friable than natural, and the peritoneum is vascular, sticky, or covered with lymph. It may arise as a local inflammation or the result of a spread from adjacent parts or from intussusception or strangulated hernia.

Symptoms. These are often the result of the accompanying peritonitis, and consist of pain, vomiting, local tenderness, collapse, distension of the abdomen, and febrile reaction. The purely infective cases above mentioned have presented the symptoms of intestinal obstruction.

Treatment must be directed to the primary cause, and in its absence is practically the same as that of peritonitis.

COLITIS

Inflammation of the colon presents the same varieties as are seen in other mucous membranes, and may thus be catarrhal or ulcerative. Catarrhal colitis is often a part of a general entero-colitis, arises from the same causes, and has very similar symptoms—namely, pain, distension, tenderness, and frequent motions in which mucus, and even occasionally blood, are present. If the lesion is near the rectum, there may also be tenesmus. Catarrhal colitis may exist in an acute or chronic form, and the treatment is not materially different from that of enteritis. Both typhoid and tuberculous ulcers occur in the cæcum and ascending colon in association with similar lesions in the ileum; syphilitic ulcers occur in the rectum; colonic ulceration may also be caused by bacillary and amœbic dysentery, *Balantidium coli* infection and intestinal schistosomiasis (*Schistosoma mansoni* and *Schistosoma japonicum*). The so-called ulcerative colitis of asylums and jails which not infrequently occurs in epidemic form is really dysentery due to the Flexner Y group of organisms. The conditions are distinct from chronic ulcerative colitis described below.

MUCO-MEMBRANOUS COLITIS

(*Mucous Colic, Mucous Colitis*)

Muco-membranous colitis is characterised by the discharge *per rectum* of large pieces of membrane or *casts*. It occurs most frequently in middle-aged neurotic females, but is also not very infrequent in children. There is commonly habitual constipation with abdominal discomfort, and other symptoms of chronic dyspepsia. An attack of the disease is accompanied by severe griping pains, which result in the discharge of membranes.

The disease is associated with sudden spastic contractions of the colon with over-production of mucus. This becomes coagulated by a ferment, mucinase, since, owing to the contractions, it is retained for some time in contact with the mucous membrane before being eventually passed. The casts may be several inches or even feet in length, are quite thin and semi-transparent, looking like skins, and embedded in them are epithelial cells, eosinophil leucocytes, cholesterin, and ammonium magnesium phosphate. *Intestinal sand* may also be passed. There is usually some catarrhal colitis present. The narrowing of the lumen of the colon may be observed by taking a series of radiograms after the colon has been filled with an opaque meal. The sigmoidoscope should also be used, in case carcinoma of the pelvic colon is present, as this may give rise to the disease. According to Lockhart Mummery, the disease may be secondary to many conditions—pericolitis, kinking, visceroptosis, displacement of the uterus, etc.

In some of these cases injection, œdema, and ulceration of the mucous membrane have been seen with the sigmoidoscope.

Treatment. If possible the primary cause should be treated. Careful dieting so as to supply a food free from all mechanically irritating particles, fibres, etc., slow eating and careful mastication, and irrigation of the bowel with from 1 to 1½ pints of warm water or 10 ounces of olive oil, are useful means of treatment. Drastic purgatives should be avoided, because by irritation of the colon they will make the condition worse. Castor oil is the most suitable. Liquid paraffin may be used. Belladonna is useful for the pain. The abdomen should also be kept warm by means of an abdominal binder. Sometimes a diet consisting of fruit and vegetables, mostly uncooked, with coarse pods and skins—the antithesis of that described above—is useful, since it attacks the constipation which the patient suffers from. The mental symptoms should be attended to, and the patient's thoughts distracted from her malady. The disease does not endanger life, but it often lasts for years. Occasionally appendicostomy has been performed, and lavage carried out through the opening.

ULCERATIVE COLITIS

(*Colitis gravis, Colitis ulcerosa gravis*)

Chronic ulcerative colitis is a disease of unknown origin characterised by the frequent passage of fæcal material associated with pus, mucus and blood. Pyrexia may or may not be present and acute and chronic forms of the disease may be encountered. Spontaneous remission is not infrequent.

Ætiology. Ulcerative colitis has a widespread distribution in Europe, America and elsewhere and affects both sexes, being most common in adult life. There may be no antecedent condition of ill-health, but certain cases have followed chronic septic disorders such as infected teeth, tonsils and sinuses, and by some this is held to support the view that a specific streptococcus (Bargen's diplostreptococcus) is the causative organism. Others regard Flexner Y bacilli as the responsible ætiological agent, but the evidence that either of these specific organisms is responsible is far from satisfactory. It has also been suggested that following dietary deficiencies or some other cause which lowers colonic resist-

ance locally, the normal bacterial flora—especially streptococci—may take on pathogenic characteristics.

Pathology. The acute fulminating cases resemble bacillary dysentery; there is generalised intense inflammation of the mucosa with exudate, necrosis of membrane and widespread ulceration. The ordinary chronic case shows hyperæmia, œdema and miliary ulceration of the mucosa of the rectum which bleeds on instrumentation or swabbing; later, as the condition progresses, the colon becomes progressively involved with a granular bleeding inflamed surface; the walls of the bowel become thickened and fibrosed and narrowing of the lumen results. At autopsy in late cases the thick contracted bowel with large shaggy ulcers and strips of intervening mucosa, inflamed or polypoid, are very characteristic; in places the ulcers may be in process of healing with regenerating epithelium. Complete healing often leads to multiple polyposis.

Symptoms. In the acute fulminating type of case the onset is sudden with diarrhœa and colicky abdominal pain. The motions are dark brown, offensive and contain much mucus, blood and pus. The tongue is furred, the breath offensive and pyrexia perhaps associated with severe sweating develops. Abdominal distension and tenderness over the colon and some rigidity occur. Marked loss of weight and anæmia result and the patients may die without any remission of symptoms.

Chronic ulcerative colitis may follow the acute type, but much more frequently it begins as an apyrexial diarrhœa with the frequent passage of foul stools containing mucus, blood and pus. Rectal discomfort or tenesmus may develop and anæmia and loss of weight may ensue. Hypochlorhydria is not uncommon.

In 5 per cent. of cases the condition starts as a granular proctitis which gradually spreads up to the pelvic, ascending and transverse colons; ultimately the cæcum may be involved. Rarely segmental areas of the large bowel are affected without involvement of the rectum. Complications include hæmorrhage, perforation, stricture, polyposis of the bowel, carcinoma and arthritis; 20 per cent. of cases showing polyps develop malignancy later.

Diagnosis. The clinical history and appearance of the stools should arouse suspicion as to the nature of the malady, but diagnosis must be confirmed in every case by sigmoidoscopy and X-ray examination. Rectal examination may show an atonic sphincter and polyps may be palpated, while the gloved finger is covered in blood. Sigmoidoscopy reveals a uniformly inflamed, granular surface, bleeding readily on swabbing or instrumentation, and miliary or large-sized ulcers may be observed. The lumen of the rectum and colon is narrowed, its walls are inelastic and rigid so that distension with air causes pain. General anæsthesia is never necessary for sigmoidoscopy, and the patient may be examined in the knee-chest or dorsal positions. In a well developed case X-ray reveals a tubular, shortened bowel with complete loss of haustration, and if extensive ulceration be present, the colon presents a feathery and moth-eaten appearance. (Plate 29, A).

Prognosis. The fulminating cases may remain febrile throughout their course and may die in two to nine months from onset. The chronic cases may never develop fever, and in them remission of many months' or even years' duration may occur; in these circumstances all symptoms disappear and the bowel may even present a normal picture on sigmoidoscopy and X-ray. Later relapses generally occur; the course extends over many years and in some cases the general health is but little affected.

Treatment. Where fever is present rest in bed is essential. A nutritious, smooth, high calorie, high vitamin diet is desirable, and though it may be low in residue at first, fruits and puréed vegetables are included as soon as possible. A diet mainly of apples is sometimes successful. Eradication of septic foci is advisable, while treatment with autogenous streptococcal vaccine, Bargen's anti-ulcerative colitic serum and anti-dysenteric serum (the latter daily in doses

of 10, 20, 40, 60, 80 and 100 c.c. intramuscularly or intravenously) are advocated by some; but deaths have occurred from anaphylaxis. Colonic lavage with saline, sodium bicarbonate, protargol and albargin (1/500), pure potassium permanganate (1 grain to the pint), tannic acid (1 to 2 grains to the ounce) and eusol my prove useful. Duodenal irrigation every other day with warm sterile saline, sufficient in amount to wash the bowel free, is sometimes successful. A 5 per cent. suspension of bismuth subgallate in olive oil may be given daily. Iron therapy and blood transfusion may be advisable if the patient be anæmic, and acid. hydrochlor. dil. B.P. (½ to 1℥) given after food thrice daily. Operative intervention is dangerous owing to the risk of streptococcal peritonitis and should be reserved for intractable cases where medical treatent is of no avail. Appendicostomy, cæcostomy and ileostomy have their advocates; they permit lavage with antiseptic solutions and the last operation rests the bowel completely.

APPENDICITIS

Ætiology. This disease is much more frequent in early life than in middle or old age, and in the male than in the female sex. The greater prevalence of the complaint in recent years, though generally admitted, is quite unexplained.

Pathology. Appendicitis is usually caused by infection by the *Bacillus coli communis*, which is a natural inhabitant of the bowel. Streptococci, staphylococci, *B. pyocyaneus*, and other pyogenic organisms, the tubercle bacillus, the typhoid bacillus, and actinomyces are sometimes concerned. The infection may be excited by a foreign body in the cavity of the appendix, obstructing the lumen. This may be a cherry stone, orange pip, seed, bristle, or similar substance. In many cases a concretion is found of the size of a pea, yellow or grey in colour, and consisting of fæcal matter, mixed with mucus, lime salts, and numerous bacteria. This is now regarded as being formed subsequently to the catarrh of the appendix.

Morbid Anatomy. There is infiltration and thickening of the coats of the appendix, distension of its cavity with catarrhal products or pus, and, finally, ulceration and gangrene. In most conditions the trouble spreads to the peritoneal covering. The peritonitis may be localised and adhesive, matting the appendix to the adjacent bowel, and forming a more or less resistant mass in the right iliac region. An appendix abscess may be formed round the appendix, being shut off by adhesions from the general peritoneal cavity, while the appendix is usually found to be perforated or gangrenous. The appendix sometimes perforates or sloughs before adhesive peritonitis has occurred, and then a general peritonitis, of a very fatal kind, is rapidly determined. Occasionally a peritonitis, at first local, gradually extends with the formation of peritoneal abscesses in different parts of the abdomen, *e.g.* perinephric abscess, subphrenic abscess, or pelvic abscess. Exceptionally infective organisms are carried to the liver by the portal vein, and suppurative pylephlebitis and hepatic abscesses are the result.

If sloughing or suppuration does not take place, the apparent subsidence of the inflammation is by no means always the end of the disease; the condition may relapse, and from six months to two or three years after the attack acute inflammation is again lighted up, and either terminates in one of the above processes or subsides again, perhaps to be active after yet another interval. In these intervals, as shown by operation in certain cases, the appendix presents thickening and infiltration of its walls, often with constriction in the middle, and dilatation at the distal end, with perhaps concretions in its cavity, and peritoneal adhesions externally; or the cavity may be obliterated and the organ fibrous.

Symptoms. *Acute Attack.* The onset is often somewhat sudden. Spontaneously, or after a period of dyspepsia with or without some constipation or diarrhœa, the patient is taken with severe abdominal pain, at first diffused over the abdomen, but soon more pronounced in the right iliac fossa, with malaise,

nausea, vomiting, and some febrile reaction. The tongue is furred, the appetite fails, there is thirst, and the bowels are constipated. The abdomen may be somewhat distended, but is generally rigid and tender in the right iliac fossa. The rigidity may be absent if the appendix is situated in the pelvis. The tenderness is often definitely situate at a point about 3 inches from the right anterior superior spinous process, on a line drawn from this process to the umbilicus—*McBurney's point*. These symptoms may continue for a few days, the vomiting, pain, and tension may diminish under treatment, and the trouble may subside. The pain at the onset is not always diffused over the abdomen generally or situated over the appendical region: it may be epigastric or on the left side, it is frequently umbilical, and it may begin on the left side and go to the right side. There may be pain in the ilio-psoas muscle, elicited by hyper-extending the right hip while patient lies on his left side, or pain in the obturator internus muscle, elicited by rotating the right thigh outwards, with the knee bent, the latter when the appendix is in the true pelvis (*obturator sign*), occasionally there is pain in the penis.

When *perforation* with abscess formation takes place, and the appendix is situated above the brim of the true pelvis, the rigidity or resistance becomes more definitely localised and may form a definite tumour, bounded externally and below by the crest of the ileum and Poupart's ligament, and extending by a convex border half or two-thirds of the distance from Poupart's ligament to the umbilicus. It is often quite dull to percussion, and sometimes it has a modified tympanitic note, while the rest of the abdomen is supple and resonant. The temperature may rise to 103° or 104° F., the pulse to 100 or 120. The pain may be irregular or paroxysmal, and often shoots down the right leg. In favourable cases, if operation is delayed, the tumour may subside, gradually becoming less definite and smaller, so that it disappears in from ten to twenty days from the time it was discovered, while the fever and other unfavourable signs diminish. On the other hand, when the appendix is in the true pelvis perforation may lead to cessation of pain, while there is no abdominal rigidity, and the diagnosis may be missed, even though there is pelvic peritonitis. Apart from the "obturator sign" described above, a deep-seated abscess may be felt *per rectum* or *per vaginam*, or by its proximity (*a*) to the bladder may cause frequent micturition or (*b*) to the rectus may cause diarrhœa and tenesmus.

In cases of early *sloughing* of the appendix, the local indications may be entirely absent, or so slight that they are scarcely noticed by the patient, or of such short duration that the case is from the first, or quite early, one of general peritonitis (*see* Peritonitis).

Hyperalgesia, *i.e.* a feeling of soreness, or merely hyperæsthesia, *i.e.* increased tactile sensibility, may be valuable in diagnosis. They are elicited by drawing a pin over the skin held at a constant angle, or lightly picking up the skin between the finger and thumb. In acute appendicitis these signs are found in about 60 per cent. of cases and nearly always in the right iliac fossa, though there may be additional areas posteriorly and on the left side (**58**). Hyperalgesia is a referred pain, and the fact that it can be produced artificially by stretching the walls of a healthy viscus, and may last an hour or so after the stretching has ceased, shows that it has not necessarily anything to do with inflammation, but is the result of the secondary dilatation and stretching of the appendix walls or possibly a segment of ileum or cæcum.

In the relapses of appendicitis which have been already mentioned, the symptoms are precisely the same as occur in primary attacks; but the liability to general peritonitis is probably less, because adhesions will have formed around the lesion.

In subacute appendicitis deep pressure in the appendix region may cause a little pain, and thickening may be felt. Frequently it gives rise to troublesome symptoms, which are apt to be misleading, because they suggest disease

remote from the appendix. Thus the patient suffers from attacks of pain in the epigastric or umbilical region, sometimes even on the left side, or in the rectum, if the appendix is in the pelvis. In the last case there may be frequency of micturition, and in the other cases vomiting. The pain lasts from a few hours to one or two days. An important group of cases is that in which the symptoms are deceptively like those of gastric ulcer or less often of duodenal ulcer. In some cases pressure over the appendix causes a painful sensation in the epigastrium. The pain is aggravated by exercise or exertion. Attacks occur at intervals over some years, and in the intervals of the severe attacks the patient is in many cases not entirely free from pain. This simulation of gastric and duodenal disease is called *appendix dyspepsia;* and the symptoms are attributable to a dyspepsia produced reflexly from the appendix region.

Diagnosis. An apparently spontaneous acute general peritonitis in a boy or girl is nearly always the result of appendicitis; in older patients many lesions may be confounded with it. Nearly all the causes of the acute abdomen have been at different times mistaken for it (*see* p. 320). The past history, the seat of maximum pain and tenderness, and the local conditions as ascertained by examination externally and *per rectum*, must be carefully considered.

At a later stage, when a tumour has formed, this has to be distinguished from fæcal accumulations, malignant growth of the cæcum, movable kidney, inflammation of the pelvic organs in women, and psoas abscess.

The diagnosis of appendix dyspepsia depends on some local signs being elicited in the appendix region, and on the absence of occult blood in the stools, (though it must be remembered that chronic appendicitis and peptic ulcer not uncommonly occur together), and on other negative evidence of peptic ulcer or cholecystitis. A valuable confirmatory test is *Bastedo's sign*. This is the occurrence of pain or tenderness in the right iliac fossa when the colon is inflated with air, slowly pumped in through a rectal tube. In the healthy person this produces some discomfort, but only pain in high degrees of distension, and then on both sides equally. When appendicitis is present, the inflation causes pain in the right iliac fossa; and the appendical region becomes tender to pressure, or, if previously tender, the sensation is aggravated. Sometimes also pressure in this situation will, after inflation, set up the very same pain in the epigastrium, which the patient has spontaneously suffered (Hurst). In a high percentage of cases the appendix can be seen by X-rays from six to eighteen hours after giving a meal of barium sulphate and buttermilk (Spriggs) or barium sulphate and water (Redding). More important than visualisation of the appendix itself is local tenderness, abnormal fixation of the cæcum and terminal ileum and delay in passage of food through the ileo-colic sphincter, *i.e.* deficiency of the gastro-ileal reflex, which is tested for by giving a meal four hours after a barium meal and examining the cæcum an hour later (**35, 36**).

Prognosis. In recent statistics from the London Hospital there was a 1·2 per cent. mortality of all cases of appendicitis operated on within the first twenty-four hours from the beginning of the attack. This had risen to 3·9 per cent. during the second day and to 8·7 per cent. during the third day. The earlier the operation, the better the prognosis.

Treatment. The facts that appendicitis may progress to the stages of gangrene and suppuration with so few symptoms, and that it is so difficult to ascertain without operation the extent of the danger, have led to the conviction that the removal of the appendix should be undertaken whenever a certain or highly probable diagnosis of appendicitis has been made; and this should be done at the earliest possible moment. If there is doubt about the diagnosis, or the symptoms are less urgent, it may be justifiable to wait; and then the patient should be put to bed, and fed only on milk, Benger's food, and similar articles of diet; hot boric lint or fomentations should be applied, and all aperients should be withheld, except a simple enema if the bowels have not recently acted.

Whether every case which has recovered under medical treatment should be operated on some months later to prevent recurrence is an open question; but if a second attack occurs, certainly the opportunity should be taken to operate. The precaution should be taken to examine other parts of the abdomen, and particularly the gall bladder, for associated disease.

DIVERTICULOSIS

Multiple diverticula of the large intestine, which project out into the appendices epiploicæ through a series of small openings in the mucous membrane, may be found in any part of it, but the pelvic colon is affected in about three-quarters of the cases. The *prediverticular stage* is a local affection of the bowel and results from irritation. There is a little abdominal pain and local tenderness. The diagnosis is made by X-rays after an opaque meal (120 grains barium sulphate suspended in 500 c.c. Horlick's Malted Milk or buttermilk) or opaque enema (**59**). There is a ragged appearance of the outline of the colon (Fig. 49, B), while the segmentation between the normal haustra may be obliterated if that part is affected (A). The next stage is the formation of diverticula, flatulent distension being probably a predisposing cause (C). When there is fæcal accumulation in the diverticulum it forms a stercolith, the barium only partly fills it, so that there is a cup-shaped shadow which moves as the haustrum contracts (D), and at times may be completely shut off from the colon by a strong contraction of the neck (E) (*see also* Plate 29, B, p. 370).

DIVERTICULITIS

Diverticulosis may continue for years without symptoms; but *diverticulitis* may supervene at any time. The earliest radiological sign of this is shown at the neck of the diverticulum owing to infiltration at this point. The haustrum shows further excavation, with blunting of the re-entering angle (F). Most characteristic is the fact that the natural movement of the haustra shown by serial films is completely inhibited. In some cases the diverticula are shut off by the inflammatory thickening (I), or the necks may become so wide that the pouches become V-shaped (G, H); while an extreme obliterative stage from fibrous hyperplasia is shown at J. Other changes that may affect diverticula are (*a*) suppuration; (*b*) perforation and peritonitis; (*c*) fistulous communication with neighbouring organs; (*d*) torsion of a diverticulum with strangulation; (*e*) secondary development of carcinoma.

The symptoms of diverticulitis are those of a low form of inflammation in the large bowel, usually in the left lower abdomen, spreading to neighbouring structures. *Abdominal discomfort*, less often pain, not as a rule related to food, is situated about or below the umbilicus, but especially in the left iliac fossa, and is frequently intermittent. It may take the form of a dragging sensation and backache. General flatulence and a feeling of distension are usually mentioned and may be the only symptoms; an advanced state of diverticulitis may, indeed, be present with but little complaint. *Constipation*, irregularity of the bowels, diarrhœa, or a sense of incomplete evacuation is frequent. In cases of implication of the bladder there may be *frequent micturition*, sometimes painful, after the bowels are opened; or a painless micturition may be followed by pain. A sausage-shaped *tumour*, sometimes tender, but not always, can be felt in the left iliac fossa, except in the very obese. It may become acutely inflamed, with pyrexia and vomiting. Diverticulitis sometimes occurs at other parts of the colon. Hæmorrhage, per rectum, is not usual; the inflammatory lesion lies, as a rule, without the mucous membrane.

Symptoms may arise from complications. When suppuration occurs there may be an acute inflammatory disturbance in the left iliac fossa resembling

the pelvic colon to be recognised (*see* p. 370). X-rays also may be used for diagnosis. An opaque enema, consisting of barium sulphate suspended in water by mucilage, is run into the rectum. If the funnel is held 2 feet above the anus, the mixture passes round to the cæcum, completely filling the colon, if the patient breathes deeply and at times alters his position. The colon must be emptied before the examination by giving castor oil thirty-six hours previously, supplemented by water enemas on the morning of the examination and the evening before. Any narrowing of the lumen or irregularity in its outline is suggestive of carcinoma (*see* Plate 30, A and B). An opaque meal traced downwards through the colon is of much less assistance in diagnosis.

In the later stages the patient may present the signs of acute intestinal obstruction, of chronic intestinal obstruction, or he may complain of an abdominal lump, which may be confounded with other lesions. Affecting the cæcum, it may resemble a chronic appendicitis, or enlarged glands; in the colon an enlarged kidney, a diverticulitis, an enlarged gall bladder, or an aneurysm if it overlies the aorta.

The treatment is surgical, and the prognosis good in the early stages. In inoperable cases deep X-ray therapy may be tried.

Polypoid growths, adeno-papillomas of the colon and rectum, occur in schistosomiasis.

Inflammatory Strictures of the Rectum. *Syphilis* rarely affects the alimentary canal between the pharynx and the rectum, but it sometimes causes stricture in this last situation. Gummas form in the submucous tissue and slowly lead to cicatricial contraction, owing to secondary inflammatory changes. Stricture may also result from gonorrhœa and more rarely from tubercle (**48**). They occur equally in both sexes, and little may be known of them till symptoms of stricture are observed, and the constriction is recognised by digital examination.

INTESTINAL OBSTRUCTION

The intestine may be obstructed in several ways: (1) foreign bodies; (2) intussusception or invagination; (3) changes in the intestinal walls, such as strictures caused by healed ulcers, or by malignant growths; (4) volvulus; (5) strangulation by bands or through apertures; (6) diminution of the calibre due to traction on the intestine, or to compression from outside in various ways.

Foreign Bodies. Among the foreign bodies found obstructing the bowels are fruit stones, pebbles, coins, bullets, pins, needles, hooks, and false teeth. Some large masses are formed of vegetable fibre, wool, or husks of oats, matted together. It is especially in lunatics that foreign bodies of these kinds are found. Occasionally a large gall stone is the cause of a fatal obstruction, or it passes *per anum* after more or less difficulty. Fæcal masses may accumulate in the same way as has been described under Constipation, and form a serious obstacle in the rectum or colon.

Intussusception. This presents special features which make it desirable to consider it separately (*see* p. 380).

Strictures. These occur both in the small and large intestines; they arise either from contraction of cicatrices of ulcers, or from new growths, and very occasionally from tuberculous infiltration in the intestinal walls. Simple tumours, such as *adenoma* and *fibroma*, are also occasionally the cause of intestinal obstruction.

Volvulus. By this term is meant the twisting of a loop of bowel upon itself, so that it becomes "strangulated," *i.e.* the pressure due to the twist is sufficient to interfere with venous return from the loop, but not with the arterial supply, so that congestion, hæmorrhage and gangrene supervene.

Strangulation by Bands and through Apertures. This class of case may be

called internal strangulated hernia; a loop of intestine, commonly the ileum, slips through an aperture, such as the foramen of Winslow, and is strangulated by the margin of the aperture grasping its neck. But more frequently the constricting ring is formed by a band of adhesion stretching from one part of the abdomen to another, under which the loop of gut passes. A frequent cause of this form of obstruction is the congenital abnormality known as *Meckel's diverticulum*. This forms a finger-like projection from the unattached side of the ileum, from 2 to 4 inches in length, and $\frac{1}{2}$ to $\frac{3}{4}$ inch in diameter. It is a remnant of the omphalo-mesenteric duct, by which the primitive alimentary canal communicates with the yolk sac. It arises from the ileum, at a point 18 to 24 inches from the cæcum, and its blind termination is generally free; but it may be attached by a fibrous band to the anterior abdominal wall at the umbilicus, or to the mesentery, or to the peritoneal surface at some other point. A ring is thus formed, through which a loop of gut may slip, and then become strangulated.

Compression and Traction. This class includes acute kinking due to traction by an isolated band; adhesions compressing the gut; and matting together of several coils.

Pathology. In a fatal case of acute obstruction of the intestine, the bowel above the seat of obstruction is found enormously distended, while that below is collapsed and empty. The distension begins immediately above the constriction, and affects the bowel for a greater or less distance, according to the severity or duration of the obstruction. Thus in obstruction at the sigmoid the whole colon and much of the small intestine are affected; in obstruction of the ileum the small intestine is distended and the colon is collapsed. In the upper distended portion is a quantity of fæcal matter, light brown or yellowish brown in colour and of uniform thick liquid consistence; and this is the same whether the obstruction is in the small or large intestine. In chronic cases the distended bowel may become gradually hypertrophied from its efforts to overcome the obstruction; eventually the bowel may yield in the distended portion above, and so-called *stercoral ulcers* may be formed, some of which may perforate. In acute strangulation sloughing may occur at the seat of constriction, from direct interference with the circulation.

Continued acute intestinal obstruction is a fatal disease, and the higher the place of obstruction the quicker is the onset of death. Biochemical changes, somewhat similar to those of an allergic attack, are present (*see* p. 138); *i.e.* in the blood there is a rise of non-protein nitrogen and bicarbonate, with alkalæmia, and a fall in the chloride, which disappears into the tissues (**61**), and the same explanation of a sudden protein catabolism or protein shock may well hold good. It has also been suggested that there is an abnormal proliferation of *B. welchii* with absorption of the toxin from the small intestine; this may initiate the protein catabolism. Favourable results from injecting the antitoxin have been reported (**62**). Another suggestion is that the presence of bile in the intestine is a necessity, and this is hindered. Favourable results from rectal injection of bile have also been reported (**63**).

Symptoms of Acute Obstruction. In a case of strangulation by a band the patient is seized with intense pain in the abdomen, generally in the neighbourhood of the umbilicus; he may be walking about, or having a meal, or he may be awakened from sleep. The patient then vomits. Neither motion nor flatus is passed *per anum;* and the vomiting, at first gastric, then bilious, becomes ultimately stercoraceous. The effect upon the patient is very grave. Collapse soon sets in; the face is drawn, the eyes are dark and sunken, the pulse small and quick, the temperature normal or subnormal. The tongue is dry, and there is constant thirst. Abdominal distension is usually a later sign and varies with the position of the obstruction; if this is in the upper part of the small intestine, the abdomen may be flat, or distended only at the upper part, above the umbilicus; if the lower part of the ileum or large intestine is strangulated, distension

occurs sooner and the abdomen is uniformly enlarged. Tenderness is usually delayed till distension takes place. If the condition is unrelieved, death supervenes, either from exhaustion or from acute peritonitis, of which a general diffused tenderness may be the chief indication. The duration of the case is from four to six days.

When the intestine is obstructed, but not strangulated, the onset is more insidious; the pain is intermittent and less severe; fæculent vomiting and distension are delayed, and the abdominal wall remains flaccid.

The symptoms due to obstruction by a gall stone are often characteristic. At first they are acute, due to ulceration into the duodenum, and afterwards to obstruction of the duodenum by the stone; there is passage or vomiting of blood. Then they disappear as the gall stone passes along the small intestine, to reappear acutely in a day or so if the stone is held up at the ileo-cæcal valve.

Symptoms of Chronic Obstruction. In chronic obstruction such as is due to malignant disease of the pelvic colon or of the descending colon, the symptoms are at first only indicative of a moderate interference with the passage of fæces; there are some local pain and occasional vomiting, not particularly related to the ingestion of food. Constipation occurs irregularly, but it can be overcome by aperients. From time to time the constipation is very troublesome, vomiting is more frequent, yet not stercoraceous, the abdomen becomes greatly distended, and the hypertrophied coils become visible in peristaltic movements on the surface of the abdomen. With the peristaltic movement can be heard gurgling sounds, or borborygmi.

From time to time some fluid motions may be passed, and there may be several large evacuations of liquid fæces, by which the abdomen is rapidly reduced to its normal capacity, and all the symptoms are relieved. This sequence of events may recur more than once, but in some such attack the obstruction becomes complete, and acute symptoms supervene as described above.

Position of the Stricture. The differences to be noted between strictures of the small intestine and those of the large are that in the former vomiting occurs earlier, and is more determined by the ingestion of food; in the latter, as already described, distension is greater, and the proximity of the stricture or growth to the anus may lead to alterations in the shape of the motions, which may be ribbon-shaped; and tenesmus is frequently present. When the distension mainly affects the colon, a number of enlarged vertical coils may be seen, due to the distended ascending and descending colon and to the transverse colon, which bends downwards in the middle and forms two others. When the small intestine is chiefly distended, and the colon is collapsed, the distended coils lie transversely across the abdomen, forming the so-called "ladder pattern."

Diagnosis of Obstruction. Before distension takes place acute intestinal obstruction is distinguished from the various acute abdominal catastrophes such as *perforation* of *peptic ulcer*, *appendicitis*, *acute hæmorrhagic pancreatitis*, and *cholecystitis* and the *colics* (*see* p. 363), by the absence of rigidity and by the more frequent vomiting which tends to become fæculent. When distension is present intestinal obstruction must be distinguished from the later stage of acute peritonitis due to any cause. The presence of acute stasis may be determined by administering two turpentine enemas at a few hours' interval; the first empties the lower bowel; the second proves the constipation. The rectum should also be examined by the finger; it is often empty and dilated, or "ballooned," in cases of obstruction.

The other conditions that must be differentiated are *mesenteric embolism* and *thrombosis* and *Henoch's purpura*, which all produce similar symptoms; but some blood will usually be obtained by an enema. Acute obstruction may be simulated by some conditions of nervous or toxic origin in which mechanical or inflammatory lesions have no part. One is the *gastric crises* of tabes dorsalis, in which pain and vomiting occur; but the abdomen is retracted, and the vomited

fluid, though abundant, is dirty green and watery, but not fæcal. A history of similar attacks in the same patient, and the absence of knee jerks and of the pupil light reflex, would speak for tabes. Another condition is the acute pain of commencing *diabetic coma*, which has more than once nearly led to operation; the patient is generally beginning to be drowsy, and sugar and aceto-acetic acid are found in the urine, if looked for. *Uræmia* may be difficult to diagnose, especially as similar biochemical changes occur; but the vomiting will not be fæculent. The possibility of obstruction from an extra-abdominal hernia, whether inguinal, femoral, or obturator, should not be forgotten.

Treatment. When the diagnosis of acute intestinal obstruction is established the operation of *laparotomy* or opening the abdomen should be performed without delay; and the cause should be ascertained and an attempt made to remove it, or if necessary the bowel should be simply opened at the most distended part above the obstruction, and a fæcal fistula established. Saline infusions and rectal injections of 6 per cent. dextrose may be given with great advantage. Treatment with anti-Welch serum (80 c.c. intramuscularly repeated as required daily) and with rectal injections of bile have already been mentioned. It is rarely wise to give opium or morphia for the relief of pain: it has the serious disadvantage that, while easing the pain and checking sickness, it removes two important symptoms, and may lull to a false security while the fatal mischief is progressing. Locally relief may be furthered by the application of turpentine stupes; or of flannels wrung out of hot water, and sprinkled with tincture of belladonna, or opium; or of hot linseed-meal poultices.

In *chronic* obstruction, which is chiefly the result of strictures and growths, whether in the small or large intestine, the diet must be carefully selected, with the object of ensuring regular digestion and the easy passage of the intestinal contents through the constriction. Enemas, and occasionally laxatives, may be used to maintain a periodical evacuation. If an obstinate constipation ensues, and especially if great distension and sickness occur, the treatment should be similar to that of an acute obstruction. Opium may be given, with or without belladonna, while food must be given in only small quantities, or *per rectum*, when relief may be shortly obtained. Eventually, if life is to be prolonged, an operation will become necessary.

For fæcal accumulations large and frequently repeated enemas generally suffice, but the case requires to be long under treatment by careful diet, exercise, electricity or massage, to restore the bowel to its former power.

INTUSSUSCEPTION

If one segment, say a few inches, of the intestine slips into the portion immediately adjacent, it forms an *intussusception* or *invagination*. It will be at once seen that this must present from without inwards to the centre of the bowel three layers of bowel wall, of which the innermost may be called the *entering* layer; the outermost, the *receiving* layer or *sheath;* and the portion joining these two, the *middle* layer. It is clear that a portion of bowel might slip into a segment above, forming an *ascending* intussusception, or into the bowel below, forming a *descending* intussusception. It is with the latter that we practically always have to do.

Intussusceptions occur at any part of the bowel, and have received names accordingly; thus those of the small intestine are called *enteric*, those of the large intestine *colic* or *rectal*. But at the point of junction with the ileum and the colon two varieties occur—(1) the *ileo-cæcal*, in which the ileum and cæcum pass into the ascending colon, the ileo-cæcal valve forming the most advanced point, the ileum the entering layer, and the cæcum the most advanced part of the middle layer; (2) the *ileo-colic*, in which the lowest part of the ileum is inverted through the ileo-cæcal valve—that is, an enteric intussusception continued into the colon

Of the different forms the ileo-colic is the rarest, and the ileo-cæcal is the most common, forming nearly half of all cases.

Very important changes, dependent on the anatomical relations of the intestines, ensue upon an intussusception. The intussusception, if at all extensive, forms a thick cylindrical swelling, partly from containing three layers of bowel all round instead of one, partly on account of the congestion and œdema to be presently explained. From the mesenteric connections of the bowel this cylinder has a curved shape, since the vessels which supply the inner and middle layers are of the same length as those supplying the receiving layer, and yet have not only to reach the border of the intussusception, but to go into its interior between the inner and middle layers, so that they drag upon the upper end of that part of the bowel. As the intussusception increases it moves farther along the gut, and the internal cylinder of an ileo-cæcal intussusception may even reach the rectum and project from the anus. At the same time the tumour becomes larger. The disposition of the vessels just described leads to their compression and strangulation, and consequently to congestion and œdema of the walls of the intussusception, and even to hæmorrhage from the mucous surface, and the discharge of blood *per rectum*, an occurrence of the greatest value in diagnosis. If the case is not quickly fatal, inflammatory changes ensue in the layers of the bowel, binding them together, and interfering both with the further progress and with the reduction of the intussusception; and, lastly, from the strangulation of the blood supply to the entering and middle layers, these may become gangrenous, slough off, and be discharged *per rectum*. If this has been preceded by the secure adhesive union of the entering layer to the angle between the outer and middle layers, the canal of the bowel is practically restored, and an actual cure may be the result, though this is very rare; if the union is imperfect, the detachment of the inner cylinder is followed by a fatal extravasation.

Ætiology. Enteritis is the commonest predisposing cause of intussusception. Sometimes intussusception has arisen after direct injuries. Sometimes intestinal polypi and carcinomatous tumours are responsible, and in Henoch's purpura it appears to be caused by hæmorrhage into the intestinal wall. It may happen at all ages, but is much more frequent in children. Little that is definite can be said as to the immediate mechanism of intussusception, except that it is due to an irregular peristaltic action.

Symptoms. The onset of an acute intussusception is not unlike that of strangulation by bands—that is, the patient is rather suddenly seized with pain, which is more or less constant, though aggravated from time to time, and griping in character. In the baby, the onset is indicated by screaming. Nausea and vomiting also occur, but constipation is not generally present at first; on the contrary, the bowels are usually moved, and either thin fæces, or (what is especially characteristic of intussusception) *blood* with or without mucus, is passed. Indeed, blood is passed *per rectum* in four-fifths of the acute cases; and often a certain amount of tenesmus is present. The abdomen is not always much swollen, but an examination reveals generally another characteristic feature—the presence of the *tumour* which results from the intussusception. Its position is, of course, related to the site of the lesion; in the more ordinary ileo-cæcal form it is at first situate in the right flank, but as the intussusception increases it is felt in the umbilical region, and is generally oval, cylindrical, or sausage-shaped, lying transversely across the abdomen above the umbilicus. Subsequently it passes into the left flank and left iliac fossa, and ultimately can be felt by the finger in the rectum, or actually projects from the anus. Sometimes there is complete constipation, with much distension, and fæculent vomiting; at others collapse sets in rapidly, and death takes place in twenty-four hours, or from two to five or six days. Death is especially rapid in quite young infants.

But the symptoms are not always so acute; indeed, an intussusception may exist for weeks or even months. In these more chronic cases the extent of bowel

involved is generally less, and the canal is not completely obstructed. The bowels may thus be opened, though blood is passed at the same time in about half the cases. The patient suffers from paroxysmal griping pains, not necessarily of great severity. The abdomen is flaccid, and the tumour presents an important characteristic, namely, a varying consistence, so that it hardens simultaneously with the griping pains, but soon becomes soft, and even imperceptible when they subside.

The terminations of the subacute and the chronic cases are various; they may ultimately lead to death by exhaustion, or to complete obstruction with vomiting, constipation, abdominal distension, and visible coils; or they may set up a local peritonitis, followed by the formation of abscess, or by a more general peritonitis; or the intussuscepted portion may separate by sloughing, and so the intestinal canal may be re-established.

Diagnosis. Spasmodic pain, vomiting, the passage of blood *per rectum* and the presence of an oval or elongated tumour which varies in consistence from moment to moment, and lies in the course of the colon, or occupies the rectum, are the chief features of intussusception; but the tumour cannot always be felt, especially in infants with a much-distended abdomen, unless an anæsthetic is given. *Enteritis* and *dysenteric diarrhœa* in children may resemble it, and a piece of contracted gut sometimes forms a tumour; the blood is more often mixed with mucus. In Henoch's purpura there may be lesions elsewhere and also multiple arthritis. X-ray examination after a barium enema may be used.

Treatment. An *acute* intussusception should, as soon as possible, be met by an effort at reduction, and though cases have been successfully treated by injection of fluids into the rectum and colon, it is safer and more certain for the surgeon to perform laparotomy and reduce the intussusception by careful traction. In the longer-standing cases adhesions may render reduction impossible; and then a portion or the whole of the mass must be resected.

In *chronic* forms when the nature of the lesion is recognised, operation should also be performed.

HIRSCHSPRUNG'S DISEASE

(*Megacolon*)

This is a rare disease, of which the feature is chronic dilatation and hypertrophy of the colon. In many cases the symptoms begin in the first few weeks of life, in others in early childhood, and in others later. There is constipation, obstinate and repeated, the bowels remaining unopened for two or three weeks at a time. The abdomen is distended enormously, so that the pressure on the chest may itself be a danger. The distended coils of the colon may be seen through the abdominal walls. Peristaltic movements are visible in the coils. The child is emaciated, and in the older patients defective nutrition and sallow skin are observed. The disease does not run a rapidly fatal course; but death from intercurrent disease and toxæmia is to be feared. After death the colon is found to be dilated to two or three times its normal diameter, and often much elongated; and in long-standing cases the muscular fibres, especially the circular layer, are much hypertrophied. There are two types of cases, about equally common, according as the dilatation begins immediately above the anus, or above the pelvi-rectal flexure. The most reasonable view of the pathology is to correlate the disease with chronic dilatation of the œsophagus and to regard it as secondary to obstruction (achalasia) of the anus or pelvi-rectal flexure (**64**).

Diagnosis. Megacolon is not so very uncommon; large amounts of gas are seen in the intestines by X-rays, forcing up the left diaphragm and rising above the liver. A sigmoidscope is introduced with ease and a dilated colon is seen; this is also shown by barium enema.

Treatment. Attempts must be made to keep the colon free. Purgative

drugs are of little value. In the anal variety the colon may be readily washed out daily through a rectal tube; the latter may be left in at night. In the pelvi-rectal variety the treatment is not so easy; but enemas of oil or glycerine may do good.—Pituitrin—1 c.c. injected—electricity and abdominal massage may also help. The anal sphincter may be dilated. An operation may be necessary, either a colostomy, or ileocolostomy, or complete resection of the dilated part of the colon.

EXAMINATION OF THE LIVER

The liver occupies the right hypochondriac region, under the ribs, and stretches across the upper part of the epigastrium. Normally it can scarcely be felt even in the latter situation, and there only when the abdominal wall is very thin. Percussion gives dulness (*hepatic dulness*) in the mammary line, from the upper border of the sixth rib to the costal margin. In the axillary line the hepatic dulness begins at the eighth rib, and in the line of the scapular angle at the tenth or eleventh rib. When the organ is enlarged it projects below the costal margin, its lower margin extending across the abdomen from the right flank to the left costal margin. The dulness extends to a corresponding degree down into the abdomen; but from the presence of the intestines behind it the dulness is not so complete near the free edge as it is higher up. The liver only encroaches on the chest when the enlargement is (1) localised rather than general, such as that due to carcinoma, hydatid, or abscess; or (2) when the liver is itself pushed up by something below.

Apparent enlargement of the liver arises from tight-lacing, and from tumours or pleuritic fluid in the chest. The former elongates the organ vertically; in the latter the whole liver is displaced. Displacement of the liver downwards, or ptosis, occurs also as a part of *Glénard's disease* (*see* p. 339). A distended gall-bladder may be felt as a globular prominence at the lower border of the hepatic dulness, in the mammary line.

The hepatic artery supplies about 20 to 30 per cent. of the blood flowing to the liver and the portal vein the remainder; the liver of a dog receives each minute about four-fifths of its weight in blood. The true anatomical division of the liver is into two equal lobes, indicated by a line drawn from the fundus of the gall-bladder to the groove for the inferior vena cava and not by the falciform ligament. The portal vein contains two more or less separate blood currents side by side; the "stream line" from the mesenteric area goes to the right lobe and that from the spleen to the left (**65**). The spleen and liver can be made opaque to X-rays by injecting intravenously a preparation of thorium (thorotrast), which is taken up by the reticulo-endothelial system (**66**).

LIVER FUNCTION AND FUNCTIONAL TESTS

Accurate knowledge of the function of the liver dates from the operation devised by Mann for removing the livers from dogs (**67**). After the operation the animal appears normal for three hours or more, but severe symptoms of muscular weakness come on rather suddenly, and later there are twitchings and convulsions. These are due to hypoglycæmia and can be arrested by giving sugar, so that the animal again becomes normal for a time; but then more severe symptoms appear in spite of treatment and the animal dies in coma. Hypoglycæmia results because the body burns up sugar continuously, and the one source of supply, the liver, is missing. Other biochemical changes are a fall in blood urea and in the ammonia and urea of the urine, while there is a rise in the amino-acids; the reason is that in the liver deamination with the formation of urea is naturally brought about, and some of this urea is converted into ammonia by the kidneys. There is a rise in blood uric acid, because the liver

naturally destroys it, though there is some doubt about this in man. There is jaundice, because bilirubin is formed by the reticulo-endothelial cells of the spleen and marrow (also by the Kupffer cells of the liver) by splitting off the iron-containing part from blood pigment. The liver cells collect this bile pigment, secreting it into the bile canaliculi and then into the bile ducts (**68**). All these changes have been observed from time to time in severe liver disease, *i.e.* acute necrosis and carcinoma. In addition, the liver has detoxicating properties, and in disease the blood fibrinogen, which is produced by the liver (**69**), may be diminished, leading to hæmorrhage, and the serum calcium also falls. There may be urobilinuria, because normally bilirubin is converted into urobilin in the alimentary canal, some of which is excreted as the stercobilin of the fæces, but the rest is absorbed by the alimentary canal and returns to the liver to be reconverted into bile pigment; when liver function is impaired, it escapes into the general circulation and is excreted by the kidney as urobilinogen.

The normal liver has great powers of regeneration, so that if 70 per cent. is removed the normal amount will be found in a few weeks. Quite a small amount of liver is sufficient for most of its activities, so that marked changes, like hypoglycæmia, are only found in the most severe stages of the disease, and in the milder forms the so-called functional tests, of which a very large number have been described, are apt to lead to rather uncertain results. The more important ones are described below.

Lævulose Test. This test depends on the fact that when lævulose is absorbed from the alimentary canal and reaches the portal circulation, it is almost entirely taken up by the liver, and so does not reach the systemic circulation. If the liver is diseased, the lævulose is not retained. It passes through into the systemic circulation and causes a rise in blood sugar (*see* p. 462). In performing the test, a dose of 50 grams of lævulose is taken by the mouth. The blood sugar is estimated first beforehand, and half an hour, one hour, and two hours later. Normally there may be a very slight rise, which is less than 0·01 per cent. Thus if the blood sugar is 0·10 per cent. it will not be higher than 0·11 per cent. after an hour. If the liver function is deranged, as may occur in catarrhal jaundice, or in arsenobenzol poisoning, the blood sugar may rise to 0·15 per cent. in half an hour and 0·19 per cent. at the end of an hour, and it then slowly returns to normal (**70**). Simultaneously with the rise in blood sugar the lævulose often appears in the urine, as the kidney very readily excretes it. This test should be compared with that for mild diabetes mellitus (*see* p. 464). *Galactose* (40 gram. in 400 c.c. water) is also employed as a test like lævulose, since normally there is no rise of blood sugar, or at most 0·03 per cent., though with children higher rises up to 0·1 have been found (**71**). The urine normally contains less than 1 gram. of galactose during the succeeding three hours (**72**), or 2 grams in six hours.

Gross inefficiency of hepatic function may be shown by the occurrence of jaundice or ascites, which will now be described. In this connection certain special tests are available, viz. Van den Bergh's tests, Hay's test for bile salts, and the examination of the urine for urobilin (*see* pp. 386, 509).

JAUNDICE

The term *jaundice* (from *jaune*, yellow), or *icterus*, denotes the circulation in the blood of constituents of bile. In the past the term has been used solely for the yellow staining of the skin and mucous membranes by bile pigment, but it is now used in a wider sense and includes those cases where bile salts appear in the blood without bile pigment—one form of *dissociated icterus*, and cases where the bile pigment is present in such small quantity that no colour is produced (*latent icterus*).

Symptoms. Owing to the colour of bile pigment the skin has a more or less deep yellow tinge, the conjunctivæ are yellow, and the visible mucous mem-

branes have their natural colour obviously modified by the yellow tint. In long-standing cases the colour of the skin becomes deeper, and finally of a greenish or olive-brown tint. This, formerly distinguished by the name of *green* or *black jaundice*, is due to the gradual conversion in chronic cases of bilirubin, the yellow pigment of the bile, into biliverdin by oxidation in the skin. The yellow colour must be distinguished from other changes of colour in disease, such as the lemon yellow tinge of cases of pernicious anæmia, the sallow tint of malarial cachexia, the brown colour of Addison's disease, and the yellow colour due to the pigment *carrotin*, which appears in the skin after eating large amounts of green vegetables and carrots. The colour can be generally well recognised in the conjunctiva, but in some people small masses of subconjunctival fat give a tint which is not very unlike it.

The colour of the *urine* is at the same time altered, from the presence of the biliary pigment. In small quantity this gives it a bright saffron colour, which is best seen in any froth which may form on the surface; if there is more the urine becomes brownish yellow, or yellowish brown, or even dark brown like porter. If linen or paper is dipped in the urine, it is stained bright yellow; but the presence of bile pigment can be more certainly proved by the application of chemical tests which will be mentioned presently. Of the other secretions of the body the sweat is sometimes tinged yellow. The milk of nursing women, tears, and saliva are rarely stained. The cerebro-spinal fluid is not usually stained. At the commencement and at the end of an attack of jaundice the urine often contains urobilin, a derivative of bile pigment, but none of the bile pigment itself, and there is a group of cases in which bile pigment is absent from the urine (*see* Acholuric Jaundice).

In most cases of jaundice the *fæces* are altered in colour, becoming whitish or clay-coloured; this is due to the presence of an excess of fat and to absence of urobilin in those cases of jaundice where the bile is unable to find its way into the duodenum. It has recently been shown that the intestinal contents are slightly acid and that fat is absorbed in the form of a compound of free fatty acid with bile acids. The presence of bile, also, probably prevents putrefaction and stimulates the muscular fibres of the intestinal wall. Accordingly constipation is frequent, though by no means invariable. When diarrhœa occurs, it has been attributed to the irritation of the putrescent fæces.

Other symptoms are often present in jaundice, which are due to the circulation in the blood of bile salts. These are: (1) *bradycardia;* the *pulse* becomes slowed to fifty or forty per minute; (2) *itching;* it may be so intense that sleep is rendered impossible, and blood crusts, papules, or wheals of urticaria are produced by the incessant scratching.

Some patients have a bitter taste in the mouth, and digestive disturbances are frequent. Hæmorrhages take place under the skin or from the mucous surfaces, and the bleeding from wounds is not readily checked; the coagulation time of the blood is prolonged. In some cases, serious cerebral symptoms arise, such as delirium, convulsions, and coma; but these are probably always due to the presence in the blood of other poisons than those contained in the bile. Yellow vision (*xanthopsia*) is sometimes observed. A disease of the skin named *xanthelasma* or *xanthoma* occurs in some cases of long-standing chronic jaundice (*see* Diseases of the Skin).

Clinical Tests for Jaundice. *Van den Bergh's Test for Bile Pigment in Serum.* Besides indicating the presence of bile pigment in serum, this test differentiates between the pigment retained in the blood from obstruction of the bile passages and that due to hæmolysis. Ehrlich's diazo reagent is used. This consists of (*a*) sulphanilic acid 1 gramme, conc. HCl 15 c.c., distilled water 1,000 c.c.; and (*b*) sodium nitrite 0·5 gramme, distilled water 100 c.c. The two are mixed just before use in the proportion of 25 c.c. of (*a*) to 0·75 c.c. of (*b*). *Direct Reaction.*—One cubic centimetre of serum obtained from blood, allowed to clot on standing,

and 1 c.c. of the reagent are mixed. A bluish-violet colour reaction begins immediately, and is at its maximum in ten to thirty seconds. This indicates obstructive hepatic jaundice. If there is no direct reaction, a delayed reaction may occur, beginning after one minute. This is due to hæmolytic or toxic and infective jaundice. A biphasic reaction, which begins at once, but only slowly devleops, indicates the presence of a mixed type of jaundice. *Indirect Reaction.*— If no direct reaction is given, 2 c.c. of 96 per cent. alcohol are added to 1 c.c. serum and centrifugalised. To 1 c.c. of the clear liquid 0·5 c.c. of alcohol and 0·25 c.c. of the reagent are added. A violet-red colour, which is of maximal intensity almost at once, is obtained, and this indicates hæmolytic or toxic and infective jaundice. The tests may be carried out quantitatively (**73**); the normal range is 0·2 0·5 unit, a unit being 1 part bilirubin in 200,000.

Tests for Bile Pigment in the Urine. The essential feature of these tests is the production of a green colour by the oxidation of yellow bilirubin into green biliverdin; in some processes other tints are temporarily developed. *Gmelin's test* may be carried out as follows: A few drops of urine are placed upon a white plate, and a little strong nitric acid is dropped close by, and then the two fluids are gently run into one another. At the line of contact the colour of the urine changes, becoming green, blue, violet, red, and lastly yellow or brown. Ryffel has devised a modification of this test capable of detecting very small quantities of bile pigment. The urine is saturated with ammonium chloride and made alkaline with ammonia. Ammonium urate is thus precipitated and carries down any bile pigment with it. The urate is filtered off, and nitric acid is added to the residue on the filter paper. A green colour indicates bile pigment.

Hay's Test for Bile Salts in Urine is carried out by sprinkling powdered sulphur on to the surface of fresh urine in a small conical flask illuminated from the side. If bile salts are present the surface tension is lowered and the sulphur sinks, and the test is positive if there is definite sinking in five minutes (**71**). This test, which has been much discredited in the past, is now regarded as reliable; but the test is also given if large amounts of sandal-wood oil, copaiba, cubebs and turpentine have been taken by mouth. A test for the presence of bile salts in the intestine, depending on the fact that they facilitate absorption of fat, has also been described (**74**).

Pathology of Jaundice. Bilirubin exists in two forms: (1) as an alkaline salt which is excreted into the bile passages. This gives Van den Bergh's direct reaction; (2) as a free acid circulating in the blood which gives Van den Bergh's indirect reaction (**77**). That the liver is not necessary for the production of bilirubin has already been pointed out, and it is also shown by the fact that this pigment is formed locally from old blood clots anywhere in the body. If something goes wrong with the formation by the reticulo-endothelial system, which forms bilirubin, or blood destruction in the body is excessive so that the manufacture of bilirubin by these cells is greatly increased, pigment will not all be taken up by the liver and excreted as bile, but will gain entrance to the circulation. This result may also occur if the liver cells are damaged. There are thus three types of jaundice:

1. *Hæmolytic Jaundice,* a group which includes the blood disease of this name, since owing to excessive blood destruction bilirubin is present in the serum. The group includes the jaundice that may result from paroxysmal hæmoglobinuria, transfusion with incompatible blood, phenyl hydrazine poisoning, hæmolytic septicæmias, lobar pneumonia, malaria and icterus neonatorum. Pernicious anæmia is sometimes included, though the bilirubin accumulates probably because the formation of hæmoglobin is defective.

2. *Jaundice due to Primary Liver Damage.* The causes are (*a*) congestion from heart failure; (*b*) primary disease of the liver, such as most cases of catarrhal jaundice, acute necrosis (yellow atrophy), Hanot's cirrhosis, multilobular cirrhosis in the later stages, and certain conditions classified previously under the

heading *toxic and infective hepatic jaundice ;* the agents are—(*i*) *chemical poisons*, such as tetrachlorethane (*i.e.* dope for aeroplanes), T.N.T., chloroform, phosphorus, toluylene-diamine, nitrobenzene, arsenobenzol derivatives, arseniuretted hydrogen, mushrooms, snake venom, etc. ; (*ii*) *bacterial poisons*, such as occur in relapsing fever, malaria, the enteric group, typhus, pneumonia, influenza, syphilis, yellow fever, septicæmia, leptospiral jaundice, etc.

3. *Obstructive Hepatic Jaundice.* In this group there is some obvious obstruction of the bile ducts: (1) gall stones and inspissated bile, very rarely hydatids, liver flukes, and foreign bodies from the intestinal canal, including *Ascaris lumbricoides ;* (2) stricture or obliteration of the duct from congenital defect or atresia, or from former ulceration of the duodenum or of the bile duct itself: catarrhal or inflammatory swelling or carcinoma of the wall of the bile duct: spasm of the duct; (3) compression from the outside by glands in the portal fissure : by tumours of the head of the pancreas, stomach, colon, kidneys, omentum, ovaries, or uterus : by abscess or hydatid of the liver : by an abdominal aneurysm, accumulated fæces, or pregnant uterus. In many cases of obstructive hepatic jaundice the bile distends the gall bladder and the bile ducts, and then passes into the lymphatics and blood vessels, circulates in the latter, and gives the characteristic tinge to the skin and other parts. An interesting fact in the secretion of the bile makes it likely that a complete obstruction is not necessary—that is, that the bile is secreted under very low pressure, such that in guinea-pigs a pressure of 20 cm. of water will force the secreted bile back into the circulation. Where there is a complete obstruction, as from a gall stone in the common duct, or a tumour pressing upon it, the bile is unable to reach the intestines, and the fæces, as already stated, are white or clay-coloured. When the obstruction is relieved the symptoms disappear.

While the first and third of these types of jaundice are clearly differentiated, since they give respectively the indirect and direct Van den Bergh reactions, members of the second group commonly give a biphasic reaction. In the past the jaundice in these cases has been looked upon as due to a cholangitis affecting the smaller bile ducts and therefore obstructive ; but this view has been attacked by Brulé, who points out that sometimes the bile salts alone are retained in the circulation and at other times the bile pigments alone—these are the two types of *dissociated jaundice*—so that the liver cells themselves must be implicated (**74**). He regards the jaundice due to cirrhosis, concussion or congestion in heart disease as belonging to the same group. It has been found that in obstructive jaundice the blood phosphatase is increased, and this may be helpful in diagnosis (**75**).

Latent Jaundice means that there is bilirubin in the blood, but not enough to produce a typical yellow colour or to cause the kidney to excrete bilirubin. In such cases the urine commonly contains plenty of urobilin, which is probably a transformation product of bilirubin by the tissues. However, it must be noted that urobilinuria is commonly absent when bilirubinuria is marked. Latent jaundice may be present in heart disease and may suggest the onset of failure. Its presence will differentiate pernicious anæmia from secondary anæmia due to hæmorrhage. It may indicate damage of the liver after treatment with arsenobenzol, and in various infective diseases. It is very commonly present in cirrhosis.

Icterus Neonatorum. Jaundice is not infrequent in new-born children. It lasts only a few days or a week or two, and is unaccompanied by any symptoms. Bile pigment, as indicated by Van den Bergh's indirect test, begins to appear in the blood in measurable quantities at about the fifth month of intrauterine life, due to a physiological hæmolysis, and this process suddenly increases after birth, causing jaundice. The suggestion has been made that the maternal liver helps to prevent hæmolysis in the fœtus, and that after birth the infant's liver is slow in taking up its full anti-hæmolytic function. (*See* Pernicious Anæmia.) The yellow colour affects first the face and trunk, and later the limbs ; and is recognised by

pressing the reddened skin, so as to exclude the blood colour. The fæces are generally normal, and the urine is untinted by bile pigment, except in the severer cases. The patients recover, and no treatment is required.

Grave Familial Jaundice of the Newly-born. This condition affects several members of the same family. Jaundice begins on the first day, occasionally the second day after birth, and rapidly increases in intensity. There is drowsiness and loss of weight. The infant dies about the fourteenth day, often with convulsions. The urine contains urobilin and often bilirubin; hæmorrhages are sometimes seen. The stools are normal in colour. The liver and spleen are sometimes enlarged. The *treatment* consists in giving intramuscular injections of 5 to 15 c.c. of the mother's serum into the buttock daily until the bile pigment in the blood diminishes. The serum is anti-hæmolytic. With this treatment the prognosis is good (**90**). Other cases of jaundice that must be distinguished are: *Familial acholuric jaundice*, in which " the patients are more icteric than sick " ; *congenital obliteration of the bile ducts*, associated with white stools and biliary cirrhosis, and the liver is hard ; *congenital syphilis ; infective jaundice*, in which there is an obvious source of infection and the temperature is high.

ASCITES

By this term is meant the presence of serous fluid in the peritoneal cavity. Like other effusions into the serous cavities, it is commonly alkaline, of a pale straw colour, of specific gravity 1,015 to 1,018, highly albuminous, and containing chlorides. It arises (1) from obstruction of the portal circulation, either in the trunk of the portal vein, or in its distribution in the liver; (2) as a result of diseases of the peritoneum; and (3) as a part of the general dropsy of renal disease, or cardiac disease.

The portal vein trunk may be obstructed by the pressure of tumours and enlarged glands in the portal fissure, by carcinoma, abscess, or hydatid in the liver itself, and by coagulation of blood in its interior (*thrombosis, pylephlebitis*). In the liver the chief cause of portal obstruction is the compression of the interlobular veins by the fibrous overgrowth of cirrhosis. It is thought by some that portal obstruction is not an adequate cause of ascites, which they attribute to toxins produced in the diseased liver, or absorbed from the intestine and undestroyed by the liver. Another cause of portal obstruction is perihepatitis. A third kind of obstruction is formed by the different forms of cardiac and lung disease, in which the right side of the heart is dilated and the passage of the blood through the chest is impeded (*see* p. 146).

The peritoneal diseases causing ascites are—acute and chronic peritonitis, tuberculous peritonitis, and carcinoma of the peritoneum.

In Bright's disease the peritoneum is the seat of effusion, in common with the other serous cavities.

Physical Signs. The abdomen is enlarged, and in the early stages of a considerable ascites it is generally tense, and the form tends to be globular, with a decided prominence in a forward direction. Later the walls of the abdomen become stretched, and as the patient lies in bed the fluid gravitates backwards in each flank, and gives a broader and flatter shape to the belly. The liquid then poured out may amount to 3, 4, or 5 gallons, and the abdomen becomes proportionately enlarged so that it may measure from 40 to 42 inches or more in circumference. The presence of fluid is detected by three methods of examination—*percussion, fluctuation*, and *displacement*.

Percussion. Normally the surface of the abdomen is resonant from the air contained in the stomach and intestines; but when fluid is poured out this collects at first in the flanks and hypogastric region, so as to give a dull note to percussion in these parts, while the centre of the abdomen remains resonant. If the patient be turned upon one side and again percussed, it will be found

that the anterior and central regions have become dull, and the flank, which is now uppermost, gives a resonant note. This is due to the gravitation of the fluid to the lowest part and the floating of the air-containing bowel to the highest, and this occurrence is the most conclusive proof of the presence of fluid in the peritoneum and provides the most delicate test for ascites.

Fluctuation is obtained by laying one hand on one side of the abdomen and sharply tapping or flipping the other side with the finger. The applied hand then feels the transmission of a wave across the abdomen. This is a less certain sign than the former. Very fat abdominal walls may transmit a wave without the presence of fluid, and to prevent this the edge of the hand, or of a book or card, should be pressed on the centre of the abdomen while fluctuation is tried.

The method of *displacement* has only a limited application, but it provides in some cases earlier evidence of ascites than either percussion or fluctuation. If in a case of ascites the liver is enlarged, it sinks in the fluid, and a small quantity of fluid lies between its anterior surface and the abdominal wall. By placing the fingers on the abdomen at this spot, and suddenly pressing them in, the fluid is displaced, and the surface of the liver may be felt. This is a proof of the presence of fluid, since, if there were none, the liver would be in close apposition with the anterior abdominal wall.

Ascites is, however, sometimes simulated by one or other of the different kinds of cyst which may occur in connection with the abdominal or pelvic viscera, by a pregnant uterus, or by a distended urinary bladder. These cysts are ovarian, parovarian, hydatid, and renal cysts. They are excluded if the percussion test is successful; on the other hand, they may give the fluctuation test; and if the whole surface is dull there may be some difficulty in distinguishing between one of these and an ascites in which the intestines are bound down. An ovarian cyst is chiefly distinguished by the abdomen being dull in front and resonant in the flanks, into which position the intestines are pressed by the cyst, and by the swelling due to the cyst, which begins on one side, though later on it is central. Not infrequently also the outline of the cyst can be recognised at the uppermost part, especially if looked for during the movements of respiration.

Chylous and Chyliform Ascites. In exceptional cases the fluid contained within the peritoneal cavity is opalescent and milky instead of being a clear serum.

Sometimes this is due to the extravasation of chyle from the thoracic duct or lacteal vessels into the peritoneum, either from rupture or from obstruction of the vessels by disease or by the presence of parasites (*see* Filariasis). This is true *chylous ascites*. The fluid is then of a yellowish-white colour, has a specific gravity of 1,012 or more, and an odour dependent upon the food which is being taken. On standing fat separates and forms a creamy layer on the surface; fatty globules are seen under the microscope, but few cellular elements. A clot of fibrin may form in it after removal from the body.

In another group of cases, *chyliform ascites* or *pseudo-chylous asoites*, the fluid is pure milky white, of a specific gravity less than 1,012. The amount of fat is variable: it may form a creamy layer on the surface, or there may be only traces of it; but in any case the opalescence is not due to the fat, but to minute granules of a compound of lecithin and globulin, held in suspension by inorganic salts. Microscopically cellular elements containing fat may be present. The presence of lecithin enables this fluid to resist putrefaction for a long time.

These chyliform effusions are not distinctive of any one pathological condition; but in a large majority of the cases there has been found either carcinoma, or tubercle, or cirrhosis of the liver, or chronic nephritis; and generally the prognosis is bad.

Both chylous and chyliform liquid may occur simultaneously in other serous cavities; and there is no means of knowing, until paracentesis has been performed on one or other cavity, whether an effusion is of the kind under discussion.

DISEASES OF THE LIVER

ABSCESS

Pathology. Abscesses of the liver arise from the introduction of some septic agent by one of three channels: the hepatic artery, the portal vein, or the bile ducts in suppurative cholangitis (*q.v.*).

In the first case they form part of a general pyæmia, such as results from wound or injury in any part of the body, but especially injuries to the head; they are small in size, and numerous, or at least multiple. They are known as *pyæmic abscesses.*

The portal vein is responsible for a still larger number of cases, the septic agents being carried from lesions within the portal vein area, as described in suppurative pylephlebitis (*q.v.*) and tropical dysentery. The abscesses may be single, few, or multiple; and when they are multiple the condition may be spoken of as *portal pyæmia.* Sometimes the portal vein and its branches are filled with broken-down purulent clot, and the walls of the veins are inflamed, constituting *suppurative pylephlebitis.*

Abscesses of the liver vary in size from a pin's head up to that of a hazel-nut; they may contain well-formed pus, or sanious liquid and *débris*, or more bulky sloughs that have only just been separated. In cases originating in pylephlebitis it may be easy to show that much of the suppuration is in the course of the distribution of the portal vein. The capsule of the liver is frequently inflamed where abscesses approach the surface.

Symptoms. Cases of multiple abscesses in the liver are often very obscure, especially when they form a part of a general illness like pyæmia. There is severe constitutional disturbance, with fever of hectic type, rapid pulse, dry brown or furred tongue, and early prostration. Vomiting is often present, but the action of the bowels is variable: sometimes there is constipation, at others diarrhœa. The liver is mostly enlarged, and in some cases may reach to the level of the umbilicus; it is painful and tender. Jaundice is sometimes, but not necessarily, present; it probably requires the compression by an abscess, or the obstruction by gall stones, of some larger bile duct. The condition of the urine and of the fæces as to the bile pigment will, of course, vary with it. The duration of the illness is from one to several weeks, but the end is certainly fatal.

Diagnosis. This must depend on the fact that an enlarged liver is involved in an acute process, with severe general toxæmia, especially if these symptoms are associated with some lesion which can be recognised as the primary cause.

The **Treatment** must be mainly symptomatic. An attempt must be made to improve the general condition by nourishment, quinine, and stimulants. Opium and local applications, poultices, fomentations, etc., will be required to relieve pain.

COMMON INFECTIVE HEPATIC JAUNDICE

(Catarrhal Jaundice; Acute Hepatitis)

This is one of the commonest forms in which jaundice occurs. The name catarrhal jaundice arose from the belief that it was due to obstruction at the bile papilla with a small piece of inspissated mucus or swelling of the mucous membrane. It is not impossible that occasional cases may be due to such a cause.

Ætiology. Infective hepatic jaundice is especially frequent in early life. It may be associated with evidences of gastro-duodenal catarrh. It is usual to associate with it the well-known instances of jaundice from fright, the main features of which are, at any rate, similar.

Common infective hepatic jaundice has often been observed to occur in epidemics, known as *epidemic jaundice.* In many of these children are alone or

chiefly attacked ; in a smaller number of instances adults suffer most. Neither to the sporadic cases, nor to the epidemic cases, has a definite bacteriology been assigned, but where there has been opportunity to examine the gall bladder and bile passages these have been found to be empty of bile, indicating that liver secretion has failed, owing to acute hepatitis, which is doubtless the true cause of the condition. However, a duodenitis reflexly stops the outflow of bile and so may be responsible for some cases (**76**). Infectious jaundice, which is of leptospiral origin, is described elsewhere.

Symptoms. The patient may have indigestion, weight, pain, or distension of the stomach after food, with, perhaps, occasional sickness for three or four weeks before the jaundice ; and in other cases it may occur after unusual indulgence in particular kinds of food ; but in very numerous instances the patient knows absolutely nothing of his illness until he himself sees in the looking-glass, or is told by his friends, that his skin is acquiring a yellow tinge. Occasionally the jaundice is preceded by severe pains in the limbs, or the case progresses to become one of acute necrosis of the liver. The skin and conjunctivæ are of a bright yellow colour ; the urine is yellowish brown from bile pigment and contains ketone bodies ; the fæces are pale or clay-coloured. The serum usually gives Van den Bergh's direct test or a biphasic reaction. The temperature is generally normal, and there may be no constitutional disturbance, the patient being able to do his work as usual ; but often he is languid, indisposed for exertion, with a bad appetite, and some nausea. There is mostly no pain in the hepatic region, and not even tenderness ; but both may be present in moderate degree. The liver also is often not at all enlarged, but sometimes its dulness reaches one or two finger-breadths below the margin of the ribs, and the edge may then be felt, as well as the distended gall bladder. The bowels are variable, most often constipated, occasionally loose. The pulse may be unaffected, but it is especially in this form of jaundice that abnormally slow pulses have been recorded. The illness lasts from two to five or six or more weeks, and the jaundice gradually disappears, the urine becoming normal in colour first, and the skin more slowly recovering.

In the epidemic form the incubation period is from three to five weeks.

Diagnosis. It is occasionally possible to make the diagnosis before the onset of jaundice, since enlargement of the liver, which is an early sign, may suggest that functional efficiency tests for the liver should be carried out, and a functional deficiency may be found. The painless, or almost painless, onset of jaundice in a young person previously healthy, or at most suffering some gastric disturbance, as a rule, distinguishes it from the jaundice of *gall stones*, of *carcinoma*, and of *cirrhosis*, the other most common causes. If the jaundice lasts more than five or six weeks, the possibility of one of the above three diseases or of a more general cholangitis should be considered. The epidemic form must be distinguished from leptospiral jaundice (*q.v.*). The blood count may help. In the former, except possibly during the first few days, there is an increase of mononuclear cells, in the latter a polymorphonuclear leucocytosis.

Prognosis. With the rare exception of the onset of acute necrosis, this is entirely favourable.

Treatment. The patient need not be confined to bed, unless there is fever ; but should take a diet with plenty of carbohydrates, especially glucose, and avoid fats and stimulants ; and a saline laxative should be given if necessary.

ACUTE NECROSIS OF THE LIVER

(Acute Yellow Atrophy)

In this remarkable disease the liver undergoes a rapid degeneration of its tissues, and diminishes in size to two-thirds, or even one-half, of its normal bulk.

Ætiology. It is more common in females than in males, and the majority

of patients are under thirty years of age, though it is very rare in children. Indeed, at any age it is a disease of extreme rarity. Its onset is often preceded by severe mental disturbances, and many of the cases have occurred in people who have led a dissipated life, in the subjects of syphilis, and in women who are pregnant. It has also occurred within twenty-four or forty-eight hours of a surgical operation; this has mostly been an abdominal operation, performed under chloroform. Acute necrosis, giving rise to toxic jaundice, results from poisoning with trinitrotoluene (T.N.T.), tetrachlorethane (aeroplane dope), arsenobenzol derivatives (*see* p. 117), phenyl-cinchoninic acid (*see* Gout), and in cases of leptospiral jaundice. Acute necrosis on the one hand and cirrhosis of the liver on the other may be different phases of essentially the same process, viz., poisoning of liver cells, in the one case acute, in the other extremely chronic. Further, there is a whole series of cases of *subacute atrophy*, or *multiple nodular hyperplasia*, that bridge the gap between the two. Again, its infective origin in some cases, from common infective jaundice, has already been mentioned. The biochemical changes are described under Liver Function.

Morbid Anatomy. 1. *The Acute Type.* In the most acute cases the liver is large and canary yellow in colour. When the disease is not quite so acute the liver is very much diminished in size; it may be only 30 or 28 ounces in weight. It is soft, flaccid, almost like a bag of fluid, and its capsule, which is wrinkled, appears too large for its contents. On section the liver is of a yellow colour, with patches of rather bright red; or in some parts it is entirely red, in others all yellow. The essential change is a granular and fatty degeneration, by which the hepatic cells are more or less completely destroyed. The necrosis begins in the central zones of the lobule. In the yellow parts of the liver the destruction is less advanced, and some bile-stained cells may still perhaps be found. In the red parts the colour is due to the more complete necrosis of the tissue, by which the vessels are left alone to represent the substance of the liver. Under the microscope one can often see nothing but granules of albuminous matter, fat and pigment, and larger globules of fat. Leucin and tyrosin are also found in the liver, and will spontaneously crystallise on the surface of sections some hours after death. The bile ducts are empty, and are stained by bile pigment: the gall bladder is also empty, or contains a small quantity of viscid grey mucus.

Other organs undergo fatty degeneration, especially the kidneys, in which the secreting cells are granular and fatty, and the heart and muscles. Petechiæ are found under the skin, in the mucous membranes, under the serous membranes, in the kidneys, and other parts.

2. *Subacute Atrophy, or Multiple Nodular Hyperplasia.* The liver is not so much reduced in size, and regeneration of liver tissue is the chief feature. Adenomatous-looking nodules, yellow in colour, are seen set in a stroma of fibrous tissue. They may be small or large, depending on the amount of regeneration, and microscopically they contain newly formed liver cells and bile ducts, though necrotic cells are also present in abundance. To the naked eye the liver has a curious appearance, the arrangement of the fibrous tissue being similar to cirrhosis, and the yellow nodules resembling in appearance the acute form of the disease.

Symptoms. The symptoms are at first obscure. Often it begins with a jaundice indistinguishable from catarrhal jaundice, or with gastro-intestinal symptoms, such as nausea, vomiting, and irregularity of the bowels; and pains in the hepatic region may occur comparatively early. These symptoms may last two or three weeks, or much longer when the more characteristic features develop. These consist of marked cerebral disturbances—at first headache and restlessness, then delirium and gradually developing coma, with convulsive twitchings, or more rarely epileptiform fits, towards the end. Jaundice then appears, or if it has been present early it becomes deeper. The blood serum may give either a direct, indirect or biphasic reaction with Van den Bergh's test. The

temperature is rarely high, but may be from 101° to 102°. The pulse, which may have been slow with the early jaundice, now becomes quick. The tongue is dry and brown, and as the symptoms progress sordes collect about the lips and teeth. There is, besides, pain in the hepatic region, and decided tenderness, which may be recognised even during the stage of coma, if pressure be made there. The extent of dulness diminishes with great rapidity, so that finally its vertical measurement is only an inch or less.

The abdomen is natural, or towards the end it is retracted. The spleen is mostly enlarged. The urine contains bile and not infrequently albumin, especially towards the end, and casts; and there may be also blood, the indication of a general hæmorrhagic condition which may be further shown by coffee-ground vomit; by the fæces, which appear to be mostly pale, and deficient in bile, containing blood; and by epistaxis, metrorrhagia, or petechial hæmorrhages under the skin. With increasing coma death finally takes place, the severer symptoms lasting only from two to four days. Pregnant women, as a rule, abort.

Sometimes a case lasts a much longer time, several months or two years, and these cases have been called *subacute atrophy*. In other cases the attack is quite mild, and the patient recovers. In fact, in cases of T.N.T. and arsenobenzol poisoning it is only the worst cases that die. It was formerly believed that acute yellow atrophy was almost invariably fatal; but these cases of recovery prove that a mild form of the disease does exist. There is often a remarkable latency in the T.N.T. poisoning cases, since jaundice may only be noticeable some years after exposure to the poison has ceased.

Diagnosis. This depends upon the occurrence of cerebral symptoms and rapid diminution of hepatic dulness in a jaundiced patient. X-ray examination is a valuable method of diagnosis (Strathy and Gilchrist). In the vertical position there is a diminution in the height of the shadow. The upper surface is more dome-shaped owing to relaxation of the capsule and traction of the lung, and the lower border is rather more vertical than normal.

Prognosis. Acute necrosis when the symptoms are developed is exceedingly fatal; but cases have temporarily improved, to relapse and die later. These are the subacute cases. The milder cases may recover completely.

Treatment. In the final stage little can be done; but in the earlier stages attempts may be made to remove or neutralise the toxic factor, and so possibly prevent the further progress of the disease. Rest in bed, the administration of glucose bymouth (10 per cent.) and intravenously (6 per cent.), of 10 per cent. calcium gluconate intravenously (10 c.c. daily), and of sodium thiosulphate intravenously (0·6 gram) with abundance of fluid should be tried.

CIRRHOSIS OF THE LIVER

The name *cirrhosis* is given to diseases of the liver where there is infiltration with fibrous tissue. The name *cirrhosis* (κιρρός, yellow) was used owing to the general yellow colour of the liver in portal cirrhosis, and not in reference to the presence of excess of fibrous tissue. Nevertheless the name has been often applied to chronic fibrous changes in other organs of the body—*e.g.* cirrhosis of the lung and cirrhosis of the kidney; but the term "fibrosis" is much to be preferred for these organs.

There are *three* chief types of cirrhosis: (1) *portal cirrhosis*, in which chronic irritants reach the liver through the portal vein and in which circulatory disturbances causing gastric hæmorrhage and ascites are the prominent clinical features; (2) *biliary cirrhosis*, in which jaundice is the prominent feature, and ascites occurs only as a terminal condition; (3) *pericellular cirrhosis*, occurring in congenital syphilis (*see* p. 397).

PORTAL CIRRHOSIS

(Multilobular, Alcoholic Cirrhosis, Hobnailed Liver)

Ætiology. In the great majority of cases portal cirrhosis is dependent, wholly or in part, upon the excessive use of alcohol, in the form of beer, wine or spirits. Little is known as to the amount that is required to produce cirrhosis; there are the widest individual differences. Some people may drink freely all their lives without acquiring it, whereas in others a few months' indulgence seems sufficient for the purpose. In some children that have been the subjects of it the fact of alcoholism has been proved. But there are cases of undoubted cirrhosis of the liver in which alcohol as a cause can be certainly excluded. It is possible also that intestinal toxins may cause some forms of the disease. The cirrhosis due to syphilis is considered later. Some slight degree of fibrous overgrowth may result from chronic heart disease, but this is not cirrhosis as ordinarily understood. Cirrhosis of the liver occurs as a late result in some cases of splenic anæmia (*see* Anæmia), and the cases are then described as *Banti's disease.*

A large-livered cirrhosis is also associated with pigmentation in cases described as *hæmochromatosis.* Iron pigment in the form of hæmofuscin and hæmosiderin (the latter gives the Prussian blue reaction—Perl's test) is deposited in large amounts—ten times the amount normally present in the whole body—in the liver and in the pancreas, but also in other organs, voluntary muscle, cœliac lymph glands and skin, producing bronzing; it is uncertain whether the cirrhosis precedes or follows the pigment in the liver; in bronzed diabetes —*diabète bronzé*—diabetes follows upon the deposition of hæmosiderin in the pancreas. It has been suggested that hæmochromatosis results from prolonged copper poisoning.

The tropical infectious disease, Kala-azar, is accompanied by a moderate degree of cirrhosis; a somewhat similar combination of cirrhosis, enlarged spleen and bone marrow changes, but without the Leishman-Donovan bodies, is endemic in Egypt (Day and Ferguson); and a curiously localised portal cirrhosis is found as a result of bilharzia infection (*see* Bilharziasis).

Morbid Anatomy. The organ varies much in size; it may be very large, or about the normal size, or very much smaller: in the former case, sometimes called *hypertrophic* cirrhosis, the surface may be fairly smooth or present rather fine granulations; in the latter case, sometimes called *atrophic* cirrhosis, the shape is often much altered from the extensive and irregular contraction of the fibrous tissue, which forms coarse knobs on the surface (hobnailed liver). When ascites has constantly reappeared during life, after tapping, the capsule of the liver is found to be thickened (*see* Perihepatitis). In all cases the organ is very much tougher and harder than normal, from the development of fibrous tissue, which runs in all directions through it. The liver presents on section a number of yellow, brownish-yellow, or brown areas surrounded and separated from one another by broad tracts of grey translucent fibrous tissue. If it can be examined in the earliest stages of cirrhosis, there are found large numbers of round cells infiltrating the tissue about the portal canals (Glisson's capsule), and in some cases penetrating more or less between the lobules, or even within them. Later on white fibrous tissue is developed, which forms a large part of the section in an advanced case. The bands of fibrous tissue running through the organ break it up into islands of hepatic tissue, each of which may consist of several lobules (*multilobular cirrhosis*); but the fibrous tissue not infrequently breaks right through a lobule, and sometimes single lobules are surrounded by it. There is great variety. The cells are atrophied and mostly stained yellow or brown by pigment granules. In the fibrous tissue are numerous newly formed blood vessels, which can be injected from the hepatic artery, and regenerating liver cells are also seen. In fact, the production of cirrhosis may be looked upon as the attempt of the body at repair, which follows necrosis of the middle and outer

zones of the lobule. The newly formed, highly vascular, fibrous tissue is an advantage since it supplies nutriment to the regenerating liver cells (**78**). Later on it becomes useless when it contracts, and thus compresses more and more the hepatic cells, the branches of the portal vein, and perhaps the bile ducts. The organ is at first enlarged by the overgrowth of connective tissue, and some large cirrhotic livers also contain a quantity of fat. The liver cells and fat may eventually disappear, and the organ may be reduced much below its normal weight. The varying size of the liver is thus, in part at least, dependent on the stage of the process.

Cirrhosis carcinomatosa is the name given to cases in which a primary carcinoma develops in a cirrhotic liver (*see* p. 400). It presumably results from the chronic irritation—in the same way as an epithelioma of the tongue follows a chronic syphilitic glossitis.

Symptoms. The symptoms of portal cirrhosis are mainly due to increasing obstruction of the portal circulation. Jaundice and other signs of hepatic deficiency are often absent or come on late in the course of the disease. The serum may give Van den Bergh's biphasic reaction. There is frequently, as a result of free drinking, a gastritis which produces loss of appetite, furred tongue, and vomiting, especially in the morning. An examination of the abdomen at this stage may, however, reveal a considerable enlargement of the liver, of which the patient is entirely ignorant. The next symptom is not infrequently *hæmatemesis ;* this is due to the commencing obstruction in the portal circulation ; as the blood in the portal vein finds a difficulty in passing through the liver, the radicles of this system, viz. the mesenteric, gastric, and splenic veins, are, of course, congested, and tend to bleed on to the mucous surfaces. But sometimes the blood proceeds from a rupture of the veins at the lower end of the œsophagus, which have become varicose in the course of establishing a free communication between branches of the portal vein and branches of the inferior cava vena or azygos vein. The hæmatemesis may be followed by melæna. Piles are not infrequently present at the same time, and hæmorrhage from other parts (gums, nose, and lungs) is liable to occur in the course of cirrhosis.

The most important and constant result of the portal obstruction is the effusion of fluid from the distended veins into the peritoneal cavity, constituting the form of dropsy already described as *ascites.* In many cases, when ascites has developed, the liver is still enlarged, and can be felt 1 or more inches below the ribs ; the edge is firm, and very sharp or rounded, but the surface will be smooth if there is much perihepatitis ; but it is commonly granular or nodular. The spleen is often enlarged and palpable. The surface of the abdomen is covered by large veins, running between the iliac and thoracic trunks. This collateral circulation is a means by which the portal circulation is relieved. This is an important point, for it must be remembered that the portal system is not completely shut off from the general circulation, but that there are, even in health, means of communication which in cirrhosis become greatly enlarged, and allow of some of the blood in the portal vein radicles reaching the right side of the heart without passing through the liver itself. Those which have been described are communications (1) between the gastric and œsophageal veins at the opening in the diaphragm ; (2) between the inferior mesenteric and the hæmorrhoidal branches of the internal iliac vein ; (3) between the coronary veins of the stomach and branches of the phrenic veins ; (4) between branches of the mesenteric vein and the spermatic vein, or others in the abdominal wall. Frerichs described (5) vessels forming in the adhesions between the liver and the diaphragm ; and (6) a large vein (accessory portal of Sappey) has sometimes been found running along the round ligament of the liver, by which the portal vein communicates directly with branches of the epigastric and internal mammary.

The bases of the lungs are often seriously compressed by a large ascites. Hydrothorax and œdema of the legs often occur. By the time that ascites is

well developed the patient is in other respects often seriously ill. He is thin, weak, with sunken eyes, a slight tinge of jaundice, and small stellate venules on the face. The temperature is mostly normal, but fever is sometimes present. Death may result within a few months of the appearance of ascites, with cardiac failure, or with cerebral symptoms (delirium and coma) from chronic alcoholism. Occasionally hæmatemesis is fatal. Secondary infections, such as peritonitis, also commonly cause death.

Diagnosis. Cirrhosis is often latent until hæmatemesis, ascites, or slight jaundice discloses the secret, or its onset may be suspected owing to alcoholic habits, and may be proved by a positive lævulose or galactose tolerance test. Examination may discover an enlarged rough liver in a tippler who has no decided trouble. Most commonly the diagnosis has to be made when ascites has already appeared, and then the history of drinking and of hæmatemesis, the presence of an enlarged liver, enlarged spleen, and slight jaundice, are sufficient to determine the case. Of the other conditions of the liver and peritoneum causing ascites the most important are *carcinoma*, which may obstruct the portal vein, or its largest branches, and the association of *perihepatitis* with *chronic thickening of the peritoneum* (*see* Perihepatitis). *Carcinoma* and *tubercle*, apart from the liver, also cause a peritonitis, which results in ascites. The former may be recognised by the occurrence of nodules of growth in different parts of the abdomen. The latter often presents a thickening of the omentum, which may be mistaken for an enlarged liver. Hæmatemesis is frequently the result of cirrhosis, and is valuable in diagnosis ; but it also commonly occurs in acute gastric ulcer and splenic anæmia.

Prognosis. In the early stages, especially if the condition has been disclosed by a functional test, the prognosis is good if alcohol is stopped. When ascites has developed the patient may still live for some years with repeated tappings. In some cases in children ascites has occurred as the first symptom, and yet the patient has lived for eight or ten years.

Treatment. Little, if anything, can be done with the cirrhotic liver itself ; and treatment resolves itself into the prevention of further mischief, and the attempt to obviate the effects of the damage already done. In alcoholic cirrhosis the first essential is that the ingestion of alcohol should be absolutely stopped ; and in early stages the liver may become normal again. It is, however, impossible in such a case to say how far fibrosis has progressed. The diet should contain plenty of carbohydrate, and proteins should be restricted ; the bowels should be kept active, and sickness and any dyspeptic symptoms may be treated as previously described. When ascites occurs it has been considered unsafe to cause its disappearance by diuretics such as salyrgan, because of the toxins it contains, though these have often been employed. Of purgatives sulphate of magnesium, bitartrate of potassium, compound jalap powder, or elaterium may be employed. When the abdomen becomes very tense, paracentesis is required, and it may sometimes be repeated with success as the fluid reaccumulates. Attempts to develop a collateral circulation based on the view that ascites is mainly mechanical in origin have been made (1) by opening the abdomen, scraping the peritoneum on the opposed surfaces of the liver and diaphragm, and bringing them into contact by stitches (Drummond and Morison, Talma), and (2) by uniting the great omentum to the anterior abdominal wall (*epiplopexy*). It is even claimed that 30 per cent. of these operations have met with some success.

BILIARY CIRRHOSIS

1. Hanot's Cirrhosis (*Hypertrophic Biliary Cirrhosis*). The ætiology of this disease is obscure. It is not known whether the liver parenchyma or the bile ducts are primarily affected. It is a rare disease, commoner in males than females, and often occurring in children. There is considerable enlargement of the liver, and often in children still greater enlargement of the spleen, stunted

growth of the patient, deep pigmentation of the skin, and marked clubbing of the finger ends (*splenomegalic cirrhosis*). Jaundice is a marked feature of the disease, and the urine contains bile pigment, whereas ascites is not present until just at the termination. The disease may last for several years. Towards the end the patient becomes delirious, even violently so, and relapses into coma. The temperature is high, hæmorrhages occur under the skin and from the mucous membranes, and he dies in three or four days.

The liver, besides being smooth and large, is deeply stained with bile on section. The fibrous tissue is much more delicately arranged than in portal cirrhosis, each lobule being surrounded by fibrous tissue (*unilobular cirrhosis*). Some fibrous tissue may also be present inside the lobule round the liver cells. There is marked proliferation of bile ducts. There is evidence that a large cirrhotic liver may become smaller during the patient's lifetime. Sir Frederick Taylor recorded a case in which a liver reaching below the umbilicus, in a patient with strongly marked jaundice and no ascites, was found fifteen months later to have contracted quite close under the edge of the ribs. The treatment is described under Portal Cirrhosis.

2. **Obstructive Form.** Experimentally Rous and Larimore have produced a pure unilobular cirrhosis similar to Hanot's cirrhosis by ligaturing one of the bile ducts and the corresponding branch of the portal vein. The amount of bile formed was less than before, but being unable to pass along the usual channels, it passed out through the walls of the interlobular ducts, causing irritation and fibrous tissue formation.

Again, by ligaturing the other branches of the portal vein instead, all the portal blood was diverted to the area of the liver where there was biliary stasis. A larger amount of bile was formed, which escaped out of the intralobular bile canaliculi, giving rise to a pericellular cirrhosis.

These results have naturally a great bearing on the pathology of Hanot's cirrhosis, suggesting that it may really be due to obstruction of the smaller bile passages. There exists, however, a form of obviously obstructive biliary cirrhosis, which is sometimes, but not always, met with clinically, when there is long-continued obstruction of the bile ducts due to gall stones or carcinoma, etc. The bile ducts are seen to be greatly dilated, and the liver may show unilobular, or sometimes multilobular, cirrhosis. The treatment consists in removing the cause as far as possible by surgical methods.

SYPHILIS AND TUBERCULOSIS OF THE LIVER

Syphilis may be *congenital* or *acquired*.

Congenital Syphilis occurs first as *pericellular cirrhosis*, secondly as gumma. The former change begins as a cellular infiltration, which develops into a fibroid induration; it invades the lobules, and surrounds each cell with a layer of fibrous tissue, leading to considerable enlargement of the organ. Microscopic examination may also show: (1) increased fibrous tissue round the portal canals (periportal cirrhosis); (2) numerous embryonic red cells, due to the liver continuing its hæmatopoietic functions, which may help to compensate for the destruction of corpuscles by the syphilitic toxin; (3) miliary gummas (**80**). Spirochætes are present in the connective tissue. The spleen is often enlarged at the same time. Jaundice occasionally occurs, but ascites rarely. A multilobular cirrhosis has sometimes developed in those previously the subjects of the intercellular form.

Treatment. *See* Congenital Syphilis, p. 117.

Acquired Syphilis. The jaundice that is not infrequent in the early stages of syphilis, and was known before the introduction of arsenobenzol compounds, shows that this infection may produce an acute hepatitis. In the later stages syphilis produces gumma of the liver. This presents the general features of gumma in other situations, and spirochætes are found. They are more or less spherical yellow masses, tough and elastic, surrounded by a zone of grey

fibrous tissue, from which branch off numerous bands into the adjacent hepatic substance. The contraction of the fibrous tissue produces a depression or fissure on the surface of the liver, at the bottom of which lies the gumma which has caused it; and so the organ may become coarsely lobulated and deformed. Gummas not infrequently break down in the centre into a puriform detritus; on the other hand, they may become completely fibrous, so that nothing remains but a depressed scar; or calcareous granules may be deposited in them. Gummatous livers often become lardaceous, and in consequence they may be of large size in spite of cicatricial contractions. Perihepatitis is another change resulting from syphilis. It is probable that syphilis is responsible for some cases of multilobular cirrhosis.

Symptoms. Occasionally a large gumma may form a prominence on the anterior surface of the liver, smooth and elastic, and strongly suggestive of a hydatid or other cyst; it may cause elevation of the right costal margin. More often, but probably in later stages, syphilitic livers are large, hard, irregular on the surface, and deformed, from the contraction of the fibrous cicatrices. Neither ascites nor jaundice is necessarily present, but in particular cases they may occur from the pressure of a gumma upon the portal vein or the bile duct; and there is often albuminuria from co-existing lardaceous disease of the kidney. A gumma is sometimes accompanied by decided fever of hectic type.

Treatment. In early cases, iodide of potassium will quickly reduce the gumma and check the fever accompanying it; salvarsan may also be tried cautiously, the patient being given plenty of carbohydrate. But when there are old cicatrices and lardaceous disease, little good can be expected.

Tuberculosis. This is almost invariably a part of a general tuberculosis. (*See* Miliary Tuberculosis, p. 163).

NEW GROWTHS IN THE LIVER

The only tumour of the liver that is at all common is carcinoma. Of others cavernous angeioma, simple cysts, and the lymphadenomatous deposits associated with Hodgkin's disease are the most frequent. They rarely cause definite symptoms. Cases of spindle-cell sarcoma, melano-sarcoma, cysto-sarcoma, myxoma, and adenoma have been recorded.

FATTY LIVER

Fatty Infiltration. The hepatic cells normally contain a small quantity of fat. Under certain conditions the neutral fat is immensely increased. *Fatty Degeneration.* In this condition there is a change in the physical characteristics of the fat; it may be seen histologically as globules in the cells, which are degenerated in consequence.

Ætiology. There are a large number of causes of fatty infiltration and degeneration; these include pregnancy and lactation; general obesity; starvation; congestion of the liver in heart failure; untreated diabetes; eclampsia; febrile conditions, where the toxins and high temperature damage the cell; severe anæmias; acute necrosis and other disease of the liver; poisoning by phosphorus, arsenic, carbon monoxide, chloroform, phenyl hydrazine, carbon tetrachloride, etc.

Pathology. The fatty liver is much enlarged; it has a smooth surface, is somewhat rounded at the edge, on section has a whitish-yellow colour and uniform appearance, and it may actually float in water.

Symptoms. The fatty liver is painless; it may be difficult to feel as it is of soft consistence, though large and smooth; and also the abdominal wall may be fat. In general the symptoms are those of the causal condition. In particular the section on Obesity should be consulted.

Experimentally, it was observed that in depancreatised dogs the diabetes often apparently improved with lapse of time; less sugar was passed and yet the

animal eventually died and a fatty liver was found; the animals remained healthy if raw pancreas was given by mouth. It is possible that the substance in the pancreas which is responsible for the cure is choline (**79**).

LARDACEOUS DISEASE

(*Amyloid Disease*)

Lardaceous degeneration has been already referred to in connection with empyema and phthisis; and as the liver is one of the organs which are most frequently implicated, a short account of the degeneration must here be given. It consists in the deposition in the tissues of a firm, colourless, translucent protein material containing much tyrosine (*lardacein* or *amyloid*), which is stained by certain colouring agents. Thus iodine in aqueous solution turns it a rich brown-red mahogany colour. The iodine may be applied to a section of the fresh organ after this has been washed free of blood, and the affected parts are then mapped out by the characteristic tint. The subsequent addition of dilute sulphuric acid changes this to a dark purple hue. Methyl-violet or gentian-violet turns lardaceous matter red, while the surrounding healthy tissue is stained blue.

The tissues in which it is found are, first in point of time, the walls of the blood-vessels; secondly, various connective tissues; and lastly, if at all, the gland cells of an organ. Indeed, the material is mostly intercellular in its position: thus it is found in the small arteries deposited between, and separating from one another, the muscle fibre cells of the middle coat; in the spleen it exists as streaks and patches between the cells of the pulp; and in the liver it lies in similar particles between the capillaries and the gland cells. It is, indeed, not so much a degeneration as an addition to the structure; and solid organs affected by it are generally much enlarged. Its relation to the vessels suggests that it is deposited from the blood. It occurs most often in the spleen, kidneys, liver, intestines, and stomach, and with decreasing frequency in the suprarenal capsules, lymphatic glands, thyroid, aorta, ovaries, and uterus. It is due to prolonged suppuration in any part of the body and it is specially common in phthisis, tertiary syphilis, tuberculous disease of bones and joints, and empyema, or in syphilis, without suppuration.

In the *liver* the lardaceous change is first observed in the middle zone of the lobules, where the capillaries are most intimately connected with the divisions of the hepatic artery. As the deposit increases the hepatic cells are compressed and atrophied, but they are only occasionally the seat of lardaceous deposit. The liver becomes enormously enlarged, has a smooth surface and somewhat rounded edge, and is entirely free from pain or tenderness. The disease causes no jaundice. It is accompanied by the signs of the causative disease, and often by an enlarged spleen, albuminuria and diarrhœa, the results of the deposit in other organs. A lardaceous liver, which is at the same time the seat of a syphilitic gumma or cicatrix, naturally loses its uniform smooth surface, but may be recognised by its other associations. The portal circulation is not obstructed by lardaceous change alone, and although ascites is not infrequently present, it is mostly associated with general anasarca, and must be referred with it to co-existing disease of the kidneys, or it may be due to other complications, such as cirrhosis, gumma, or chronic peritonitis. Lardaceous disease of the *kidney* often produces the appearance of large white kidney. On microscopic examination the glomerular tuft is often first altered, then successively the vasa afferentia, the vasa recta, the vasa efferentia, and the intertubal vessels. In some cases, however, the change can be found in the vasa recta before it is seen in the glomeruli. There are, in addition, the inflammatory changes of large white kidney. The lardaceous *spleen* is enlarged, hard and smooth. The change affects the splenic vessels and the Malpighian corpuscles, which last

appear as grey specks upon the surface (*sago spleen*) ; in other cases the lardaceous material is deposited between the cells of the pulp, and the organ is more uniformly pale.

The **Diagnosis** has been made by means of liver puncture. The presence of albuminuria in a case having a long-continued suppurating lesion or tertiary syphilis will suggest the possibility of the disease, especially if the spleen or liver is also enlarged. The urine may contain a few hyaline or granular casts, and, rarely, some which give the lardaceous reaction. If the functions of the kidneys are much interfered with the case may closely resemble any type of Bright's disease and there may be diarrhœa from co-existing lardaceous disease of the intestine.

Prognosis. This is very bad, but decrease of the enlargement of the liver after efficient surgical treatment has been recorded. Death may take place from increasing dropsy, uræmia, exhausting diarrhœa, serous inflammations, or hepatic insufficiency.

Treatment. The cause must be, if possible, removed. This is impracticable in phthisis, but other sources of suppuration may perhaps be treated surgically ; and potassium iodide, cod-liver oil, iron, quinine, and other tonics should be given. Mercury and potassium iodide should be used in syphilitic cases.

CARCINOMA OF THE LIVER

Pathology. Primary carcinoma occurs in two forms—as nodules appearing in any part of the liver and as a diffuse infiltration. Histologically carcinoma of the liver is of two kinds, consisting of (1) liver cells, which may secrete bile, or (2) bile duct cells. Primary carcinoma occasionally develops in a cirrhotic liver. The liver is not, as a rule, much enlarged; it presents, besides the fibrous overgrowth, multiple tumours which are at first firm and white, but later degenerate or undergo necrosis, and acquire a yellow or green colour. The clinical features are those of cirrhosis, and the condition has been called *cirrhosis carcinomatosa.*

By far the greater number of cases of carcinoma of the liver met with are secondary to carcinomatous deposits in other organs, especially the stomach, the intestine, the gall bladder, the glands in the portal fissure, the uterus, or the breast. The carcinoma cells are carried to the liver by branches of the portal vein, and lodged in the lobular capillaries. The form of the secondary carcinoma, whether soft or hard or melanotic, is determined by the nature of the primary growth.

If the carcinoma is diffused, the liver is merely enlarged; but when it exists in the form of nodules, or separate tumours, the liver takes at the same time the most varied shapes. Each nodule tends to grow evenly in every direction, and thus to keep a globular form, and when it reaches the surface it will project as a hard, convex, or hemispherical outgrowth. But as the nodules become larger—for instance, 1½ to 2 inches in diameter—they often break down in the centre into granular and fatty detritus, and as a consequence those that project on the surface, being unsupported on one side, sink in and form a central depression or *umbilication*, a condition which may sometimes be felt through the anterior abdominal wall. The lower edge of the liver is also irregular and nodulated. On section such a liver presents irregular areas of white carcinomal growth, with a more or less circular outline; the larger ones are softening in the centre, and many of them are blotched by hæmorrhages. The intervening hepatic tissue is often of a deep brown or yellow colour. Where the carcinoma has started from the gall bladder, or the bile duct, or has grown in from the portal fissure, the growth is most extensive in that region, or may be quite confined to it. Sometimes the empty gall bladder, or a gall bladder containing some calculi, is embedded in a mass of carcinoma. Carcinomatous nodules near the portal fissure may compress the bile duct or the portal vein, and the latter may be entirely filled by the new growth.

Symptoms. Carcinoma of the liver usually gives rise to a good deal of pain, affecting the right hypochondrium, shoulder, and loins. At first not much more than a sense of weight and uneasiness, it afterwards becomes severe and lancinating, and is accompanied by tenderness. Occasionally, however, pain is absent. The liver, as already stated, is enlarged; it may reach far below the umbilicus, and over towards the left side; the nodules are prominent on the surface, and the irregular outline may even be seen in profile. For the most part the enlargement is in a downward direction, but large masses may grow from the convex surface, and force up the diaphragm so as to compress the base of the lung. The surface of the carcinomatous mass is, as a rule, of almost stony hardness, distinctly more hard than cirrhosis, or lardaceous disease, and the transition from hard carcinoma to the soft normal tissue can often be recognised. Jaundice occurs in about half the cases and can generally be shown to result from pressure on the main bile duct, especially in those cases where the carcinoma starts from the portal fissure. Van den Bergh's direct test is given. Similarly, ascites is often, but not always, present, and rarely is the fluid as abundant as it may be in cirrhosis. It mostly depends on direct pressure on the portal vein or its large branches, occasionally on a co-existing peritonitis. The emaciation, pallor, and prostration common to malignant diseases of the abdominal viscera are also present. Pyrexia occurs in many cases of carcinoma of the liver, and occasionally it has exacerbations and remissions like those seen in Hodgkin's disease.

Diagnosis. A jaundice of some months' standing in an old person with an enlarged liver is, in the majority of cases, due to carcinoma of the liver or of the head of the pancreas, though occasionally the bile duct may be obstructed permanently by a gall stone. If hard, irregular nodules are felt on the surface of the liver, the diagnosis of hepatic carcinoma is highly probable; the prominence due to gumma is generally solitary, an inch or more in diameter, and soft or elastic. If the liver is of uniform and not very great hardness, carcinoma is only probable. In cases without jaundice, the large, irregular, and bossy liver and the emaciation of the patient are generally distinctive. Lardaceous and cirrhotic livers are less hard and more uniform. In both these cases the spleen is frequently enlarged also, in the first case by lardaceous deposit, in the second by venous stagnation, whereas carcinomatous enlargement of the spleen is relatively uncommon. Syphilitic livers may be irregular and painful, but often occur in younger people, and have their own special history. A long history of gall stones does not exclude, but rather favours, the possibility of carcinoma.

Prognosis. This is hopelessly bad. The duration is rarely more than twelve months, but may be two or three years. The softer forms of growth may kill within a month or two.

Treatment. This can be only palliative, and consists in relieving pain and in meeting other symptoms, mostly of the digestive organs, such as vomiting, flatulence, and constipation. The diet should be light but nutritious.

CYSTIC DISEASE

In this uncommon condition there are numerous cysts, more or less aggregated together, varying in size up to an inch or more in diameter, containing a clear or yellowish-brown watery liquid. It is very frequently associated with cystic disease of the kidneys and other organs. The liver may be enlarged, but otherwise there are no symptoms, and its diagnosis, prognosis and treatment are dependent upon the like change in the kidneys with which it is associated (*see* Cystic Disease of the Kidney).

PERIHEPATITIS

Pathology. Perihepatitis, or inflammation of the capsule of the liver, may be acute or chronic, localised or more generally diffused. It is set up by

any lesion which occurs in and about the liver, especially cirrhosis, syphilitic disease, cholecystitis, carcinoma, hydatid, and subphrenic abscess, and it may be part of a general peritonitis.

In acute perihepatitis the appearance of the surface of the liver is one of acute peritonitis. In chronic perihepatitis the capsule is opaque and more or less thickened; often the thickening is distributed in patches irregularly over the surface; and such patches may be determined by the disease which causes the inflammation of the capsule. Sometimes the liver is completely enclosed in a thick casing, from 2 to 10 mm. in thickness (German *Zuckergussleber*, sugar-icing liver). In such cases the organ has a rounded anterior edge. In the severer forms ascites is generally present, the result of the accompanying peritonitis, and the spleen is often similarly affected (*perisplenitis*).

Symptoms. In acute perihepatitis there is local tenderness and pains, especially on respiration, while a friction sound may be heard, or a rub can be felt on laying the hand over the liver. In chronic cases the liver is hard and recurrent ascites may be a feature. The underlying cause should be treated.

PYLEPHLEBITIS

This occurs in two forms, adhesive and suppurative, which have been already referred to, the one as a cause of ascites, the other in connection with multiple abscesses of the liver (*see* p. 390).

ADHESIVE PYLEPHLEBITIS

This is more generally a thrombosis of the portal vein, in which the clot adheres to the wall of the vein, and becomes ultimately organised in the same way as a thrombus in any other situation. Its causes are those changes which bring about retardation of the blood current in the portal vein or its distribution, such as cirrhosis, syphilitic disease, the pressure of tumours on the trunk of the vein or its implication in perihepatitis, or chronic peritonitis near the fissure of the liver. The obstruction to the portal vein leads to a form of Banti's disease, viz. splenic anæmia combined with cirrhosis of the liver.

SUPPURATIVE PYLEPHLEBITIS

This is nearly always due to infection from lesions in the abdomen—*i.e.* the area from which the blood is supplied to the portal vein—such as appendicitis (the most common cause), ulcers of the rectum, colon, or small intestines, gastric ulcer, and any suppuration in the abdomen or pelvis. In the new-born child the portal vein may be infected from a septic phlebitis of the umbilical vein, and rarely the lesion may be initiated by direct injury.

The mischief commonly begins in the peripheral branches of the portal vein. The wall of the vein inflames and suppurates, a thrombus forms, breaks down into pus, and its conveyance to the central branches in the liver sets up fresh centres of thrombosis, phlebitis, and suppuration. Finally, in many cases, multiple small abscesses of the liver are formed. The liver is enlarged and soft. The branches of the portal vein are filled with disintegrating thrombi, or pus, or grumous fluid; the spleen is enlarged, and there is occasionally peritonitis.

Symptoms. There are epigastric and hypochondriac pain, fever of hectic type, rigors, sweating, vomiting, anæmia and prostration. The portal vein may be sufficiently obstructed to cause some ascites, and the spleen is enlarged. Jaundice is often, but not always present; and if abscesses are numerous, there may be enlargement and pain and tenderness of the liver. The fæces generally contain stercobilin. A typhoid condition supervenes with stupor and delirium, and the disease generally progresses to a fatal termination in from one to seven or eight weeks.

Diagnosis. The disease is easily overlooked. It may be confounded with pyæmia, septicæmia, malarial fevers, acute yellow atrophy, suppurative cholangitis, tropical abscess, subphrenic abscess, typhoid fever, or pneumonia. Local evidence of the liver being involved, and evidence of a local source of infection in the portal area and enlargement of the spleen, point to suppurative pylephlebitis. When local signs are absent, the fact of an obvious pyæmia without external wound, and without endocarditis, might suggest some abdominal organ as the source of the sepsis. Symptoms of septicæmia, marked jaundice and evidence of cholecystitis or gall stones would suggest suppurative cholangitis.

Treatment. The almost necessarily fatal course of the disease renders treatment useless, except as applied to the relief of pain, sleeplessness, and other symptoms.

EXAMINATION OF THE BILIARY APPARATUS

The bile ducts are not merely conducting tubes like the ureters, nor the gall bladder merely a receptacle like the bladder. The bile ducts contain glands which secrete a colourless watery fluid which dilutes the bile, while the gall bladder has the reverse function of concentrating the bile—as much as ten times—to form a thick green fluid. If the hepatic ducts are tied they become distended with the colourless fluid—*white bile*—which collects under such a high tension as to prevent completely the liver from secreting bile into the ducts. If the common duct is obstructed the absorption of water and salts by the gall bladder, amounting in the normal to 90 per cent. of the whole volume, prevents the pressure from rising in the ducts, so that they now contain ordinary bile; but if the gall bladder is cirrhosed or destroyed, the pressure-regulating mechanism is absent and the ducts become filled with white bile, even though every other tissue in the body may be deeply jaundiced. After cholecystectomy, the bile at first leaks continuously into the duodenum, but eventually the ducts may dilate and themselves take on the functions of the gall bladder. (*See also* Diseases of the Pancreas.)

FUNCTIONAL TESTS

Cholecystography. Graham's method depends on the fact that certain dyes opaque to X-rays, after reaching the blood stream, are secreted by the liver into the bile and pass along into the gall bladder. After some hours the bile, and with it the dye, becomes concentrated in the gall bladder (but not in the ducts) so that a radiogram can be taken. The emptying function of the gall bladder may then be tested by giving a fatty meal, when normally the shadow becomes smaller (Plates 31 and 32B).

Tetra-iodo-phenol phthalein, in doses of 3 to 4 grams, according to the size of the subject, is dissolved in 40 c.c. sterile distilled water and injected into the median basilic vein (for precautions, *see* Novarsenobenzol) at 9 p.m., liquorice powder having been given twenty-four hours previously, and a plate of the gall bladder region having been taken. Fatty meals are given during the day, but no food is allowed after 6 p.m. At 9 a.m. the following morning, without food, radiograms are taken and the relation of the shadow to the duodenum determined by a barium meal. At 1 p.m. a fatty meal is taken, and two hours later another X-ray is taken. The injection sometimes causes nausea, vomiting, tingling, and rigor. To avoid this the drug (4·5 gm.) is usually now given by mouth made up into a number of small keratin-coated capsules, but absorption into the blood stream is less certain.

Absence of the gall bladder shadow may be due to blocking of the cystic duct or to the fact that the gall bladder is completely filled with gall stones. A faint shadow may be due to failure to concentrate the dye which suggests cholecystitis. The gall bladder may be shown, and gall stones may also appear in

the gall bladder shadow either as darker shadows from calcium salts or as negative shadows from cholesterin, which is transparent to the rays. The gall bladder shadow may be displaced or distorted owing to neighbouring growths, hydatids, etc.

Duodenal Intubation. Einhorn's duodenal tube provides a valuable method of diagnosing gall bladder disease, though it will not differentiate between cholecystitis and cholelithiasis. After passing the tube into the fasting stomach, which is carefully washed out with sterile water, the patient lies on the left side until the passage of the tube into the duodenum has taken place, as is shown by the fact that on suction through the tube a finely frothing fluid, slightly bile-stained, and neutral or alkaline to litmus is obtained. After washing out the duodenum with sterile distilled water, 10 to 30 c.c. of a 25 to 50 per cent. solution of magnesium sulphate is injected into the duodenum. A copious flow of bile results, which is withdrawn and examined. The presence of cholesterin crystals and leucocytes is suggestive of gall-bladder disease. Cultivation may show the presence of *B. coli*, but this is not so characteristic, as it may be found in any case where the acid of the gastric juice is much diminished.

There is some evidence that certain cases of migraine may be associated with an abnormal emptying of the gall bladder (**83**)—" bilious migraine."

DISEASES OF THE BILIARY APPARATUS

CHOLECYSTITIS

The commonest type of cholecystitis is a subacute or chronic infection by streptococci which have been isolated from inside the structure of the walls of the gall bladder (**27**). It may be a blood borne infection. However, cholecystitis is always accompanied by a pericholangitis, which suggests that the infection may gain access to the gall bladder from the liver *via* the lymphatics. Cholecystitis is commonly associated with appendicitis and peptic ulcer, and it is possible that infection may travel *via* the portal vein to the liver and so to the gall bladder; in other cases there is direct spread through the wall of the gall bladder. Bile inhibits streptococcal growth, and so the bile is usually sterile. An early form of inflammation resulting probably from this type of infection is the so-called *Strawberry Gall Bladder*; small yellowish-white specks are seen projecting from the villi. Microscopically these specks are seen to be cholesterin deposits beneath the surface layer of the mucous membrane, *i.e.* there is a *cholesterosis* of the gall bladder. It has been suggested that normally cholesterol is absorbed from the bile by the gall bladder and that these deposits become formed when the gall bladder wall is infected. Eventually some of these laden papilli are shed into the gall bladder, and so may become the nuclei round which are formed multiple mulberry-shaped calculi; these calculi are sometimes found in this condition. Hence, cholecystitis is the primary cause of gall stones, and the latter have been found at operation in 65 per cent. of cases of cholecystitis. The later results of streptococcal infection are thickening and contraction of the wall of the gall bladder, and adhesions take place to surrounding parts. Apart from the presence of stones an infected gall bladder may cause chronic pancreatitis, cirrhosis of the liver, as well as distant toxic effects on the heart muscle, joints, fasciæ, and kidneys, and lesions have cleared up after the removal of a chronically infected gall bladder (**82**).

Acute catarrhal or suppurative cholecystitis (*empyema* of the gall bladder) is an obstructive cholecystitis, commonly due to the *Bacillus coli communis*; but *B. typhosis* and occasionally other organisms are found. It may result from impacted stones, typhoid fever, and other infective diseases. In very severe forms the walls are intensely inflamed, œdematous, and infiltrated with pus (*phlegmonous cholecystitis*), and in a still more virulent form they are dark green,

soft, friable, and sloughing in more or less extensive patches (*gangrenous cholecystitis*). The inflammation may of course extend in various directions.

Symptoms. The symptoms of subacute and chronic cholecystitis of streptococcal origin, described above, are commonly insidious in onset. In fact they have been looked on as the inaugural symptoms of gall stones from the fact that the majority of cases of cholecystitis eventually terminate with gall stones. The symptoms are dyspepsia, viz. nausea, heartburn, and epigastric discomfort, and particularly flatulence; there are also aching pains and tenderness on pressure beneath the right costal margin and in the region of the right scapula. The dyspepsia may be similar to duodenal ulcer, but often has not the same striking relation to food. There is commonly pain on pressing the eleventh and twelfth right ribs and the lower dorsal vertebræ. There may also be symptoms corresponding to the complications described above—breathlessness, cardiac irregularities and angina pectoris, and symptoms of rheumatoid arthritis, fibrositis and Bright's disease.

In the case of acute obstructive cholecystitis the onset is acute with persistent or paroxysmal pain in the region of the gall bladder, and great tenderness with rigidity of the upper part of the rectus muscle. Nausea and vomiting, anorexia, a coated tongue, fever, with perhaps rigors, occur, and jaundice in about one-third of the cases. Especially characteristic are signs at the left base, viz. impairment, crepitations, and pleural friction. The right diaphragm is immobile. After a time a definite tumour may be formed by the distended gall bladder. There is leucocytosis in suppurative cases.

Diagnosis. Cholecystitis without the presence of gall stones, not at all an uncommon condition, may be diagnosed when there is severe pain and tenderness beneath the right costal margin and some dyspepsia, and when careful examination has excluded duodenal ulcer and appendicitis. Cholecystography and the " medical " drainage of the gall bladder, as described on p. 403, may be of value in diagnosis.

Prognosis. Milder cases recover with medical treatment.

Treatment. Medical treatment consists mainly in facilitating the emptying of the gall bladder. Medical drainage may be carried out several times a week. The magnesium sulphate may even be given by mouth, but it is not so effective. Fatty meals, and especially olive oil (1 to 2 ounces several times (**84**) a day) are also of assistance. Inflammation may be allayed by applying poultices and mud packs to the region of the liver and gall bladder. The bile may be disinfected by giving 10 to 20 grains of sodium salicylate three times a day or hexamine (20 grains, increasing to 60 or 80 grains) at night with sufficient alkali, *e.g.* 60 grains of potassium citrate, to make the urine alkaline and to stop irritation of the urinary tract from the hexamine, which decomposes into formalin in acid solution (**64**). The waters of Harrogate, Vichy and Carlsbad may be specially mentioned. In severe cases cholecystectomy is desirable, and operation will be necessary if there is suppuration.

GALL STONES

(*Cholelithiasis*)

Biliary calculi, or gall stones, are formed from the bile in the gall bladder, or very rarely in the bile ducts in the liver. They vary in size from a mere sand to ovoid masses of 2 inches in length by an inch in breadth; more often they measure from $\frac{1}{4}$ to $\frac{1}{2}$ inch in diameter. They are often roughly cubical in shape, presenting facets when several have been in contact; otherwise they may be more rounded. The largest have the ovoid shape, which would result from their occupying the whole cavity of the gall bladder. The chief constituents of gall stones are cholesterin, bile pigment, protein and calcium salts; and the bile pigment is mostly combined with calcium, as bilirubin-calcium. Those which consist mainly

of bile pigment are small, dark and friable. Others have a nucleus or centre of bile pigment, and are surrounded by layers of cholesterin crystals which radiate from the nucleus; these stones are generally larger, harder, and have a paler colour. Soft stones consisting mainly of calcium carbonate are found when the cystic duct is obstructed. The hard greenish calcium carbonate stone contains copper.

Ætiology. Gall stones are commoner in advanced life, and occur in women more often than in men. Sedentary occupations and over-indulgence in food, especially cholesterin-containing foods, are predisposing causes, and possibly pregnancy and typhoid fever.

Pathology. The view that a cholecystitis is the primary cause of gall stones has already been described. Given some foreign material to act as a nucleus the formation of gall stones has been proved to occur even though the bile remains sterile. They have been found in 10 per cent. of autopsies, and may remain latent (**81**), though their presence may aggravate the cholecystitis. However, in consequence of irritation in the gall bladder, due to inflammation, one or more stones may be forced out of the cavity and may pass down or be impacted in the cystic duct. The immediate effect is extremely painful spasm of the duct (*biliary colic*), but without jaundice. In the case of impaction bile is unable to enter the gall bladder, which becomes distended with mucus, or muco-pus, or pus. If the cystic duct is traversed the stone enters the common duct, and gives rise here also to biliary colic, accompanied, however, by transient jaundice, owing to the resistance offered by the presence of the stone to the outflow of bile from the liver. If the stone is impacted in the duct, obstructive jaundice results. The impaction commonly occurs at the ampulla of Vater, where the diameter of the duct is smallest. This continued obstruction has the following effects :—

(α) The liver is at first considerably enlarged from dilatation of its ducts, which are distended with bile. Sometimes the ducts are dilated uniformly, at others more irregularly into globular cysts. They exert a certain amount of pressure on the tissue of the liver, and cause it to atrophy, so that subsequently the liver becomes smaller and rather flaccid. Suppurative cholangitis may supervene.

(β) The effect of the impaction on the gall bladder might be expected to cause its distension; but this usually does not occur unless the gall bladder is simultaneously acutely inflamed, because chronic inflammation leads to fibrosis and shrinking up of the gall bladder.

(γ) When a gall stone is fixed in the ampulla of Vater, the relations of the pancreatic duct, which opens here, are of importance, since it will also probably be blocked with a retention of pancreatic juice. Micro-organisms will readily pass through the walls of the bile duct into the pancreas, and with the retained secretions set up acute or chronic pancreatitis (*q.v.*).

It is not a very uncommon event for a gall stone to ulcerate through the wall of the gall bladder directly into the duodenum or into the transverse colon; generally it is a large gall stone, an inch or more in diameter, which, if it enters the duodenum, may become impacted in the lower part of the ileum, or, if it enters the colon, may be passed *per anum* after more or less pain and difficulty from obstruction at the sigmoid or near the anus. Rarely a large stone has been vomited.

Another result of the presence and persistence of gall stones in the gall bladder is *carcinoma* of the gall bladder or bile ducts, and this has been found in about 5 per cent. of cases of cholelithiasis. Experimentally, it has been shown that the introduction of gall stones and other foreign bodies into the gall bladders of guinea pigs causes carcinoma from the chronic irritation (**85**).

Symptoms. Gall stones may remain in the gall bladder for years without giving rise to any symptoms. But in other cases the symptoms are those of subacute and chronic cholecystitis, and the dyspepsia of the co-existing cholecystitis is commonly called *gall stone dyspepsia.* The gall stones can sometimes be felt through the abdominal wall and give a sensation of crackling on being

handled. In an attack of biliary colic the patient is seized, often suddenly, with agonising pain in the right hypochondrium and lower part of the chest, or in the epigastrium and lower sternum; and it commonly radiates to the right shoulder. The pain is often so severe that he is bent double, or writhes on the floor or bed. Rigors may occur, and the patient is pale, collapsed, with profuse sweating and a small, feeble, generally quick pulse. After a time the pain becomes dull and aching, until a fresh attack of the acuter kind occurs; or the pain persists, and within a few hours or a day or two of the beginning of the pain bile pigment appears in the urine, and the patient becomes jaundiced. This may end by the passage of the stone into the duodenum, when the bile again flows freely, the pain subsides, and more gradually the jaundice clears up. When this happens, the fæces should be searched for the gall stone, which may be found by washing them with water and passing the washings through a sieve. When the stone is impacted in the common duct the symptoms are variable, but the most typical "Charcot" syndrome is recurring colic, rigors, jaundice and loss of weight. Since gall stones are usually associated with cholecystitis (*q.v.*) the corresponding symptoms may also be present.

Diagnosis. Biliary colic may be confounded with gastric pain, intestinal colic, renal colic, etc. But the passage of gall stones is not always associated with pain, and cases of impaction with jaundice may be misunderstood from the absence of this symptom. In cases of jaundice due to obstruction of the common duct, if the gall bladder cannot be felt, the obstruction is due to gall stones; if there is a lump, the obstruction is probably due to some other cause, usually a growth (Courvoisier's law). This is correct in about 90 per cent. of cases in practice. Gall stones differ considerably in the extent to which they intercept the X-rays, and thus reveal themselves by their shadows. Pure cholesterin gall stones are transparent to X-rays and give a "negative" shadow, *i.e.* a clear area in a cholecystogram (Plate 32, B). The bilirubin and calcium salts, when present, obstruct the rays (Plate 31). A very characteristic appearance is a rounded opacity with an opaque centre and a clearer layer surrounding it. Duodenal intubation should also be used.

Prognosis. This need not be unfavourable in a first attack of colic; many people recover even after several; but the possible onset of carcinoma must not be forgotten.

Treatment. The treatment of cholecystitis should be consulted.

For an attack of biliary colic the patient should be placed in a hot bath, or hot fomentations or poultices should be applied to the right side. Most relief will be obtained from the subcutaneous injection of $\frac{1}{4}$ to $\frac{1}{3}$ grain of morphia, repeated, if necessary, in three or four hours. Sometimes chloroform may be inhaled with temporary relief. Papaverine hydrochloride ($\frac{1}{3}$ to $1\frac{1}{3}$ grain) by mouth may also be tried.

When the gall stones are a constant source of trouble, or if complications are feared, cholecystotomy should be performed, and the stone or stones can be removed from the bladder or ducts. It may be advisable to remove the gall bladder.

SUPPURATIVE CHOLANGITIS

This is always due to infection by micro-organisms, *e.g.* streptococci, staphylococci, pneumococci, the typhoid bacillus, and *Bacillus coli communis;* and is either determined by local diseases, such as gall stones, the most common cause, by carcinoma, by hydatid cyst rupturing into the ducts, or by the more general infections of influenza, pneumonia, typhoid, and cholera. There is swelling and thickening of the bile ducts throughout the liver; the organ becomes enlarged; the ducts are dilated, and numerous foci of suppuration, forming smaller or larger abscesses, occur. The inflammation may extend to the pancreatic duct, and cause suppurative pancreatitis; or abscesses near the surface

may lead to localised or general peritonitis. Occasionally infection extends so as to cause a general pyæmia or infective endocarditis.

The **Symptoms** are pain and tenderness over the liver, loss of appetite, nausea, vomiting, rigors, pyrexia, which may be intermittent resembling malaria, prostration, and often jaundice. The condition is sometimes called *intermittent hepatic fever*. The liver usually increases in size as the illness progresses. The spleen may be enlarged. The duration is from a few weeks to some months, and the disease is fatal.

Diagnosis. *See* Suppurative Pylephlebitis.

Treatment. This can only be surgical. The bile ducts must be drained, where possible, by opening the gall bladder, or any ducts which may be accessible.

EXAMINATION OF THE PANCREAS

The pancreas contains two different types of secreting cells: (1) *acinar* cells, which secrete the pancreatic juice; (2) cells of the *islands of Langerhans*, which secrete a hormone necessary for the metabolism of carbohydrate. These cells may be affected by disease independently of one another.

Recent observations have shown the following relation between bile and pancreatic juice during healthy digestion. During the period of alimentary rest the liver continuously secretes bile which is stored in the gall bladder. After eating, peristaltic waves of contraction pass down the intestine from the pyloric sphincter of the stomach. Each wave is preceded by a negative wave of relaxation, so that some bile escapes through the relaxed sphincter of Oddi. This bile is mixed with the contents from the stomach, which gives it an adequate reaction to ensure the absorption of bile-salts through the intestinal mucosa. The bile-salts in their passage through the cells adsorb the preformed secretin contained in them and pass into the portal blood. The secretin causes the pancreas to secrete and the liberated bile-salt is carried to the liver to cause the secretion of a further quantity of bile. In addition the secretin in the portal blood causes the gall bladder to pass into a state of sustained contraction, so that more bile passes into the duodenum. The pancreatic secretion called forth by secretin is a dilute solution of sodium bicarbonate of the correct *p*H which washes out the preformed ferments. For the production of ferments varied stimulation is required. The activation of trypsinogen in the duodenum is caused by enterokinase, leucocytes, bacteria, etc. (**86**).

FUNCTIONAL TESTS OF THE PANCREAS

Most of the functional tests of the pancreas consist in determining whether there is a deficiency (*a*) in the external secretion from the acinar cells, (*b*) in the internal secretion from the islands. However, Loewi's *mydriatic test*, which is only positive in a proportion of cases, and is also positive in some cases of exophthalmic goitre, depends on some functional connection of the pancreas with the sympathetic system. The eyes are examined to see whether the pupils are equal and react normally. Into one of them a solution of adrenin (1 in 1,000) is dropped and the eye closed. This is repeated twice during five minutes. The eyes are not used for an hour. If during this time the pupil of the adrenalised eye is larger than that of the other eye, which is used as a control, the test is positive and indicates pancreatic disease.

Deficiency of External Secretion. *Steatorrhœa* has up to the present been regarded as one of the most characteristic signs of pancreatic disease. It consists in the passage of liquid fat in the stools, which solidifies on cooling, forming white or yellow lumps. The stools are bulky, soft and pale, and besides unaltered fat they may contain fatty acids and soaps. Where the stools are not obviously altered to the naked eye the microscope may reveal numerous fat globules and fatty acid crystals. In estimating the degree of steatorrhœa

chemically, it is important to determine not only the fat in the stools, but also to know the fat taken in the diet. In severe cases from 50 to 60 per cent. of the fat intake is lost in the stools. The normal loss is only about 10 per cent. and not more than $\frac{1}{4}$–$\frac{1}{3}$ of the dried fæces is fat, and of this not more than $\frac{1}{4}$–$\frac{1}{3}$ is split into glycerine and fatty acid.

There are two reasons for doubting that steatorrhœa is usually pancreatic in origin: (1) because it very commonly arises from defective absorption where the lacteals are obstructed from abdominal tuberculosis or growth. In these cases the fat in the stools is largely split. (2) Evidence is forthcoming that the presence of bile in the intestine is a much more important factor in fat absorption than the pancreatic juice. In fact, experimental ligature or extirpation of the pancreatic ducts do not seem to affect the absorption (**74**). Congenital steatorrhœa has been described, and in diarrhœa, cœliac disease and gastrocolic fistula the fat in the stools is increased, and the stools are bulky.

Creatorrhœa is due to the absence of trypsin. Large numbers of undigested striped muscle fibres, derived from the meat eaten, are observed microscopically in the stools. Creatorrhœa also occurs in profuse diarrhœa, so that to avoid this fallacy charcoal is taken with a meat meal, and the black stools are examined only if they have been passed between eighteen to thirty hours after ingestion (**87**).

Diastase in the Urine. The test is carried out on a twenty-four hours' specimen. To get accurate results it is essential first of all to titrate the urine with $\frac{N}{10}$ NaOH or HCl until the acidity is optimum, *i.e.* the *p*H of the urine is 6·7. This is the case when after the addition of phenol red as an indicator the urine shows a faint pink tinge (**92**). 0·6, 0·4, 0·2, and 0·1 c.c. of the urine are put in four tubes and normal saline (0·9 per cent.) added, so as to make 1 c.c. in each case. The same procedure is adopted after the urine has been diluted ten times with normal saline, so that the eight tubes contain strengths of urine corresponding to 0·6, 0·4, 0·2, 0·1, 0·06, 0·04, 0·02, 0·01. To each tube are added 2 c.c. of 0·1 per cent. soluble starch. The tubes are incubated for half an hour at 39° C. After cooling, $\frac{N}{50}$ iodine is added drop by drop to the tubes in series, starting from the tube containing 0·01 strength of urine, until there ceases to be a change of colour. The first tube in which the blue colour ceases to be developed gives the amount of diastase in the urine, which is reckoned by dividing 2 by the strength of the tube. If, for example, the blue colour is not found in the 0·06 tube, the amount of diastase would be 33 units. The normal amount of diastase varies between 10 and 40. In pancreatic disease the amount of diastase in the urine (*i.e.* the diastase index) is increased. It is possible that this test is really concerned with the *internal* secretion of the pancreas. Cammidge believes that a deficiency of this leads to liberation of hepatic diastase into the blood and its increase in the urine.

Deficiency of Internal Secretion. In a marked case this leads to glycosuria, and in less marked cases there may be a decrease in *sugar tolerance*. This is best tested by giving a patient a dose of dextrose and observing the rise in the blood sugar, as well as whether any sugar is excreted in the urine (*see* p. 463). The work of Cammidge, Forsyth and Howard is of very great theoretical interest, and may lead to valuable means of detecting a deficiency of the internal secretion of the pancreas in its earliest stages. They consider that the liver contains an amylolytic ferment which breaks down glycogen through a stage of dextrin-like bodies into dextrose. The activity of this ferment is normally kept in check by the internal secretion of the pancreas. If the latter is deficient, there is first of all an excess of these dextrins in the blood and in the urine, into which they are excreted, while the blood sugar remains at about its normal level. In a later stage these dextrins are broken down completely into dextrose, so that there

is now hyperglycæmia and glycosuria, while the dextrins disappear from the blood and urine. This latter is the condition found in diabetes mellitus. The amount of dextrins in the blood was measured by hydrolysing them with hydrochloric acid so that they were converted into dextrose. The total dextrose was then estimated. The "difference value" between this quantity and the amount of dextrose present in the original blood before hydrolysis gives the amount of dextrose which was due to the dextrins. The same method may be used for the urine, or a direct method involving the use of iodine can be employed. These determinations take the place of the original Cammidge's reaction, which is not reliable.

DISEASES OF THE PANCREAS

ACUTE PANCREATITIS

Pathology. Experiments and clinical observations show that acute pancreatitis is in the majority of cases due primarily to bacterial infection, which activates the pancreatic juice by converting the trypsinogen into trypsin. The characteristic appearances of the diseased gland are due to its digestion by the active pancreatic juice. Acute pancreatitis is predisposed to by obesity, and the attacks may be recurrent, ending in one final catastrophe. It is commonly associated with gall stones or cholecystitis; but it is not very common in acute pancreatitis for a gall stone to be found impacted in the ampulla of Vater, and when this is the case the stone is probably large enough to block the exit of Wirsung's duct, and so prevent bile from passing up it into the pancreas. However, it is possible that small stones cause intermittent stasis in the pancreatic duct by impaction at the ampulla, and the associated infection spreading from the bile ducts starts the attack. It is quite common for a history of repeated mild attacks of biliary colic to be obtained, which would fit in with this hypothesis. Acute pancreatitis may start from other neighbouring foci of infection, such as duodenal ulcer and cholangitis, and it sometimes occurs in infective diseases, such as enteric fever, pyæmia, and septicæmia, and also in mumps, which is of interest from the structural resemblance of the pancreas to the salivary glands.

In *acute hæmorrhagic pancreatitis* the organ is swollen, friable, and mottled red or brown to black, with hæmorrhages on the surface and in the interstitial tissue; and the blood may extravasate in the surrounding structures, or there may be blood-stained fluid in the peritoneal cavity. Microscopically the parenchymatous tissue is found to be necrosed, and there is usually associated inflammation, as shown by infiltration with polymorphonuclear cells. This is probably secondary to the digestion by pancreatic juice. *Fat necrosis* is always a prominent feature. In the pancreas, and in the subperitoneal fat adjacent, sometimes in the perinephric, mediastinal, and pericardial fat and even in the subcutaneous fat, are small masses of dull yellow or opaque white colour, sharply differentiated from the adjacent healthy fat, and sometimes surrounded by a narrow hæmorrhagic zone. They are produced by the action of the fat-splitting ferment (*lipase*) of the escaped pancreatic secretion upon the fat; the liberated fatty acids combine with calcium base, while the glycerine is absorbed.

At a later stage, or if the process is more chronic, *suppurative pancreatitis* occurs. The organ is large, swollen and infiltrated with pus; or it contains separate abscesses. An abscess may burst into the peritoneal cavity, or into the stomach or bowel; thrombosis and infection of the portal and splenic veins may also occur with metastatic abscesses in the liver. The *Bacillus coli communis* and pyogenic organisms are found in different cases. In both forms death may follow from acute peritonitis.

Symptoms. When pancreatitis occurs in the course of mumps, there

are vomiting and epigastric pain, with swelling and tenderness in the epigastric region. The more intense *hæmorrhagic pancreatitis* is characterised by severe, even excruciating, pain in the upper part of the abdomen, radiating through to the back; it is worse than the pain of perforated peptic ulcer, and is often unrelieved by morphia. However, there is usually not very much rigidity, since owing to the antiseptic nature of the fluid there is usually no general peritonitis. Shock, accompanied by cyanosis, comes on early, possibly owing to the absorption of proteolytic substances. The symptoms often come on quite suddenly in the midst of apparent health. Occasionally, after a few hours, a circumscribed, tender swelling appears in the upper part of the abdomen, but the difficulties of diagnosis are such that the abdomen has often been opened for the relief of a supposed intestinal obstruction. The cases are generally fatal within four or five days, but some have recovered after laparotomy. The symptoms of *suppurative pancreatitis* are similar, but less pronounced and acute, and the case may last several months. A tumour is only felt in one quarter of the cases, and this is due to accumulation of fluid in the lesser peritoneal sac. Symptoms referable to failing pancreatic functions have not very often been reported, but this is probably because they have not often been looked for. Glycosuria and an increase in the urinary diastase would be a valuable help in diagnosis. Jaundice is sometimes present.

Treatment. Laparotomy should be immediately performed if the symptoms are urgent. The condition that is found may suggest local measures. Thus with a hæmorrhagic lesion the organ has been incised, the hæmorrhage checked by ligature, and drainage instituted with success. In a case of suppurative pancreatitis, incision of the abscess and drainage are absolutely necessary. In any operation the gall bladder and common bile duct should be examined for cholecystitis and gall stones and the gall bladder drained.

CHRONIC PANCREATITIS

This affects the interstitial tissue, producing considerable fibrous growth, with consequent atrophy of the glandular structures, analogous to the changes in cirrhosis of the liver; and, as in that disease, the fibrous network may enclose large groups of acini (*interlobular*), or much more rarely single acini (*interacinar*). The head of the organ is usually most affected. The substance is rendered extremely dense and hard, and in the less frequent interacinar form considerable enlargement may take place. The ætiology of chronic pancreatitis is much the same as that of acute pancreatitis. It commonly arises from the spread of adjacent inflammations, such as those of the peritoneum, of the bile duct, of the stomach and of the intestines, such as appendicitis, by which infective organisms may be conveyed up the pancreatic duct. It also results from the presence of concretions in the pancreatic duct, or of retained pancreatic secretions; from compression of the duct by cancer; from the venous congestion of heart disease; and possibly from syphilis, and the abuse of alcohol. Gall stones are a common cause of chronic pancreatitis, especially when one lies in the ampulla of Vater, or in the common duct, or when there is suppurative cholangitis, the result of their presence. In most of these instances of duct obstruction and infection it is the interlobular form which is caused. Arterio-sclerosis is also a cause of chronic pancreatitis, which is then commonly of the interacinar variety.

Morbid Anatomy. In the interlobular form the pancreas is dense and hard, with broad bands of fibrous tissue running between the lobules and embedded areas, some of disintegrating glandular substance, some of well-preserved tissue. As a rule the islands of Langerhans are untouched. In the interacinar form the acini are separated from one another by coarse strands of fibrous tissue, the acini are atrophied, and the islands of Langerhans are frequently involved in lymphoid-cell infiltration and sclerosis.

Either form of chronic pancreatitis may be complicated by a large deposit of fat, *lipomatosis*, especially in persons the subjects of obesity.

Symptoms. A case of the writer's was a man aged 49 who had symptoms exactly simulating duodenal ulcer, with a small transverse stomach, emptying rapidly, but no deformity of the cap and no occult blood. Operation was carried out for suspected gall stones, but the biliary tract, etc. were normal. Other cases have no symptoms, or ill-defined dyspeptic symptoms, or there may be emaciation with well-marked pancreatic deficiency. Again, the swollen head of the pancreas may compress the common bile duct which it surrounds, and thus cause obstructive jaundice, which often leads to operation, when a hard pancreas is felt; in about one-third of the cases the lump is due to pancreatitis, and in two-thirds to carcinoma of the head of the pancreas.

Where diabetes mellitus results from chronic pancreatitis, Opie states that it results almost entirely from the interacinar form, in which especially the islands of Langerhans are injured, and from the interlobular form only in extreme instances when the islands, situated in the centres of the lobules, are reached by the degenerative process.

Treatment. As the chronic inflammation is attributable in so many cases to disordered conditions of the biliary and pancreatic ducts, and of the gastro-intestinal mucous membrane, the treatment of these primary disorders is the first consideration. The former will often require operation for the removal of calculi, and the latter will need suitable dietetic and medicinal treatment. Cases have been reported where prolonged drainage through the gall bladder has been successful in relieving symptoms.

PANCREATIC CALCULI

These may occur in middle-aged men; they are by no means common. They are attributable to catarrh of the ducts with delayed secretion, and consist of calcium carbonate and calcium phosphate, and sometimes calcium oxalate. They may be like grains of sand, or as large as hazel-nuts, and are usually round or oval, occasionally irregular or branched. In colour they are white or greyish white, sometimes brown or nearly black. They sometimes block the duct or its branches, and lead to dilatation of the ducts, retention cysts, acute inflammation with suppuration or chronic induration, and even to inflammation in the parts around. They rarely produce symptoms, except through their secondary effects—for instance, by the inflammation which they excite, or by the formation of cysts, or by the production of atrophy and cirrhosis of the gland.

Diagnosis is made by means of radiography and by examination of the stools for calculi. They have occasionally been removed successfully by operation, in most cases from the duct of Wirsung.

NEOPLASMS OF THE PANCREAS AND CYSTS

Carcinoma, which is nearly always primary, is the most important tumour of the pancreas. It is often confined to the head of the gland. It is an irregular nodular hard tumour, which may be of sufficient size to be felt under favourable circumstances through the abdominal parietes. As the nodules increase in size the pancreatic duct is liable to be obstructed, with the formation of a cyst as a result; and the common bile duct is not infrequently blocked either by pressure or by the spread of a chronic inflammation, so that jaundice is produced. This is, indeed, a common cause of jaundice in persons of middle and advanced age. In other instances the carcinoma may involve the stomach, duodenum, peritoneum, vertebræ, or other structures. The symptoms resemble those of chronic pancreatitis; but emaciation becomes usually marked.

Pancreatic Cysts. These develop more frequently in the tail and body of the gland; they may be retention cysts from obstruction of the duct of Wirsung by

calculus or by pressure from without. Others are formed in the substance of the gland as the after result of a hæmorrhagic pancreatitis. Pseudo-cysts develop in the neighbouring peritoneum, and are due to the out-pouring of fluid to dilute the irritating pancreatic juice which is liberated as the result of acute pancreatitis.

A cyst of sufficient size forms a globular tumour in the upper part of the abdomen, either in the median line or to one side of it; it may project below the transverse colon, resembling an ovarian cyst, though it may be pushed upwards on palpation from below; it may project forwards between the stomach and transverse colon or between the liver and stomach. Its relations can be determined by X-ray after an opaque meal or by percussion after insufflation of the hollow viscera. A pancreatic tumour is often stationary during deep inspiration, but if in contact with the diaphragm, it may move downwards ½ or ¾ inch. The fluid within it is turbid, brown or greenish in colour, alkaline, albuminous and of specific gravity 1,010 to 1,020; it may contain altered blood pigment and the various pancreatic ferments. There is emaciation and sometimes pain or jaundice. The urine sometimes contains sugar.

The swellings most likely to be confounded with it are a hydatid cyst of some other organ, hydronephrosis, circumscribed peritonitis, and ovarian disease; if much to the left and moving on inspiration it may resemble a splenic or renal tumour. The nature of the aspirated fluid should help. Congenital cysts and hydatid cysts of the pancreas occur rarely.

Treatment. Pancreatic cysts have often been successfully treated by incision and drainage. Other tumours are less easily dealt with, and treatment must be directed to the relief of symptoms. If the tumour cannot be removed, some relief may be obtained by cholecystotomy or cholecyst-enterostomy.

DISEASES OF THE PERITONEUM

ACUTE PERITONITIS

Ætiology. Acute peritonitis may be due to a blood-borne infection, *i.e.* pneumococcal peritonitis, and very rarely streptococcal peritonitis. The most frequent cause is some lesion of the abdominal viscera, such as perforated peptic ulcer, perforated typhoid and tuberculous ulcers of the ileum, and dysenteric ulcers of the colon, inflammation and sloughing of the appendix cæci, abscess of the liver, suppuration of the gall bladder, acute intestinal obstruction with strangulation, infarction and abscess of the spleen, the numerous inflammatory lesions which are apt to involve the female pelvic organs—metritis, parametritis, ovaritis, salpingitis, and pelvic hæmatocele, and sometimes infection spreading from a pyelonephritis, perinephritis, psoas abscess, acute pleurisy or empyema; but empyema is much less commonly a cause of peritonitis than a peritoneal abscess is a cause of empyema.

In many of these cases the peritonitis is set up by the discharge into the abdominal cavity of liquids, such as food, fæces, or pus, carrying with them infective micro-organisms; this happens in the case of the perforation of gastric and intestinal ulcers, in appendicitis, and in rupture of abscesses. In other cases there is an extension of inflammation to the serous layer; that is, the micro-organisms penetrate the tissues without coarse rupture. Wounds of the peritoneum, whether from injury or surgical procedure, are liable to be followed by peritonitis. Bright's disease, whether acute or chronic, is an occasional predisposing cause of peritonitis.

Bacteriology. The micro-organisms causing peritonitis are usually the *Bacillus coli communis* when the peritoneum is infected from the intestine, as in appendicitis or perforation of the bowels, or from the biliary passages; streptococci and staphylococci are found in peritonitis derived from lesions of the pelvic organs, or the abdominal walls. The pneumococcus is also met with; the

peritonitis may be primary or it may be associated with pneumonia, or it may be part of a pneumococcal septicæmia. Other bacteria less frequently found are *B. typhosus*, *B. pyocyaneus*, *B. lactis aerogenes*, *Micrococcus tetragenus*, and the gonococcus. The amœba coli has been found in amœbic dysentery; the tubercle bacillus occasionally causes acute inflammation, but much more commonly a chronic form.

Morbid Anatomy. The changes which take place in the peritoneum are not unlike those which occur in the pleura when it is inflamed. There is at first redness from increased vascularity, and if the cavity of the abdomen is examined in this early stage, the redness of the intestines is commonly seen to form parallel streaks along the intestine in the position where three peritoneal surfaces meet, *i.e.* two coils of intestine and the anterior abdominal wall or three coils of intestine. The pressure is lower at this position than elsewhere, so that congestion and exudation occur first here, forming a space along the gut which is triangular in section. The exudation coagulates, producing a yellow flaky deposit, which is often loosely spoken of as *lymph*, but which consists of fibrin and leucocytes, and there may be present a varying amount of turbid fluid in addition. The exudation appears with great rapidity, as may be seen in some traumatic cases, where a quantity of yellow lymph may be formed in less than eighteen hours. In some less severe or less extensive cases, the exudation may be replaced by fibrous tissue (*organisation*); and the different viscera are united together, or the peritoneal cavity is obliterated, by the adhesions which are thus formed. In other cases, the quantity of leucocytes increases, or is more numerous from the first, and the inflammatory products are entirely purulent; this is often quickly fatal.

Acute circumscribed peritonitis or *peritoneal abscess* results from the localisation of the infection. The *appendix abscess* is the commonest type of peritoneal abscess. Peritoneal abscesses occur in the pelvis, in the lumbar regions, iliac fossæ, or beneath the diaphragm—subphrenic abscess, which is considered later. They may point externally or open into one of the hollow viscera, or they may rupture into the chest and set up pleurisy or pneumonia. A peritoneal abscess not infrequently contains air from direct communication with the stomach or intestines by perforation of an ulcer.

Symptoms. *Acute general peritonitis* begins with pain, which is mostly very severe, and, if at first localised to one spot, soon becomes diffused over the whole abdomen. The pain is constant, but aggravated by every kind of movement, by coughing, straining, or vomiting. It is not relieved by pressure; on the contrary, there is marked tenderness over the whole of the abdomen. There is immobility of the whole abdomen on respiration, which is entirely thoracic, and a rigidity on palpation which is never relaxed—a very important sign. The legs are frequently drawn up to prevent stretching of the abdominal parietes, and every movement is avoided by the patient. The pulse is generally quickened, and the temperature is raised; but sometimes the temperature is low, though the pulse is rapid, and this is to be regarded as a sign of severe infection, as the pulse rate is a more important indication of severity than the degree of temperature. Vomiting, as a rule, soon sets in, and occurs repeatedly, either spontaneously or after attempts to take food. At first the gastric contents are brought up, subsequently bile, and later still the vomit is almost feculent in character. Sometimes also rigors occur at the commencement, but there is always a considerable degree of collapse. In the later stages the patient lies on his back, with shrunken face, dark sunken eyes, anxious expression, dry furred tongue, and quick small pulse. The abdomen becomes swollen from paralysis of the muscular coat of the intestines and the accumulation of gas within them. The surface is resonant, but if much fluid is poured out, it may cause dulness at the flanks, or occasionally all over. Hiccough is a frequent symptom. Constipation is the rule, but sometimes, after two or three days, one or more

motions may be passed, or even diarrhœa may set in ; and occasionally there is diarrhœa from the first. The urine is scanty ; it may be passed with pain, or be retained.

In cases of perforated peptic ulcer there is at the beginning generalised abdominal rigidity and shock, with livid, anxious face, cold, damp extremities, subnormal temperature, rapid, weak pulse. The later signs of acute peritonitis eventually appear. Gas may escape into the peritoneal cavity and cause extensive resonance or even splashing from mixture with the liquid. The extravasation of gas into the peritoneum is sometimes recognised by its lying in front of the liver and replacing the natural hepatic dulness by resonance. But it must be remembered that the liver may be displaced from its contact with the anterior thoracic wall by much gaseous distension of the viscera, without any escape of gas from their interior.

The patient gradually gets exhausted by vomiting and pain, the tongue becomes drier and brown, sordes form on the lips and teeth, the pulse is smaller and quicker, the bases of the lungs are compressed, and after an illness of from two to six days death takes place. It is not, however, every case that presents all the characteristic signs. Fever is absent in some cases ; there is but little distension in others ; occasionally a patient, instead of lying prostrate on his back, will throw himself about in the agony of pain.

In *pneumococcal peritonitis*, which usually arises as part of a pneumococcal septicæmia, there is pain and tenderness of the abdomen, and diarrhœa. There may be rigidity, but more often the wall is flaccid. The toxic symptoms are pronounced, with high temperature and delirium, and the respiration rate is raised, and there may be herpes labialis or evidence of pneumococcal infection elsewhere, in the lungs, joints, etc. After a time an abscess forms in one part of the abdomen, and this is indicated by the appearance of a swelling in the particular region.

In *acute circumscribed peritonitis* the general symptoms are much the same, but the local conditions are more or less limited to the region affected. The commonest cause is appendicitis with perforation, and this has already been described.

Diagnosis. As a rule, this is not difficult : the severe pain, tenderness, vomiting, rigidity, and immobility of the abdomen during respiration, followed by distension, constipation, small quick pulse, and collapse, form the important features. But peritonitis may be simulated by the severe pain of colic, by ruptured aneurysm, mesenteric thrombosis, and by acute hæmorrhagic pancreatitis ; it may itself be mistaken for intestinal obstruction ; and it may be set up, and cause death without its presence being suspected, in enteric fever, and after operations on the abdominal walls, such as herniotomy. *Colic* and *hysterical pain* are mostly to be distinguished from peritonitis by the contracted abdomen and the absence of tenderness, indeed, the relief on pressure, in the former case, and the extreme sensitiveness to the merest touch, without pressure, in the latter. *Rupture* of an *ectopic gestation* causes pain and collapse, and may be mistaken for the perforation of a gastric ulcer. There may be a history of vomiting, and menstrual irregularity ; owing to profuse hæmorrhage there is blanching of the lips ; there is tenderness and swelling of the abdomen, and sometimes free fluid, but no true rigidity, and pelvic and rectal examination discloses a tense lump. A valuable means of confirming a diagnosis of *perforated peptic ulcer* is in use at Lewisham Hospital. An X-ray film in the vertical position by a clear area between the liver and right diaphragm in the peritoneal cavity indicates the presence of free gas (*see* Plate 32, A). Perforative peritonitis is sometimes simulated by the fatal coma of *diabetes*. This occasionally begins suddenly, with severe abdominal pain and small, thready pulse. The air hunger of diabetes and the presence of much aceto-acetic acid in the urine and absence of abdominal rigidity should clear up the diagnosis.

As to the differential diagnosis of peritonitis, its cause must be looked for in the preceding history. Where severe acute peritonitis ensues in a person previously considered well, ulceration of the appendix cæci, perforated gastric ulcer, and lesions of the pelvic organs are the most likely causes. The first is more probable in both sexes before and about the age of puberty; the last occurs almost exclusively in females, and in girls the possibility of a neglected vulvo-vaginitis causing gonococcal peritonitis should be thought of. The characteristics of a primary pneumococcal peritonitis, which occurs chiefly in children, have already been described.

Prognosis. General peritonitis is a very fatal disease. The probable result must be estimated by the character of the pulse, the persistence of vomiting, the amount of collapse, and the probable extent of the inflammation. Severer cases can only be judged of from day to day. There is more hope when some days have elapsed, but in cases that are apparently improving accumulations of pus may reveal themselves, and become dangerous in the way indicated. Pneumococcal and gonococcal forms are relatively favourable.

Treatment. The majority of cases of peritonitis, and especially those due to perforation of a gastric, duodenal, or typhoid ulcer, or sloughing of the appendix cæci, or other similar accident, are only likely to recover if promptly treated by surgical methods: the abdomen must be opened, and the causative lesion dealt with, and collections of pus must be drained. In peritonitis having its origin in a septicæmia, *e.g.* pneumococcal peritonitis, an operation should not be carried out unless an abscess has formed, since it will not be possible to remove the primary focus.

Supposing it has been decided not to operate, the first principle of treatment is to keep the intestines completely at rest. For this purpose the patient must, of course, be in bed; food may be given by means of rectal enemas containing 6 per cent. dextrose; and purgatives should be strictly avoided. The patient's thirst may be quenched by small pieces of ice sucked from time to time, but no food should be allowed by the mouth. Opium or morphia should not be used, as their administration may mark an increase in the symptoms which might render operation necessary. Relief is afforded locally by the application of hot linseed-meal poultices, or flannels wrung out of hot water and sprinkled with turpentine or liniment of belladonna. Ice compresses or pieces of ice between layers of flannel are sometimes used, but they do not generally give so much relief as the hot applications. Stimulants are often required, and are best given in the form of brandy, in small quantities frequently. When there is distension, anti-Welch serum may be injected (*see* p. 380).

Subphrenic Abscess may occur in the peritoneum or in the cellular tissue beneath the diaphragm. The most frequent positions are classified as follows: (1) the right anterior intra-peritoneal abscess is above the right lobe of the liver and to the right of the falciform ligament; the pus often spreads beneath the liver posteriorly. The commonest causes are appendicitis, perforated duodenal ulcer and hepatic abscesses. (2) The left anterior intra-peritoneal abscess, due principally to perforated gastric ulcer, is situated above the left lobe of the liver and around the spleen. (3) The right extra-peritoneal abscess is situated in the cellular tissue above and behind the liver, and originates from inflammation in the liver, right retro-peritoneal tissues and the thorax. There is little subphrenic cellular tissue on the left side, so that inflammation here tends to produce a lumbar abscess. Suppuration in the lesser peritoneal sac, which arises from perforated gastric ulcer, is not so common as in the other situations mentioned (**91**). Pain is the earliest symptom of subphrenic abscess. Besides the general symptoms of a febrile disturbance due to suppuration, there are important localising signs, viz. an abdominal swelling which does not descend on inspiration, bulging of the thoracic walls on the side of the abscess, with deep tenderness. At the base of the corresponding

lung there are dulness and diminution of breath sounds, vocal resonance and tactile vocal fremitus. X-ray examination shows that the corresponding diaphragm is raised and immobile. When the abscess contains air, as may happen if it results from perforation of a viscus, a pneumothorax is simulated by the occurrence of tympanitic note, amphoric breathing, metallic tinkling, and bell sound. Exploratory puncture is best carried out under an anæsthetic, and if positive the cavity should be drained by open operation.

CHRONIC PERITONITIS

This may arise as a sequel of acute peritonitis, especially in its local forms; it is often the result of local irritation about particular organs—for instance, the liver or the spleen may be surrounded with a thickened capsule (perihepatitis, perisplenitis). The growth of tubercle and carcinoma in the abdominal cavity gives rise to forms of chronic peritonitis which will be spoken of shortly. It may occur in Bright's disease.

Adhesions and Bands between the viscera may be another form of chronic peritonitis resulting from acute or chronic inflammation, and leading occasionally to acute intestinal obstruction as already described. Much importance has been attached to adhesions in regard to intestinal stasis and alimentary toxæmia. But it has been shown that they can be found in the majority of persons of all but the youngest ages, being most frequent about the colon, and especially the ascending colon and hepatic flexure, and that even in fœtal life an adhesive process sets in at the splenic and hepatic flexures, and in some cases fixing the ileum in the pelvic fossa. Their action in impeding the flow of the bowel contents is open to investigation by X-rays after a bismuth or barium meal.

Symptoms. When there is little or no fluid the abdomen may present irregular resistance where the intestines are matted together. Otherwise the symptoms are those of the primary disease.

Diagnosis. The mere diagnosis of chronic peritonitis is not sufficient. It is necessary to find out the primary cause, and the **Prognosis** and **Treatment** depend on this. (*See also* Ascites.)

TUBERCULOUS PERITONITIS

Ætiology. Tuberculous peritonitis occurs at all ages, but most commonly in children and young adults. It is very commonly associated with tubercle in other parts of the body. It is hence often secondary to pulmonary phthisis, to tuberculous ulceration of the intestine, to caseous mesenteric glands, and to diseases of the pelvic organs—*e.g.* the Fallopian tubes, or the testes and vesiculæ seminales. It may form part of an acute general tuberculosis. Sometimes, no doubt, tubercle bacilli may pass through the bowel wall when there is no obvious lesion.

Pathology. There are four types of tuberculous peritonitis: (1) The *ascitic* type. The surface of the peritoneum is covered with small, flat whitish grains, from 2 to 5 mm. in diameter, slightly raised above the surface, and closely aggregated together. These tubercles are most abundant on the under-surface of the diaphragm and in the flanks. There is an exudation of serous fluid, which may amount to several pints, and the abdomen may be as much enlarged as it is in ascites from cirrhosis or heart disease. More rarely the liquid is sero-purulent or purulent. (2) The *adhesive, fibrinous* or *plastic* type. The exudation of fluid is much smaller in quantity, and fibrin is deposited extensively between the coils of intestine. Organisation takes place so that the coils adhere together and the peritoneal cavity becomes obliterated. In later stages firm fibrous tissue is formed. The tubercles may not be at all obvious. (3) The *caseous* type. The tubercles become larger, and in places they coalesce to form yellow caseous lumps. This often occurs in the great omentum, which becomes contracted up,

forming a sausage-shaped mass across the abdomen. Extensive ulceration of the bowel occurs in this form. The adherent intestines may open into one another through the bases of the ulcers, and render it impossible to trace the natural course of the alimentary canal. Perforation may take place, causing acute general peritonitis, or there may be collections of pus shut off from one another in different parts of the peritoneal cavity. The mesenteric glands are often caseous, and when these form large palpable lumps, the type is often called (4) *tabes mesenterica*, which term is used to denote a primary tuberculosis of the mesenteric glands, involving the peritoneum secondarily. The glands may suppurate and burst externally or into the peritoneal cavity. It must be remembered that cases often do not correspond to these types in any hard-and-fast way. Mixtures of all of them may be present, and the case may change from one type to another during the course of the illness.

Symptoms. The symptoms are sometimes *acute*, and the case is similar in every respect to acute peritonitis from other infections. More often they come on insidiously, consisting of pain or discomfort in the abdomen. The patient loses strength and flesh; there is irregular pyrexia; the appetite is diminished, and the bowels are irregular, but often loose and undigested. The abdomen may be enlarged from ascites. In the adhesive form the abdomen is also swollen and presents to palpation increased resistance in certain parts, or a doughy sensation. In the caseous form and in tabes mesenterica there are firm rounded masses with a more or less definite outline. Such tumour-like masses often occupy the lower half of the abdomen, reaching perhaps higher on one side than on the other; they are irregular or nodular on the surface. Sometimes the indurated masses of tuberculous infiltration are felt as bands running across the abdomen. Thus the thickened omentum often forms a transverse band at its upper part, and the tissue about the obliterated urachus forms a vertical band below the umbilicus. Occasionally the abdomen is retracted from the excess of fibrous tissue and consequent contraction. Tuberculosis of the abdominal lymphatic glands with obstruction of the lymphatics causes steatorrhœa.

Diagnosis. A distended abdomen associated with a chest showing undue prominence of the ribs and recession of the intercostal spaces from wasting is very characteristic of advanced tuberculous peritonitis. Obvious veins may be seen on the surface of the abdomen, and there is some tenderness. Cæcal tuberculosis and peritonitis may resemble an appendix abscess of long standing, or a case of abdominal Hodgkin's disease. The acute forms may resemble one of the enteric fevers.

There are three conditions in children, characterised by wasted limbs and a large abdomen, which are liable to be spoken of as "consumption of the bowels." They are tuberculous peritonitis and tuberculosis of the abdominal lymphatic glands, cœliac disease, and simple indigestion with diarrhœa. Of these the last is the most common. The X-rays may help in doubtful cases. In tuberculous peritonitis, owing to the adhesions, the opaque meal forms small aggregations at irregular points in the small intestine, whereas normally it passes uninterruptedly through to the end of the ileum. The infiltrated omentum may be mistaken for the lower part of an enlarged liver, but the resonance of the stomach above it should prevent this error. Sometimes, but not always, the diagnosis may be confirmed by the presence of tubercle in other parts of the body. In children or young people, a simple ascites, otherwise unexplained, is likely to be tuberculous, but it is often difficult to distinguish from the ascites of hepatic cirrhosis, which indeed sometimes co-exists; and it has often been mistaken for an ovarian cyst until operation has proved the contrary. The liquid withdrawn by paracentesis may be tested by inoculation into a guinea-pig, or tuberculin may be used (*see* p. 170).

Prognosis. This is more hopeful than the prognosis of many other tuber-

culous lesions, and many patients treated early have apparently recovered completely. Not only does liquid become absorbed, but large masses of induration, infiltration, or matting have disappeared entirely in some cases.

Treatment. Rest in bed is important, and this should be combined with fresh air, as described in the sanatorium treatment of phthisis. Exposure of the body to sunlight (*heliotherapy*) is a valuable method of treating non-febrile cases not only of tuberculous peritonitis, but also of tuberculosis of the lymphatic glands, bones and joints. The extent of body surface exposed is gradually increased from day to day, beginning with the feet and passing upwards, until finally the whole body is exposed for two or three hours a day. The head is kept covered. Albinos and people whose power of responding by producing pigment is limited are not very suitable subjects (**89**). Cod-liver oil and general tonics may be used internally, and the diet should be easily digestible. Mercurial ointment applied to the abdomen is an old method of treatment. Excess of fluid may be removed by paracentesis ; but a laparatomy is an even better method, as it enables localised collections of fluid to be evacuated. Steatorrhœa should be treated by reducing the fat in the diet.

PERITONEAL EFFUSIONS AND CONTENTS

Liquid effusions into the peritoneal cavity are: (1) The serous, serofibrinous and purulent liquids which result from inflammation or peritonitis. The names *polyorrhomenitis* (ὀρρός, serum) or *polyserositis*, or Concato's disease, are given to the condition of simultaneous inflammations of two or more of the four great serous membranes, pericardium, pleuræ, and peritoneum. This association may occur in tuberculous, streptococcal and pneumococcal infection, and in acute rheumatism. It must be distingiushed from Pick's disease (*q.v.*). (2) The liquids effused in the different forms of hepatic, cardiac or renal dropsy, and the chylous and chyliform liquids sometimes present. (3) Liquids provided by the rupture of vessels, or other adjacent structures. Thus (*a*) blood may be found in the peritoneal cavity as the result of traumatism, rupture of an aneurysm, hæmorrhagic pancreatitis, embolism or thrombosis of mesenteric vessels, rupture of vessels in carcinomatous growths, extra-uterine pregnancy and other conditions. (*b*) Bile may reach the peritoneum during rupture of a hydatid cyst in the liver, and possibly from rupture of the gall bladder. (*c*) A hydatid cyst, whether simple or suppurating, may rupture and discharge its contents into the peritoneum. (*d*) Pus from abscesses and (*e*) the contents of any of the hollow abdominal viscera may from traumatism or disease be passed into the cavity, for instance, those of the stomach, intestines or bladder, etc.

NEW GROWTHS IN THE PERITONEUM

One of the most common growths in the peritoneum is *carcinoma*, secondary to disease in the viscera, especially the stomach and the ovary. It occurs mostly at an advanced age. It occurs in the form of flat circular deposits, covering the abdominal surface, and, like tubercle, it is most abundant on the diaphragm and in the flanks ; similarly the omentum may be thickened and infiltrated, and eventually large carcinomatous nodules may occur all over the abdomen. *Colloid carcinoma* is present in a certain number of cases. Considerable liquid effusion is commonly present (*carcinomatous peritonitis*), and blood is not infrequently mixed with it, so that it acquires a brown, brownish-red, or even red colour. Occasionally nodules of carcinoma are felt in the skin around the umbilicus, and the glands in the groin may be infiltrated with the same growth. Colloid carcinoma must be distinguished from so-called *pseudo-myxoma peritonei*. If an organ, *e.g.* the appendix, affected with catarrhal inflammation, ruptures, mucus may be extruded through the opening into the peritoneum, forming large masses, to which this name is given.

Sarcoma is another common form of malignant disease ; it occurs in the retroperitoneal tissues, in the omentum, mesentery, or broad ligament. Retroperitoneal *myxo-sarcoma* may form very large tumours.

Symptoms. Apart from the symptoms of chronic peritonitis already described, these depend on the seat of the primary growth.

Prognosis is absolutely unfavourable, and **Treatment** must be directed to the relief of symptoms, the temporary removal of fluid when it is considerable, or an operation for obstructed bowel. Sarcoma may do well with deep X-ray therapy.

REFERENCES

1	A. Rendle Short	1925	*Brit. Med. Journ.*, ii., p. 254.
2	A. Bulleid	1931	*Guy's Hosp. Rep.*, **81**, p. 116.
3	C. B. Henry	1930	*Lancet*, ii., p. 35.
4	H. Lloyd Williams	1925	*British Dental Journ.*, Dec. 9th, p. 60.
5	R. D. Paterson; A. Brown Kelly	1919	*Journ. Laryng.*, pp. 285, 289.
6	P. P. Vinson	1922	*Minnesota Medicine*, p. 107.
7	W. W. Payne and E. P. Poulton	1923	*Quart. Journ. Med.*, **65**, p. 53.
8	G. W. Rake	1926	*Guy's Hosp. Rep.*, **76**, p. 145.
9	G. W. Rake	1927	*Guy's Hosp. Rep.*, **77**, p. 141.
10	G. L. Scott	1922	*Lancet*, ii., p. 988.
11	A. E. Barclay	1922	*Lancet*, ii., p. 261.
12	J. M. H. Campbell and J. J. Conybeare	1924	*Guy's Hosp. Rep.*, **74**, p. 354.
13	Bolton and Goodhart	1922	*Lancet*, i., p. 420.
14	Baird, Campbell and Hern ..	1924	*Guy's Hosp. Rep.*, **74**, p. 23.
15	H. D. Rolleston	1896	*Trans. Path. Soc.*, **47**, p. 37.
16	A. F. Hurst	1914	*Quart. Journ. Med.*, **8**, p. 300.
17	T. L. Hardy	1929	*Lancet*, i., p. 711.
18	H. Maclean and W. Griffiths	1928	*Journ. Physiol.*, **65**, p. 63.
19	Morell Roberts	1930–31	*Quart. Journ. Med.*, **24**, p. 133.
20	Campbell, Mitchell, Powell ..	1928	*Guy's Hosp. Rep.*, **78**, p. 279.
21	A. F. Hurst (Goulstonian Lectures)	1911	*The Sensibility of the Alimentary Canal. Oxf. Med. Publications.*
22	W. W. Payne and E. P. Poulton	1927	*Journ. Physiol.*, **63**, p. 217.
	E. P. Poulton	1928	*Lancet*, ii., pp. 1223, 1277.
23	W. W. Payne and E. P. Poulton	1928	*Journ. Physiol.*, **65**, p. 157.
24	Meunier (L'etat dyspeptique)	1924	Masson et Cie., Paris.
25	Sir B. Bruce-Porter	1924	*Lancet*, ii., p. 495.
26	P. C. Conran	1922	*Quart. Journ. Med.*, **15**, p. 144.
27	D. P. D. Wilkie	1928	*Brit. Med. Journ.*, i., p. 481.
28	D. P. D. Wilkie	1922	*Brit. Med. Journ.*, ii., p. 1219.
29	D. P. D. Wilkie	1933	*Brit. Med. Journ.*, i., p. 771.
30	D. C. M. Ettles	1927	*Guy's Hosp. Rep.*, **77**, p. 216.
31	K. Faber	1927	*Lancet*, ii., p. 901
32	J. Sherren	1924	*Lancet*, i., p. 477.
33	K. Faber..	1922	*Lancet*, i., p. 65.
34	A. E. Barclay	1929	*Lancet*, ii., p. 1272.
35	A. E. Barclay	1929	*Lancet*, ii., p. 1322.
36	A. Bruce Maclean	1932	*Brit. Med. Journ.*, ii., p. 1055.
37	M. J. Stewart	1923	*Brit. Med. Journ.*, Nov. 24th and Dec. 1st.
38	J. W. McNee	1922	*Quart. Journ. Med.*, **15**, p. 215.
39	T. G. Bonar	1924	*Lancet*, ii., p. 261.
40	A. F. Hurst, R. P. Rowlands, etc.	1926	*Guy's Hosp. Rep.*, **76**, p. 156.
41	E. C. Rosenow	1923	*Journ. Infect. Dis.*, **32**, p. 384.
42	A. F. Hurst	1923	*Brit. Med. Journ.*, i., p. 1074.
43	J. J. Conybeare	1922	*Guy's Hosp. Rep.*, **72**, p. 174.
44	Sir B. Moynihan..	1923	*Lancet*, i., p. 631.
45	E. I. Spriggs and O. A. Marxer	1922	*Lancet*, i., p. 725.

46	J. Morley	1923	*Lancet*, ii., p. 823.
47	G. F. Still	1923	*Brit. Med. Journ.*, i., p. 579.
48	H. Tyrrell Gray and F. N. Reynolds	1921	*Lancet*, ii., p. 891.
49	T. I. Bennett	1923	*Lancet*, ii., p. 275.
50	A. F. Hurst and A. Newton	1913	*Journ. Physiol.*, **47**, p. 57.
51	T. I. Bennett, D. Hunter and J. M. Vaughan	1932	*Quart. Journ. Med.*, **1**, p. 603.
52	Discussion on Summer Diarrhœa	1923	*Brit. Med. Journ.*, ii., p. 857.
53	G. Leighton (The Loch Maree Tragedy)	1923	W. Collins, Sons & Co.
54	W. M. Scott	1930	*Brit. Med. Journ.*, ii., p. 56.
55	R. E. Smith	1931	*Lancet*, ii., p. 925.
56	T. K. Monro and W. W. N. Knox	1923	*Brit. Med. Journ.*, i., p. 279.
57	N. L. Lloyd	1925	*Guy's Hosp. Rep.*, **75**, p. 410.
58	Z. Cope	1924	*Lancet*, i., p. 121.
59	E. I. Spriggs and O. A. Marxer	1927	*Lancet*, i., p. 1067.
60	H. Hartmann	1922	*Lancet*, i., p. 307.
61	R. L. Haden and T. C. Orr	1923	*Journ. Exp. Med.*, **37**, p. 365.
62	B. W. Williams	1927	*Lancet*, i., p. 907.
63	R. St. L. Brockman	1927	*Lancet*, ii., p. 317.
64	A. F. Hurst (Essays, etc.)	1924	Heinemann, p. 123, etc.
65	J. W. McNee	1932	*Brit. Med. Journ.*, i., pp. 1017, 1071.
66	P. H. Whitaker, T. B. Davie, and F. Murgatroid	1933	*Quart. Journ. Med.*, **2**, p. 49.
67	Mann	1927	*Medicine*, **6**, p. 419.
68	A. R. Rich	1930	*Bull. Johns Hopkins Hosp.*, **47**, p. 338.
69	D. R. Drury and P. D. McMaster	1929	*Journ. Exp. Med.*, **50**, p. 569.
70	J. C. Spence and P. C. Brett	1921	*Lancet*, ii., p. 1362.
71	Y. Akerran	1934	*Experimental Changes in Liver Function*, Upsala.
72	D. T. Davies	1927	*Lancet*, i., p. 380.
73	J. W. McNee	1922	*Brit. Med. Journ.*, i., pp. 716, 783.
74	M. Brulé (Recherches sur les Ictères)	1924	Masson et Cie., Paris.
75	W. Morrell Roberts	1933	*Brit. Med. Journ.*, i., p. 734.
76	C. Newman (Goulstonian Lectures)	1933	*Lancet*, i., pp. 785, 842, 896.
77	G. A. Collinson and F. S. Fowweather	1926	*Brit. Med. Journ.*, i., p. 108.
78	Sir H. Rolleston (Discussion on Degenerative Diseases of Liver)	1922	*Brit. Med. Journ.*, ii., p. 1055.
79	C. H. Best	1934	*Lancet*, i., p. 1274.
80	Review on Syphilis	1923	*Med. Sci.*, **8**, p. 182.
81	P. Rous, P. D. McMaster and G. O. Broun	1923	*Lancet*, i., p. 449.
82	D. P. D. Wilkie	1933	*Brit. Med. Journ.*, ii., p. 767.
83	T. C. Hunt	1933	*Lancet*, ii., p. 279.
84	B. B. V. Lyon	1920	*Amer. Journ. Med. Sci.*, **160**, p. 515.
85	A. Leitch	1924	*Brit. Med. Journ.*, ii., p. 451.
86	J. Mellanby	1926	*Lancet*, ii., p. 215.
87	R. Coope (Pancreatic Disease)	1927	London.
88	J. F. Brailsford	1926	*Proc. Roy. Soc. Med.* (*Elect. Therap. Sect.*), p. 41.
89	A. Rollier	1922	*Brit. Med. Journ.*, ii., p. 741.
90	A. C. Hampson	1919	*Lancet*, i., p. 429.
91	H. L. Barnard	1910	*Contrib. to Abdominal Surgery*, p. 335.
92	A. F. Sladden	1922	*Lancet*, ii., p. 68.
93	H C. Edwards	1935	*Lancet*, ii., p. 1161.

DISEASES OF THE BLOOD, SPLEEN, AND LYMPHATIC SYSTEM

EXAMINATION OF THE BLOOD

Coagulation Time. The determinations are carried out at blood temperature. Gibbs' clinical blood coagulometer is the instrument recommended (**1**). A drop of blood is made to travel round a platinum wire loop, and its movement stops when coagulation takes place. The coagulation time of the first drop obtained from a prick varies from about 100 to 170 sec. (average 128 sec.). With later drops the time is shorter (25—55 sec.). This is because, at first, the bruising of the tissues liberates thrombokinase, while, later on, platelets become agglutinated in the wounded vessels and give rise to extra prothrombin (**2**), factors which increase the speed of clotting.

AVERAGE VALUES OF SOME NORMAL CONSTITUENTS OF BLOOD AND URINE

	Whole Blood. (Fasting).	Urine. (On ordinary diet).	
	Mgm. per 100 c.c.	Mgm. per 100 c.c.	Grams. per 24 hrs.
Amino-acid N	Up to 6	6	0·06
Chlorine	270–300	600	Up to 10
Cholesterol	120–200		
Dextrose	80–100		
Non-protein N	3		
Uric Acid	Up to 4	57	1
Urea	19–32	2,000	20–30
	Plasma.		
Chlorine	352–383	600	Up to 10
Albumin	4,400		
Globulin & Fibrinogen	2,630		
Alb.-glob. ratio	1·67 to 1		
Fibrinogen	0·2–0·4		
Inorg. phosphorus	3	90	0·9
	Serum.		
Calcium	9·6	15–17	0·3
Magnesium	3·2	6	0·16
Potassium	19·5	200–250	Up to 4
Sodium	335	300	Up to 5
Alkaline Reserve	53–75 c.c. CO_2		
Oxidised sulphur			
Inorganic	0·5–1·1	180	2·3
Ethereal	0·1–1·0	15	0·2
Unoxidised sulphur	1·7–3·5	15	0·2

Note. There is no ammonia in blood; the ammonia nitrogen content of the urine is usually 10 times the amino-acid nitrogen.

Bleeding Time. The blood from a prick is dried off with blotting paper without pressure every quarter or half minute. Normally, the bleeding ceases in one to two and a half minutes; in disease it may be prolonged up to thirty minutes or even several hours.

Sedimentation Rate. Oxalated or citrated blood is drawn into a glass tube of at least 2 mm. bore, so as to form a column 10 cm. high. The normal rate at which the corpuscles sink is such that there is left a clear column of plasma in the top of the tube, measuring up to 0·4 cm. in 15′; 1·0 cm. in 30′; 2·5 cm. in 60′. The determinations are best carried out in an incubator at 37° C. A rapid sedimentation rate suggests infection, *e.g.* focal sepsis; but anæmia and nephritis must be excluded.

Fragility of Corpuscles. In some diseases it has been found that the fragility of the red corpuscles is greater than normal, or, in other words, that the corpuscular or globular resistance to hæmolysis by dilute fluids is less. For this determination a few cubic centimetres of blood are mixed with an isotonic solution of oxalate of potassium (pot. oxal. 0·28 gramme, sod. chlor. 0·8 gramme, aq. dest. 100 grammes), centrifuged, the plasma decanted, and the corpuscles washed in a solution of 0·9 per cent. of sodium chloride, and then tested with sodium chloride solutions of different strengths. Washed normal red corpuscles show slight hæmolysis in 0·45 per cent. sodium chloride, and complete hæmolysis in 0·35 per cent. Abnormally high fragility is shown if hæmolysis occurs with stronger solutions, as is the case in acholuric jaundice.

Enumeration of Corpuscles, or Blood-count. This is effected by the *hæmocytometer* of Thoma-Zeiss or Bürker-Zeiss.

The former consists of a glass slide on which a "cell" is constructed $\frac{1}{10}$ mm. in depth and ruled at the bottom into squares measuring $\frac{1}{20}$ mm. in the side, which are again ruled into groups of sixteen small squares. In a specially constructed pipette the blood is diluted to the extent of 1 to 100 by a saline solution (sodium phosphate or chloride) which does not injure the corpuscles; and a drop of this is placed in the cell and covered with thin glass. The corpuscles settle down upon the squares, each of which corresponds to $\frac{1}{4000}$ cubic millimetre. The red corpuscles in several groups of sixteen squares are counted, and the total multiplied by 100 (the dilution) and 4,000 (representing the volume of fluid over each small square), and divided by the number of small squares counted, gives the corpuscles in a cubic millimetre. In Bürker's instrument, which is preferable to that of Thoma-Zeiss, the cover glass is first of all arranged in position by clamps, and the diluted blood is then run in by capillary attraction. Bürker's method of effecting dilution is also much superior, but this is not yet much used in this country. A second pipette provides for a dilution of 1 in 10 with 0·9 per cent. acetic acid, by which the red corpuscles are rendered invisible.

The average number of red corpuscles per cubic millimetre is usually taken to be 5,000,000 for males and 4,500,000 for females. Actually in London the average for males is 5,430,000 and the range, within which about 90 per cent. of normal values lie (2·5 × standard deviation), is 4,660,000–6,190,000; for females, 5,010,000 and the range 4,120,000–5,910,000.

The average hæmoglobin for men in London is 105 per cent., corresponding to an oxygen capacity of 19·5 per cent. and 14·5 grm. hæmoglobin; the range within which 90 per cent. of normal results lie (2·5 × standard deviation) is from 96 to 115 per cent. The average hæmoglobin for women is 98 per cent., and the range 87 to 110. These high values may be due to carbon monoxide in the atmosphere from motors.

The number of leucocytes is from 4,000 to 9,000 per cubic millimetre when counted in the morning; the maximum is 12,000 in the afternoon (*see* p. 427).

Platelet-counting. A drop of sterile 2·5 per cent. solution of sodium citrate is placed on the finger, and the latter is pricked through the drop, so that blood diffuses out into it. The mixed blood and citrate are examined fresh with the

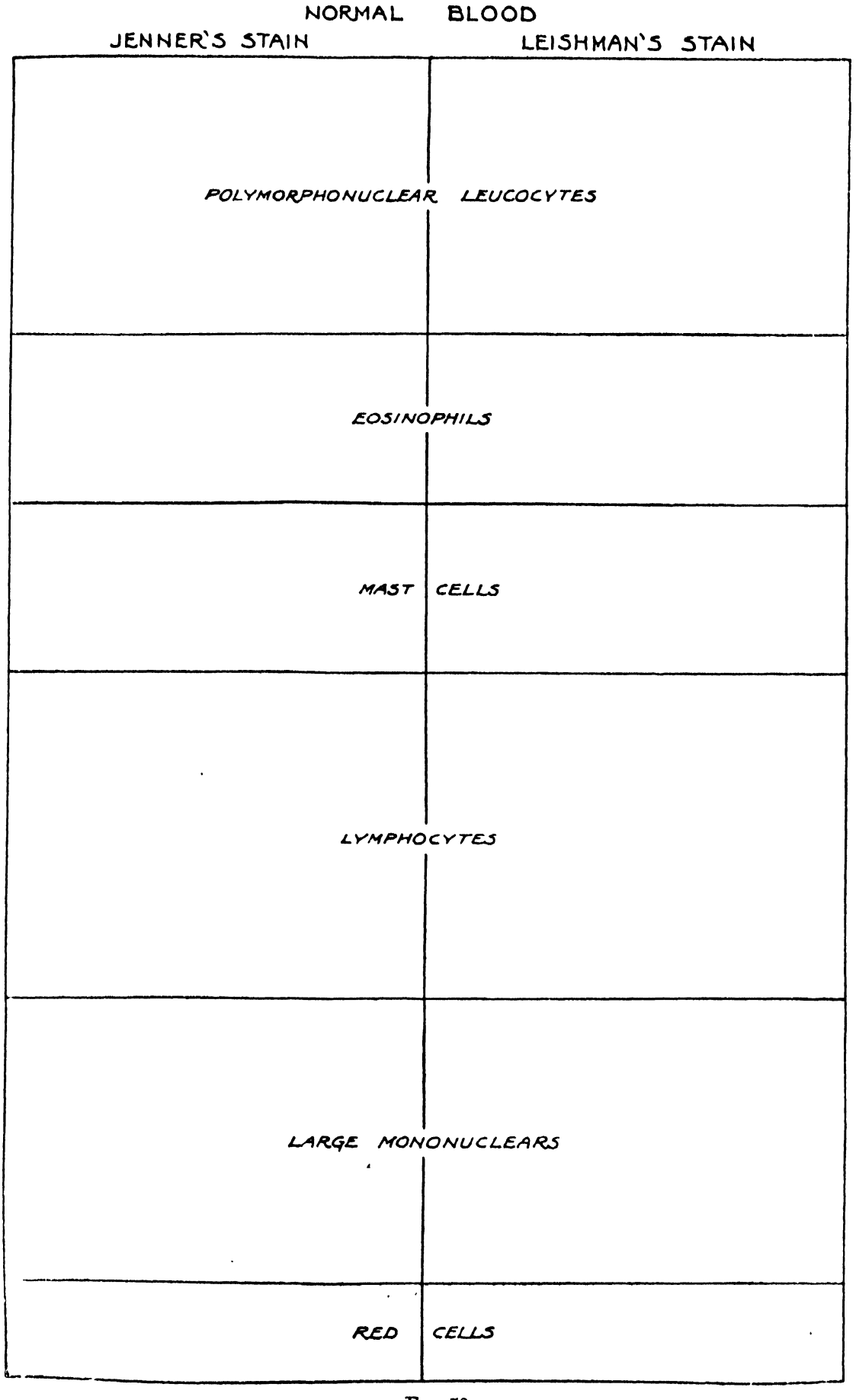

NORMAL BLOOD
JENNER'S STAIN
LEISHMAN'S STAIN
POLYMORPHONUCLEAR LEUCOCYTES
EOSINOPHILS
MAST CELLS
LYMPHOCYTES
LARGE MONONUCLEARS
RED CELLS

FIG. 50.

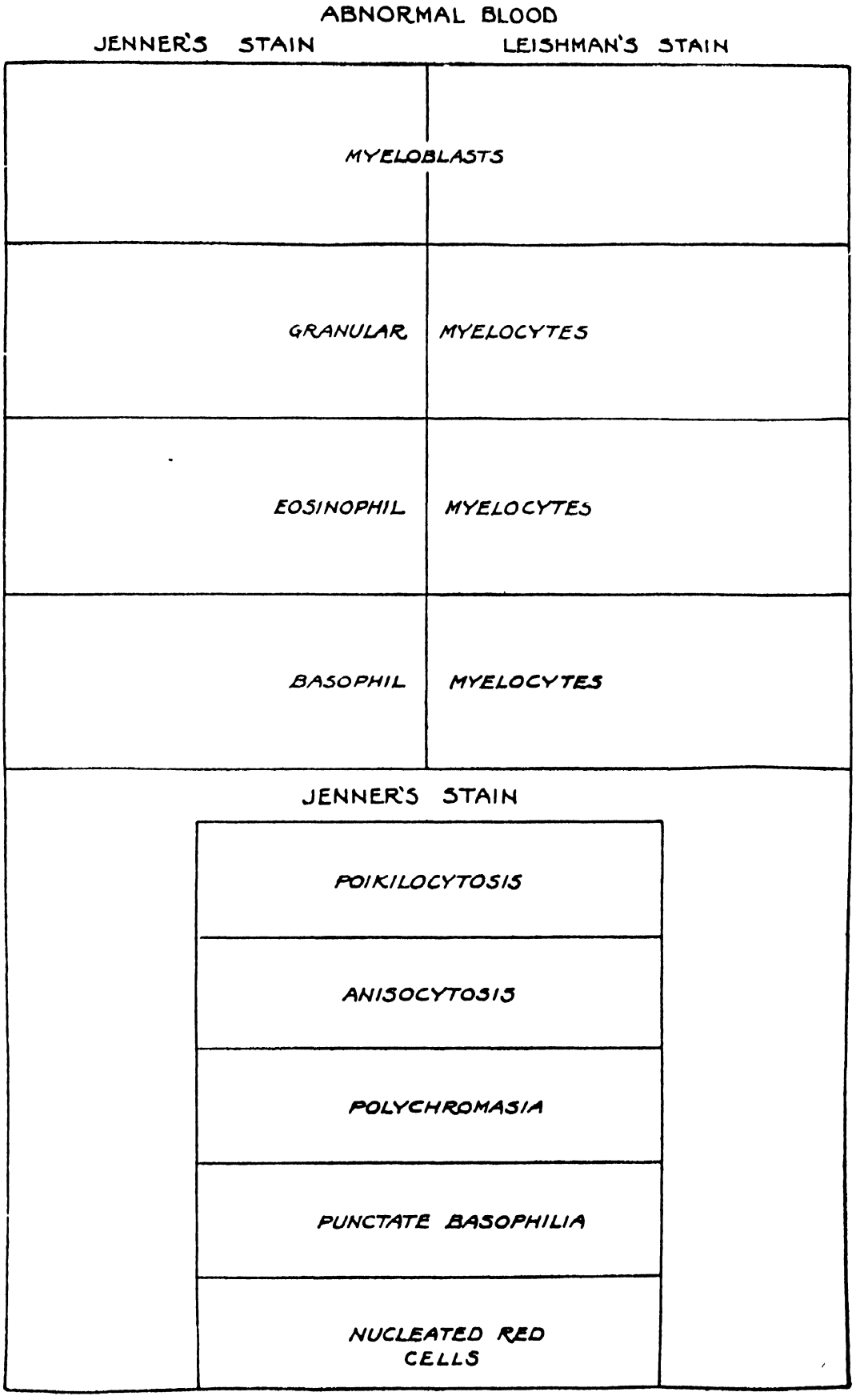

ABNORMAL BLOOD
JENNER'S STAIN
LEISHMAN'S STAIN
MYELOBLASTS
GRANULAR
MYELOCYTES
EOSINOPHIL
MYELOCYTES
BASOPHIL
MYELOCYTES
JENNER'S STAIN
POIKILOCYTOSIS
ANISOCYTOSIS
POLYCHROMASIA
PUNCTATE BASOPHILIA
NUCLEATED RED CELLS

Fig. 51.

microscope, drying being prevented by ringing the cover-slip with vaseline. If the number of red cells per cubic millimetre is known, the number of platelets can be determined from the ratio of the two in the film. The normal figure varies between 200,000 and 500,000.

Estimation of Hæmoglobin. For clinical purposes Haldane's hæmoglobinometer is the best to use. Two tubes are provided. One of them, which is the standard, contains a 1 per cent. solution of normal blood saturated with carbonic oxide, and is hermetically sealed. The other tube is graduated in divisions up to 100, and in this a measured quantity of blood is diluted till it matches the colour of the standard after saturating with coal-gas to convert all the hæmoglobin into CO-hæmoglobin. The figure on the scale which the solution then reaches represents the percentage amount of hæmoglobin. The Dare hæmoglobinometer is standardised on the same scale as the Haldane instrument; but other instruments are differently standardised.

Colour Index. The concentration of hæmoglobin in the corpuscles shows some variation in different diseases of the blood; but the size of the corpuscles varies much more. The percentage of hæmoglobin is less than that of the corpuscles if individual corpuscles are smaller than normal; the hæmoglobin percentage is greater if the corpuscles are larger than normal. This relation of the hæmoglobin percentage to the corpuscle percentage is called the *colour index*, and it may be less or greater than 1, according as the cells are on the average smaller or larger than normal (**3**). Thus with hæmoglobin 40 per cent., corpuscles 50 per cent., the colour index is $\frac{4}{5}$ or 0·8. The average colour index for men in London is 0·97 and the range 0·89–1·06, and for women the average is 0·98 and the range 0·87 to 1·1.

Microscopic Examination of the Corpuscles. Though a clinical diagnosis may often be made from an unstained film, stains, such as Jenner's or Leishmann's, should be ordinarily employed. To stain reticulocytes, an alcoholic solution of cresyl blue is evaporated to dryness on a warm slide; a drop of blood is mixed with the dye; it is then spread out and allowed to dry and examined with an oil immersion lens.

The different corpuscles which may be seen in health and disease are illustrated in Plates 33, 34, 35, 36, B, C.

Red Corpuscles or Erythrocytes. The normal red corpuscle measuring in diameter 7·5μ; small corpuscles, or *microcytes*, from 2 to 6μ; large corpuscles, or *megalocytes*, from 8 to 15μ. Inequality in the size of the red cells is called *anisocytosis*. In addition there are misshapen, distorted, often pear-shaped corpuscles, or *poikilocytes;* fragments of corpuscles are called *schizocytes;* nucleated red corpuscles (*erythroblasts*), divided according to their size and shape into *normoblasts, microblasts, megaloblasts,* and *poikiloblasts*, also occur.

Nucleated red cells occur normally in the bone marrow. Their presence in the blood indicates increased production in the marrow.

Free nuclei from rupture of erythroblasts may be seen. *Reticulocytes* are red cells containing a basophil reticulum; they are seen in the early stage of recovery in pernicious anæmia (*see* Plate 36, B, p. 433); *polychromasia* is another name for reticulocytosis. *Punctate basphilia* or stippling of the red cells is an allied condition, considered further under lead-poisoning. A *metrocyte* is a megaloblast in which the nucleus shows signs of mitosis.

Leucocytes. The white cells, of which there are several varieties, fall into two groups: (1) *granular* cells, sometimes called *leucoid*, viz., *polymorphonuclear* cells with small acid-staining granules in the cytoplasm and variable nucleus, *eosinophil* cells with coarse granules and horseshoe-shaped nucleus, and *mast* cells with granules staining purple and faintly basophil nucleus; (2) non-granular, or *lymphoid*, cells, viz. *lymphocytes*, large and small, with large, round, strongly basophil nucleus and scanty cytoplasm, which is only faintly stained, and *large mononuclear* or *hyaline* cells or *monocytes*, as they are now usually called, with

anæmia which especially occurs in constipated girls and young women between the ages of fourteen and twenty-four, though a similar condition is exceptionally seen in boys. There has been a gradual decline in the incidence of chlorosis since the beginning of the century, and this is probably due to the abolition of tight-lacing with its pressure on the liver, as well as to the better conditions under which women's work is carried on and to the greater amount of fresh air and exercise taken (**6**). It was commonest among those in domestic service.

Symptoms. Chlorosis is a microcytic anæmia; a blood count shows a low colour index, the hæmoglobin being reduced more than the red cells. Normoblasts, reticulocytes and schizocytes may be seen in serious cases. The leucocytes are normal There is amenorrhœa. The gastric juice contains free HCl. Optic neuritis occasionally occurs, and may be followed by atrophy, exceptionally also ocular paralysis, retinal embolism, and retrobulbar neuritis,

Prognosis and **Treatment.** *See* Simple Achlorhydric Anæmia.

SIMPLE ACHLORHYDRIC ANÆMIA

This disease affects women much more commonly than men, and women about the child-bearing age—most of all from forty to fifty; but it does occur in children and in the aged (**33**). However, it must be remembered that 32 per cent. of healthy men and women have achlorhydria above sixty years.

Symptoms. This is a microcytic anæmia, the blood showing a low colour index. Like pernicious anæmia it is associated with achlorhydria; but there is no excess of bilirubin in the blood, so that Van den Bergh's test is negative, and there are no changes in the spinal cord. The spleen is large and there is frequently glossitis and the inflammation spreading from the tongue on to the back of the pharnnx; there is sometimes dysphagia. The nails are concave (spoon-shaped) and thin with longitudinal ridging (*koilonychia*). The anæmia is probably due to defective absorption of iron in the alimentary tract and the absence of hydrochloric acid in the gastric juice may be partly responsible.

Diagnosis. This depends on observing achlorhydria with an anæmia of low colour index, without obvious cause, such as bleeding.

Prognosis. This is good with efficient treatment.

Treatment. Iron must be given in large doses. The scale preparation, iron and ammonium citrate, containing ferric citrate, is a favourite; but a drachm must be given daily; iron is only absorbed and acts in the ferrous condition (**7**), and so it is better to use ferrous iron. Pil. ferri. (Blaud's pill), a mixture containing ferrous sulphate and sodium carbonate (5 to 15 grains), is well known; it may be given in powdered form. The difficulty of prescribing ferrous sulphate in solution is that it is oxidised; but this can be hindered by dissolving it in 10 per cent. glucose solution, or acid. sulph. dil. 5 minims to 5 grains of ferrous sulphate may be used instead.

In many cases it will be desirable to find out as soon as possible whether the treatment is effective; for this, a reticulocyte crisis is looked for as described under pernicious anæmia. Most iron preparations contain small amounts of copper; but if necessary, this may be prescribed as a $\frac{1}{2}$ per cent. solution of copper sulphate 3–5 c.c. daily. Care must be taken to see that there is no hypothyroidism and that there is in the diet plenty of vitamin C, best given as orange and lemon juice. The anæmia in scurvy has been observed before hæmorrhage takes place. It is generally agreed that all forms of iron given by injection are valueless, and it is unnecessary to give arsenic; but liver or liver extract sometimes helps though it should not replace iron. If a laxative is required pil. aloes et ferri. (4–8 grains) containing ferrous sulphate may be useful. The naturally occurring chalybeate waters contain ferrous carbonate held in solution by extra CO_2, and these are valuable when taken by mouth fresh at the spring. In severe cases rest in bed during treatment is essential and blood transfusions may be valuable.

PERNICIOUS ANÆMIA

(*Addison's Anæmia, Glossitic Anæmia*)

Cases of this disease were first described by Addison under the name of *idiopathic anæmia*, because they presented distinctive features, and he was unable to find a cause for them. Later Biermer and other Continental writers described similar cases, under the name of *progressive pernicious anæmia.*

Ætiology. It affects both sexes equally, and 85 per cent. of cases are over the age of forty; and there is a hereditary tendency to the gastric changes responsible for this disease (**17**).

Morbid Anatomy. Besides the universal pallor of the organs, one of the most constant conditions *post-mortem* is fatty degeneration of the heart, which shows itself by alternate dark and pale striations of the muscle as seen through the endocardium (tabby-cat striation). It is due to deficient oxygen supply, owing to the diminished amount of hæmoglobin in the blood. It occurs in the left ventricle and the papillary muscles. There is also fatty degeneration of the liver and kidneys, and of the intima of the arteries. Hæmorrhages are found not only in the retina, where they have been seen during life, but in the serous membranes, the endocardium, the mucous membrane of the stomach, the lungs, the surface of the brain, and other parts. Fenwick originally observed changes in the stomach typical of gastritis, *q.v.* The spleen is sometimes enlarged, and of dark red or purple colour. The marrow of the bones has been found to be excessive in amount, of a reddish-purple colour, with large numbers of nucleated red corpuscles, especially megaloblasts. There is, moreover, an abundant deposit of iron in the peripheral zones of the lobules of the liver, in the spleen and in the kidneys, as can be shown by the organ turning blue with potassium ferrocyanide and dilute hydrochloric acid. In cases with spinal symptoms a degeneration of the lateral and posterior columns is found after death.

Pathology. The following features of the disease must be related in any consideration of its pathology: (1) The excess of urobilin in the urine, the deposit of iron in the liver, and the presence of bile pigment in the blood, which gives Van den Bergh's indirect test. Similar features have been obtained by injecting poisons such as saponin, pyridine, etc., into animals. (2) The hypertrophy of the red marrow with the irregularity in size and shape of the red cells and the presence of megalocytes and sometimes megaloblasts in the circulating blood. The disease is a *macrocytic anæmia.* The biochemical constitution of the red cells is also altered; there is an increased H ion concentration in the corpuscles, probably due to an increase in the phosphoric acid esters, so that the potential difference between cells and plasma is 28 millevolts, instead of eight or nine (**12**). (3) The absence of free HCl in the gastric juice, which is due chiefly to a gastritis, since the mineral chloride and pepsin are also low, though never completely absent (**13**); probably there is always a little "active" HCl present (*see* Fig. 47, p. 331). Inflammation elsewhere in the alimentary tract is shown by the characteristic glossitis; while the diarrhœa in certain cases may be due to an enteritis. (4) The curative effect of liver extract when given by mouth.

Up till recently the disease was considered to be due to a primary hæmolysis; but it is doubtful whether hæmolysis is at all prominent; if all the excreted bilirubin came from broken-down corpuscles, it would mean that the corpuscles of the blood would have to be regenerated with impossible rapidity; the excretion of bilirubin is very variable, while the blood picture is constant; the blood picture is very unlike acholuric jaundice, which is primarily a hæmolytic disease; the red cells may survive as long in pernicious anæmia as in health. Instead, the disease is primarily one of faulty formation of blood cells, as described on p. 429. Without the hæmatinic principle the marrow cannot produce and discharge perfect red cells into the circulation; they remain densely packed up in the marrow, giving it its red colour. On giving liver a flood of immature cells

still no response, the preparation is probably inactive. These preparations are prescribed in amounts equivalent to the original weight of liver from which they are prepared. Liver extracts are now available that need only be injected once every four to eight weeks to keep the patient in health. The daily administration of the extract from 1 lb. of liver may be required in the early stages, although the amount may be diminished to ¼ lb. or less later on. Periodical blood counts or the Van den Bergh's test are advisable. Within a few days the patients begin to feel better and eventually may develop an unusually florid red complexion, a great contrast to their previous washed-out, yellowish complexion. Sources of sepsis, whether due to teeth, tonsils, nasal sinuses, etc., should also be dealt with. It may be advisable to give a blood transfusion at the beginning of treatment in serious cases, especially if the temperature is high. The "extrinsic factor" is present in wheat germ and alcoholic extract of brewer's yeast, and marmite (**5**), and if there is sufficient of the intrinsic factor present in the stomach, giving these substances will be efficacious; or after the preliminary treatment there may be sufficient of the intrinsic factor to allow marmite to be given alone (**6**).

Other Megalocytic Anæmias. These resemble, and some of them may be considered identical with, pernicious anæmia; the bilirubinæmia is often not marked, and sometimes there is bilirubinæmia and a microcytic anæmia.

The causes are: resection of the stomach for ulcer or carcinoma, faulty intestinal absorption, gastro-colic fistula, resection of the small intestine, intestinal stenosis and tuberculous ulceration, fatty diarrhœa, including cœliac disease, sprue and infection with *Diphyllobothrium latum* (**18**). In many of these cases there is achlorhydria, which may clear up when the patient improves.

Aplastic Anæmia. This disease may result from poisoning with salvarsan and other benzol compounds (**20**), and from excessive exposure to X-rays. Infection of the bone marrow may be secondary (**21**). The red corpuscles and hæmoglobin are reduced to about 20 per cent. of the normal, and the colour index is about unity; nucleated red cells are not frequent; there is leucopenia, due to a diminution in polymorphonuclear cells. The bone marrow differs from that of pernicious anæmia in being remarkably pale and fatty, and in wanting all signs of blood regeneration. Thus there is *aplasia* of the bone marrow, which is regarded as the primary cause of the disease. In some cases (*Aleukia hæmorrhagica*) there is also a great diminution or complete absence of blood platelets, and associated with this there is a severe hæmorrhagic tendency with delay in the bleeding time, but not in the clotting time; a condition identical with a severe type of purpura (*see* p. 445). The treatment with liver is not successful, as the fault occurs at the earliest stage of blood formation (Fig. 53). Repeated blood transfusions, up to 300, have kept one patient alive for seven years up to the present (**34**).

Agranulocytosis (*Neutropenia*). This is an allied condition characterised mainly by a dimimution of leucoid (granular) cells and often accompanied by severe infection of the throat—*agranulocytic angina*—such as Vincent's angina or other infection. It is suggested that the blood condition is primary, and that infection takes place because the neutropenia means diminished resistance. There may or may not be aplastic anæmia as well. The lymphocytes may remain normal or show some reduction; but there may be a monocytosis at first (**10**) Relapses may take place over years, often with infections. It has been stated that the increase of this disease has synchronised with the popularity of amidopyrina (pyramidon) or a combination of this drug with a barbiturate (**11**). The bone marrow shows hypoplasia with absence of granulocytic cells. In granulocytic angina the mortality is over 75 per cent., but when treated with pentose nucleotide, K96, to stimulate polymorph formation it has been reduced to 25 per cent. (**8**), though some cases do not respond (**9**).

The Anhæmopoietic Anæmias of Childhood. These in a general way resemble adult anæmias.

The *megalocytic anæmias* are rare, but they have been found in infection by *Diphyllobothrium latum* and in cœliac disease from absence of the extrinsic factor, so that cure has resulted from giving marmite which contains it.

Of the *microcytic anæmias* attention may first be directed to the anæmia that may result from scurvy and cretinism, that is cured by vitamin C and thyroid respectively. Cœliac disease usually causes anæmia of this type. The commonest anæmias are *nutritional*, and an important factor is that, though there is plenty of iron in the liver and spleen at birth, the store diminishes progressively till the end of lactation, because milk contains but little iron, though breast milk is richer than cow's milk. Anæmia of infancy may be due to deficient *ante-natal* storage of iron from anæmia of the mother, premature birth before iron storage is complete, or twin pregnancy when the demand for iron is nearly double ; or from a deficient *post-natal* supply of iron, due to deficiency of iron in the milk or prolonged milk feeding. Treatment is the same as for simple achlorhydric anæmias ; ferrous sulphate (4 grains) three times a day dissolved in water with glucose and perhaps a little copper ; the latter appears to act by helping to build up the iron which is stored in the liver into hæmoglobin (**15**).

In previous editions of this book Van Jaksch's *anæmia infantum pseudo-leukæmica* (splenic anæmia of infancy) has been described as a separate disease. The blood shows a secondary anæmia with an increase of leucocytes up to 40,000 with a few myelocytes ; the liver and spleen are enlarged. The condition probably represents the infantile response on the part of the marrow to a number of factors that may cause anæmia, especially infection, and one patient developed typical acholuric jaundice (**16**).

HÆMOLYTIC ANÆMIAS

One group of hæmolytic anæmias is familial, consisting of *acholuric family jaundice;* sickle-cell anæmia, met with in negroes with jaundice, glandular enlargements and ulcers on the legs ; the very rare *erythroblastic* anæmia of infants, and *icterus gravis neonatorum* already described. Then there are the various infections of which gas gangrene causes the worst degree of anæmia, chronic suppuration, prolonged fevers, streptococcal disease, including puerperal fever, acute rheumatism, infective endocarditis commonly associated with aortic regurgitation, tuberculosis, syphilis including paroxysmal hæmoglobinuria, malaria ; then there are poisons such as aniline derivatives, lead poisoning and repeated blood transfusion, and finally pregnancy.

Symptoms. Hæmoglobinuria and jaundice follow if blood destruction is rapid ; the colour index depends on the type of bone-marrow response, as already described, and with a vigorous response there is reticulocytosis and nucleated red cells are seen. There is often enlargement of liver and spleen and occasionally of the lymph glands.

ACHOLURIC JAUNDICE

(Chronic Splenomegalic Hæmolytic Jaundice)

In this comparatively rare form of jaundice there is no obstruction of the ducts, for the fæces retain their normal colour, and the urine is, except in aggravated attacks, free from bile pigment ; but it contains urobilin. The blood serum, on the other hand, contains bile pigment, but is free from urobilin or urobilinogen. It gives Van den Bergh's indirect test. The primary cause is a defect in the red cells, which show an increased fragility (*see* p. 423). These cells are destroyed in numbers by the spleen, and the bile pigment in the blood comes from

the hæmoglobin of these cells. The patient becomes anæmic if compensatory blood regeneration is insufficient. Histologically, the spleen pulp contains an enormous number of normal-looking red cells, and in the active hæmolytic stage there is free iron pigment; the sinuses are relatively empty. The disease occurs in two forms, congenital and acquired.

Acholuric Family Jaundice. The jaundice, which occurs in several members of a family, is often noticed immediately after birth, or develops slowly at a later time; it may persist for years, or it clears up and recurs from time to time. The patient is anæmic; the red corpuscles are reduced to 3,000,000 or 3,500,000 and present moderate degrees of poikilocytosis, anisocytosis, polychromasia, and punctate basophilia; while nucleated red cells are present. A reticulocytosis of 5 per cent upwards is characteristic. The red cells have a smaller diameter but are thicker than normal. The hæmoglobin is reduced to 50 or 45 per cent., and the colour index is slightly below unity. The leucocytes are generally fewer than normal, but occasionally there is leucocytosis; the large lymphocytes are sometimes in excess, and a few myelocytes may be present. The spleen is enlarged, and appears to grow harder with the progress of the case. The liver is only slightly enlarged, and has not been known to be cirrhosed; it often enlarges during exacerbations and diminishes afterwards. The patients, as children, are not generally stunted as in splenomegalic cirrhosis (*see* p. 397), nor are the fingers clubbed. Moreover, they may be little troubled by their complaint, and may live for many years. New erythroblastic tissue may be formed outside the bone marrow; in the chest these masses may on X-ray be confused with intrathoracic neoplasm. There is a tendency to gallstones.

Acquired Acholuric Jaundice. In this form of the disease the symptoms come on insidiously in adult life; the anæmia is often pronounced, and the red corpuscles may fall to 2,000,000 or 1,500,000 or less; the colour index is sometimes above unity, as in pernicious anæmia; the jaundice is often very slight; the spleen is enlarged. The fragility of the red corpuscles is normal in a few cases. In both forms of the disease, but particularly in the acquired form, exacerbations of the hæmolysis take place, the blood picture resembling pernicious anæmia.

Treatment. Liver treatment, as for pernicious anæmia, should be tried, especially if the red cells show the same characteristic changes. Removal of the spleen has brought about recovery in both acquired and congenital cases, and this should be carried out if the anæmia is severe. It is noteworthy that if the spleen is removed in healthy animals the normal fragility of the corpuscles is diminished; but in acholuric jaundice the fragility is not diminished after operation.

Lederer's Hæmolytic Anæmia is a rare type of anæmia, more common in young children, in which a hæmolytic anæmia develops with great suddenness. The liver and spleen are enlarged. There is usually a leucocytosis which may reach 40,000 per cubic millimetre. Often gastro-intestinal symptoms are present. Treatment by transfusion usually leads to a rapid recovery.

SPLENIC ANÆMIA

This name is given to a number of conditions in which great enlargement of the spleen is associated with anæmia. Their varied pathology is described on p. 454; but in some cases the condition is undoubtedly syphilitic, and high blood pressure in the portal area is important.

Symptoms. The first event is either a general anæmia or an attack of hæmatemesis, or some complaint of pain in the left side, probably due to attacks of perisplenitis. When first observed the spleen has often reached a great size, and in the course of the illness it may be large enough to extend forwards to the umbilicus and downwards to the iliac crest. The anæmia is considerable, of chlorotic type, the red corpuscles ranging from 2,000,000 to 3,000,000, and the hæmoglobin from 35 to 50 per cent. The colour index is less than 1, but not

usually lower than 0·6. The leucocytes are generally in less number than normal (leucopenia), often only 4,000 or 5,000 per cubic millimetre. Normoblasts and a few megaloblasts may be present.

The disease runs a long course, often three or four years, sometimes ten or twelve years, and the anæmia slowly increases. The hæmatemesis may be repeated, and other hæmorrhages may occur, such as epistaxis or retinal hæmorrhage. The liver is enlarged, and there are digestive troubles; but there is no enlargement of the lymphatic glands, nor, as a rule, pyrexia. In some cases there is marked pigmentation of the skin. It occurs in both sexes, and at all ages from childhood up to late middle age. In some cases after a long time the liver becomes still more enlarged, and definitely cirrhotic. Ascites then follows, though it also sometimes occurs without cirrhosis. The supervention of definite cirrhosis of the liver with ascites is commonly called *Banti's disease.*

In other cases splenic anæmia has been associated with thrombosis of the spleen veins. Chronic perihepatitis and perisplenitis are invariably present in long standing cases.

Diagnosis. The disease may be confounded with aleukæmic leukæmia with pernicious anæmia, and with infective endocarditis. Its characteristic features are the anæmia of chlorotic type, the leucopenia, the large size of the spleen, the absence of leukæmia and of enlargements of the lymphatic glands, the long duration, and the occurrence of hæmorrhages. A confusion with malignant endocarditis is possible, because in this last disease the spleen may be very large, the anæmia may be pronounced, and purpura and hæmorrhages may occur; while hæmic murmurs may be present in splenic anæmia.

A diagnosis of Banti's disease may be too readily made in a case of cirrhosis with usually large spleen; its resemblance to Egyptian splenomegaly (*q.v.*) should be remembered.

Treatment. Iron and arsenic are of little value; and if after a period of observation the diagnosis is established the removal of the spleen is justified. Although it is not free from the danger of hæmorrhage, cases have been completely successful. Röntgen rays may be tried, as in leukæmia. Blood transfusion is a valuable palliative measure.

LEUKÆMIA

(*Leucocythæmia*)

These names are given to those cases of disease in which there is a considerable and persistent increase in the total number of leucocytes in the blood, or in a certain variety of leucocyte (*aleukæmic leukæmia, see* later), associated with changes in the marrow of the bones, in the spleen or the lymphatic glands.

Ætiology. The cause of any form of leukæmia is unknown; it may represent the response of the leucocyte-forming organs to some infection, or it may be merely a sarcoma of the white cells. Occasionally, however, leukæmia follows closely upon some septic condition. The myelocytic variety occurs in men more often than in women, and mostly in middle life, though sometimes in quite young children, but rarely in infants. Lymphatic leukæmia is more common in young people.

Pathology. There is over-production of leucoid cells or of lymphoid cells, giving rise to the two characteristic types of the disease and leading to the flooding of the circulating blood with immature fórms of leucocytes. The bone marrow, the spleen and lymph glands, may all take on the function of actively producing leucocytes, in the various types of the disease. As the latter continues, still greater pressure is brought to bear on the depôts where the white cells are manufactured, and the cells are turned out into the blood in a still more primitive form. In certain cases this increased activity of the normal depôts is accompanied by the formation of fresh leucocyte-forming areas in abnormal situations, which will

partake either of myeloid or of lymphoid character. These infiltrations may form nodules beneath the skin, or in different parts of the body (*nodular leukæmia* or *chloroma*, so called from their green colour. *See* later). There is a close relation to lymphosarcoma (*see* p. 441).

In leukæmia the basal metabolism is increased. Chemical examination shows a great increase of uric acid in the blood, which is believed to result from the destruction of the leucocytes.

MYELOCYTIC LEUKÆMIA

(*Spleno-medullary, Leucoid, Myeloid, or Granular Leukæmia; Myelocythæmia*)

Condition of the Blood. In well-marked examples of leukæmia the blood is pale and thin as it issues from a wound, and as seen after death it forms pale pus-like clots. The white corpuscles are found in number from 200,000 to 900,000 in the cubic millimetre, instead of 8,000 or 9,000; and the red corpuscles may be from 3,000,000 to 2,000,000, or even as low as 1,000,000. Nucleated red cells are numerous. The colour index is less than unity, but tends to rise if there is a megaloblastic reaction in the later stages, and then the red cells show the characters of pernicious anæmia, while, as far as the white cells are concerned, the picture is that of leucoid leukæmia, with a rather low white count.

In the earlier stage of the disease, especially if the disease is chronic, polymorphonuclear cells are most abundant; most of them are much larger than normal, and some are obviously degenerated. Metamyelocytes with horseshoe-shaped nuclei are also present, and some typical granular and eosinophil myelocytes. The eosinophil and mast cells are increased, while the lymphocytes are not so much increased. At a later stage there are few normal leucocytes present, but there are proleucocytes, myelocytes and promyelocytes and mast cells in abundance. Later still myeloblasts predominate. If the disease runs a rapid course (*Myeloblastic leukæmia*), the more primitive cells, *i.e.* myeloblasts, are seen in large numbers from the beginning, to the exclusion of other types of leucocytes, while the blood platelets are diminished.

Morbid Anatomy. The spleen often weighs 5 or 6 lbs., but a weight of 18 lbs. has been recorded. It is uniformly enlarged, and retains its normal shape; on the surface are often patches of thickening of the capsule, and the organ is more or less adherent to the abdominal wall, diaphragm, or adjacent viscera. On section it often has a brownish rather than a red colour, which is uniform, or marked with paler lines due to thickened trabeculæ. It is smooth, hard and dry. Not infrequently there are large wedge-shaped infarcts, either yellow and caseous or red and hæmorrhagic. The change in the spleen itself is one of great increase of the splenic pulp, which is full of the same cells as are found in the blood, and the outlines of the Malpighian bodies are badly defined; in long-standing cases the stroma becomes more fibrous, and the trabeculæ are increased in thickness.

The *liver* is enlarged, and may reach twice or three times its normal size. It is pale and smooth, and may present under the microscope a dense infiltration with leucocytes (myelocytic infiltration), which for the most part surround the portal vessels in their distribution, but are partly in nodular masses. The vessels also are full of leucocytes. The *kidneys* are pale and may present greyish-white deposits, running like striæ between the cortical tubules. There may be stomatitis or pharyngitis, swelling of the *tonsils*, and of the *follicles* at the root of the tongue, and swelling and superficial ulceration of the follicles, of the intestine. The *thymus*, *thyroid*, and *suprarenal glands* may also be diseased, and tumours in the skin have been recorded. Sometimes the *lungs* present hæmorrhagic infarcts. The *marrow* of the bones is either yellow and pus-like, or pink and firm, the fat of the marrow being replaced by a tissue like that of active marrow, in which myelocytes and nucleated red cells are abundant, with eosino-

phils sometimes, and myeloblasts or large lymphocytes. Besides the occasional hæmorrhage into the brain, diffuse sclerotic changes and scattered areas of acute inflammation have been found in the *brain* and *spinal cord*.

Symptoms. *Acute Myeloblastic Leukæmia.* This may be the most acute of all the leukæmias, and in one case the whole course of the disease was just under a week (**22**). The number of myeloblasts in the blood and the anæmia may both increase rapidly. There are numerous hæmorrhages as in the chronic myelocytic forms.

Chronic Myelocytic Leukæmia. One of the first indications of leukæmia, in a great number of cases, is the swelling of the abdomen from the *enlargement of the spleen*, which may have been developing for some time without giving any sign. It may then be found occupying the whole of the left side of the abdomen, forming a firm hard tumour, which extends backwards into the flank, while its anterior margin begins about the ninth costal cartilage, reaches the middle line at the umbilicus level, and not infrequently below this extends 2 or 3 inches to the right. This position is determined by its attachment to its vessels, which compel it to enlarge along the circumference of a circle of which the cœliac axis is a centre. The anterior margin is more or less sharp, and presents one or two notches. In earlier stages the spleen only occupies the left hypochondriac region, like the enlargements in malaria, and in some cases of typhoid fever. The *liver* is moderately enlarged, and can be felt for 1 or 2 inches below the right costal margin. The implication of the *bone marrow* is sometimes shown by tenderness on pressure or percussion of the corresponding bone. There may be some delay in the onset of the anæmia with its associated pallor of the skin and mucous membranes.

The altered condition of the blood shows itself in the occurrence of *dyspnœa* and of *hæmorrhages*, which last chiefly take the form of epistaxis, bleeding from the gums and mouth, and purpuric spots under the skin, but also occasionally bleeding from the lungs, stomach and intestines, kidneys, or uterus, or hæmorrhage into the brain. Hæmorrhages also occur in the retina, where they may be seen with the ophthalmoscope associated with white streaks and spots, said to consist of masses of leucocytes; and the retinal veins are often remarkably tortuous (*leukæmic retinitis*).

The course of the disease is generally progressive until its termination in death, and it lasts from six months to five years. Towards the end the pallor increases, the feet and other parts of the body become œdematous, ascites and hydrothorax may be added, the pulse is quickened, and palpitation is frequent. Diarrhœa is occasionally a prominent symptom. There is often some fever. Finally, death takes place from loss of blood, asthenia, diarrhœa, pleurisy, pneumonia, bronchitis or cardiac dilatation, and occasionally from cerebral hæmorrhage.

Diagnosis. The diagnosis depends upon the recognition of an enlarged spleen (*see* p. 453) and the examination of the blood; the last is absolutely essential. Even when the patient has a good colour there may be pronounced leukæmia.

The **Prognosis** is ultimately unfavourable, but life may be prolonged with efficient treatment. Myeloblastic leukæmia is fatal at an earlier stage.

Treatment. Arsenic is the drug which seems to have given most promise; it must be used perseveringly and in increasing doses as long as it can be borne; and under its use the spleen has diminished in size considerably, and the leucocytes in number. Under treatment by benzol remarkable diminution in the number of the leucocytes and in the size of the spleen has been observed. The daily dose is 30, 60 or 90 minims taken in capsules, with an equal amount of olive oil. This treatment was introduced by Selling, who found that benzol workers often suffered from grave leucopenia. Deep X-ray therapy, applied to the splenic region and to the epiphyses of the long bones (femur) has a decided influence both in reducing the number of the leucocytes and the size of the spleen, which may both become normal. The applications should be stopped when the number of leucocytes has fallen to between 30,000 and 40,000, as their action continues for

some time afterwards. It is also important to see that the leucocytes retain their phagocytic power (**35**).

Splenectomy has been uniformly fatal from collapse or hæmorrhage.

LYMPHATIC LEUKÆMIA

(*Lymphocytic, Lymphoid, or Non-granular leukæmia ; Lymphocythæmia*)

This is of rarer occurrence than the myelocytic form.

Condition of the Blood. In chronic lymphocytic leukæmia the lymphocytes are increased, while the number of polymorphs and other cells remain about the same. Thus, there may be a total leucocyte count of 100,000, of these 95 per cent., or in all 95,000, may be lymphocytes, and the remaining 5,000 are polymorphs, with a few *eosinophils* and mast cells. In acute lymphatic leukæmia running a rapid course the larger immature type of cell predominates, but it is difficult, if not impossible, to distinguish these from myeloblasts in myeloblastic leukæmia. On the other hand, the total number of leucocytes per cubic millimetre may not be much, if at all, above the normal ; but if the total count of lymphocytes per cubic millimetre is increased, while the polymorphs are unaltered or diminished, the condition of lymphatic leukæmia must be recognised. Such cases are often called *aleukæmic leukæmia ;* this is indistinguishable from and probably identical with lymphosarcoma, since the histological picture of the lymph glands and of the blood is the same ; in fact, cases beginning as lymphosarcoma have terminated as lymphatic leukæmia. Usually there is a secondary anæmia with a few nucleated red cells. As in myelocytic leukæmia, there may be a megaloblastic reaction so that the picture of the red cells resembles pernicious anæmia.

Symptoms. *Acute lymphatic leukæmia.* This occurs in both sexes, and at all ages between seven and fifty-eight. The illness is fatal in from two weeks to three or four months. It begins insidiously with general weakness and malaise or pains in the spleen or joints. The external glands may enlarge, but are not always very prominent ; there is slight enlargement of the spleen and liver, and the bones may be tender. The marrow is packed with lymphocytes from the first and this leads to an early marked anæmia. A striking feature in many cases has been severe stomatitis with sloughing and gangrene of the gums ; and with this there are fever, and hæmorrhages from the gums and bowels and under the skin. Many of the solid glands in the body are densely packed with lymphocytes, and hence considerably enlarged, for instance the liver, spleen, kidneys, suprarenals, pancreas, salivary glands, and lachrymal glands, while the thymus persists and is greatly enlarged, and the cardiac muscle may be also infiltrated with lymphocytes. Exophthalmos has been also observed from leukæmic infiltration of the orbital fat. Dropsy occurs commonly before the end.

As contrasted with myelocytic leukæmia the spleen in lymphocytic leukæmia is rarely quite so large, and the lymphatic glands and organs all over the body, racemose as well as ductless, are often extensively involved.

Chronic Lymphocytic Leukæmia. This disease, which may last from about six months or a year up to twelve or even eighteen years, begins in the lymphatic glands, and involves one group after another, until all the lymphatic glands over the body may be affected, and they are felt in the neck, groins or axillæ. They are moderately large, not very hard, and move freely upon one another. The mesenteric glands are even more often enlarged than the above ; the retroperitoneal, thoracic, portal, and iliac glands less so. On section the glands are whitish pink in colour, and microscopically are found to be distended with the lymphocytes. Later on, the bone marrow becomes involved, and is packed with lymphocytes, and this causes the onset of an aplastic anæmia. There is less tendency to hæmorrhage than in myelocytic leukæmia ; but patients may die

from the pressure effects of the glands on vital organs, or from their infiltration with lymphocytes or from venous thrombosis. In these chronic cases the spleen and liver may be very greatly enlarged.

Diagnosis. In any obscure illness with pallor, or enlarged glands, tonsils or spleen, or hæmorrhages, or purpura, or sloughing gums, the blood should be examined and the lymphocytes carefully estimated. The **Prognosis** is bad in the acute cases, in which there is little time for **Treatment** either by arsenic or by deep X-ray therapy. In less rapid cases these remedies should be tried.

Chloroma.—Presenting close relations with lymphatic leukæmia is the condition which has been called chloroma. In this there are numerous tumours or lymphoid deposits, especially in the orbits (so that exophthalmos may take place), in the temporal fossæ and in the periosteum of the bones of the skull. Tumours may also grow on the conjunctiva and under the skin, in various organs such as the kidneys, and sometimes even during life these tumours may have a green colour (*green cancer*), as seen through the skin; others are colourless (**36**). Cases of myeloid chloroma are rarer.

After death the various tumours are seen to have a green colour, which fades away on exposure; and the lymphatic glands, spleen, bone marrow, and other organs are in a condition similar to that accompanying lymphatic leukæmia. The nature of the green colour is not known; it is not bile pigment, but it is presumably the same as the green colour often noticed in pus.

POLYCYTHÆMIA RUBRA

Polycythæmia, or polycythæmia rubra, in which the red cells of the blood are increased, occurs (1) as a primary disease of the red cell-forming organs (*erythræmia*); (2) it also results from some disturbance in the circulatory or respiratory systems, causing oxygen want and requiring for compensation a larger number of carriers of hæmoglobin, such as in congenital heart disease. This secondary polycythæmia is called *erythrocytosis*.

Cases of polycythæmia rubra have an increased basal metabolism.

ERYTHRÆMIA

This occurs mostly in patients of between thirty and sixty years of age, though occasionally they are above or below these limits. In its pronounced form the red corpuscles vary in number from 9 and 10 to 13 and even 14 millions per cubic millimetre, and on standing the corpuscles may be found to occupy nine-tenths of the volume of the fluid. The hæmoglobin is raised to 130, 160 or 180 per cent. of the normal. The colour index is low, which shows that the red cells are small. The leucocytes are not always increased in number, but they may reach 24,000 per cubic millimetre, the chief increase being in the polymorphs. The viscosity of the blood is increased to three or four times the normal. The specific gravity and the coagulation time are not constantly either below or in excess of the normal. The blood pressure is sometimes, but not always, high.

Morbid Anatomy. The enlarged spleen is engorged, with hyperplasia of the splenic pulp and fibrosis, but generally without evidence of erythroblastic or myeloid activity. The lymph glands are generally unaffected: the liver may be engorged. The bone marrow is generally deep red in colour, and no fatty marrow is seen, so that there appears to be a great increase in the function of red corpuscle formation.

Pathology. In accordance with this, the generally accepted view of the pathology of the condition is that, from some cause or other, the bone marrow is stimulated to an excessive formation of erythrocytes, and that the other changes are secondary. There is no evidence that the polycythæmia is secondary to oxygen want in the tissues. Patients who are kept in an oxygen chamber show no alteration in the blood at the end of that time.

Symptoms. The conditions usually associated with this polycythæmia are *cyanosis* and a moderate or considerable enlargement of the spleen. The cyanosis is shown chiefly on the face, ears and mucous membranes (*see* Plate 36, A, p. 433). The face has a characteristic florid appearance; there may be jaundice and occasionally cirrhosis, the serum giving an indirect Van den Bergh reaction (**38**). The veins of the retina are engorged and very dark. The patients suffer from headache or a sense of fulness in the head, lassitude, vertigo, dyspepsia, constipation, thirst, and various forms of hæmorrhage, which include epistaxis, bleeding from the gums, menorrhagia, hæmatemesis and cerebral hæmorrhage. The arteries are sclerotic, leading to thrombo-angiitis obliterans, with intermittent claudication and erythromelalgia, or psychoses; the kidneys may be affected. There may be gout and renal calculi of uric acid (**38**). In some cases extensive venous thrombosis has occurred.

Differing somewhat from the above cases, which were first described as *polycythæmia with splenomegaly*, are some cases, less frequently occurring, in which the spleen is not enlarged, but the blood pressure is greatly increased, and may even reach 300 mm. Hg. The patients are often turgid in the face and may have hypertrophy of the heart, albumin in the urine, and signs of arterio-sclerosis. They were first described by Geisböck, who called them *polycythæmia hypertonica.*

The progress of cases of erythræmia is variable; death occurs from heart failure, or from cerebral vascular complications, or from tuberculosis.

Treatment. Periodic venesection is a good treatment for this disease. From ½ to 1 pint of blood should be removed every six months through a wide hollow needle. Citrate may be used to prevent clotting, as in the withdrawal of blood for transfusion purposes. Success has also been obtained by treating the long bones by X-rays. Recently phenyl hydrazine 0·1 grm. per diem by mouth has been used.

ERYTHROCYTOSIS

Under this term it is proposed to include the cases in which the polycythæmia is again due to increased activity of the bone marrow (Parkes Weber), but this activity is stimulated by recognisable antecedent conditions. Thus one class is constituted by chronic cardiac and pulmonary lesions, of which congenital malformation of the heart is the most striking; and others are the various forms of acquired valvular disease, emphysema and chronic pulmonary diseases, which may be accompanied by cyanosis (Ayerza's disease, *q.v.*). In these the deficient oxygenation of the blood is the stimulus to the bone marrow. Patients who have been "gassed" form another group. Here the erythrocytosis has been lessened by treatment in an oxygen chamber containing 40 per cent. oxygen (Hunt and Dufton). Another group is formed by the polycythæmia of persons resident at high altitudes, where the increase of erythrocytes compensates for deficient oxygen tension in the air available for respiration. Polycythæmia also occurs in chronic poisoning by phosphorus and carbon monoxide and in Addison's disease and diabetic coma. As in erythræmia, the red corpuscles may reach seven, eight, or nine millions; the hæmoglobin and the viscosity of the blood are raised in amount.

HÆMOGLOBINÆMIA

Hæmoglobinæmia arises when blood corpuscles are broken up in the blood vessels, so that hæmoglobin escapes into the plasma, giving it a pink tinge, and the blood corpuscles have little tendency to form rouleaux. There is commonly anæmia with some poikilocytosis and anisocytosis; very pale corpuscles (*shadow corpuscles*) are seen. The hæmoglobin is excreted by the kidneys, so that the urine is coloured deep red and is *clear;* this condition is called *hæmoglobinuria*, and is distinguished from *hæmaturia*, in which blood itself with its corpuscles

is mixed with the urine, which is *smoky*, because light is reflected from the surfaces of the corpuscles. When examined by the spectroscope, the urine in hæmoglobinuria gives the two bands in the green and yellow characteristic of oxyhæmoglobin, and another band nearer the red end of the spectrum, which is due to methæmoglobin ; the latter is produced by the action of the urine on the oxyhæmoglobin. The urine contains albumin. In slighter attacks probably only a small number of corpuscles are disintegrated, the hæmatin is disposed of in the liver, while the globulin alone is excreted in the urine ; the protein found in the urine in such conditions is globulin and not serum albumin.

A partial destruction (*hæmolysis*) of the corpuscles takes place in several circumstances : (1) The action of certain poisons, such as chlorate of potassium in large doses, pyrogallic acid, arseniuretted hydrogen, and naphthol. (2) The transfusion of incompatible blood. (3) Exposure to extremes of temperature, such as burns or frost bite. (4) The action of some fevers, so that a moderate degree of hæmoglobinæmia may result from scarlet fever or typhoid fever. (5) In malaria or blackwater fever. (6) Paroxysmal hæmoglobinuria. (7) Very slight hæmolysis may be present in the blood of normal individuals.

PAROXYSMAL HÆMOGLOBINURIA

In this comparatively rare complaint hæmoglobinuria occurs in isolated attacks.

Ætiology. It is seen in young adults and middle-aged people up to fifty years of age, and is much more common in males than in females. In a few cases there is a history of malarial poisoning, and in very many a history of syphilis. The immediate cause of an attack is exposure to cold.

Pathology. The occurrence of the hæmolysis as a result of cold is explained as follows : there is a potential toxic *hæmolysin* in the blood of sufferers from this complaint, which as an amboceptor reacts with the corpuscle. The action of cold and subsequent co-operation of the complement with the return of warmth brings about destruction of the corpuscles. The complement exists in normal blood, and it has been shown that the patient's serum will hæmolyse normal corpuscles, hence proving that there need be no specific liability of the patient's corpuscles to break down. The toxic origin of the hæmolysin is suggested by the fact that in the majority of patients there is a history or evidence of syphilis, and a positive Wassermann reaction.

Symptoms. The beginning of the attack is marked in different cases by languor and weariness, a disposition to yawn, chill or rigor, pains in the limbs, nausea, vomiting, diarrhœa, and abdominal pain. The patients often suffer from Raynaud's disease (*see* p. 310), and in this case the fingers may become livid and cold.

The temperature may rise at the commencement, but soon subsides ; and the duration of the symptoms is only from two to twelve hours. A slight enlargement of the liver and of the spleen is sometimes also observed. Either immediately after the first symptom, or after three or four hours, the blood-coloured urine is passed ; but this condition is only of short duration : in a few hours more the urine may be perfectly clear, and free from albumin and hæmoglobin ; and in the intervals between the attacks it is always perfectly normal. Towards the end of an attack an icteric tinge of the skin is observed ; and after many attacks in quick succession the patient develops a microcytic anæmia. Paroxysmal hæmoglobinuria is not in itself dangerous.

Treatment. Exposure to cold must be carefully and systematically avoided by the use of warm clothing, residence in warm rooms, and protection from night air as far as possible. The syphilis should be treated chiefly with potassium iodide, mercury or bismuth. During the attack the patient should be kept in bed.

METHÆMOGLOBINÆMIA AND SULPHÆMOGLOBINÆMIA

(*Enterogenous Cyanosis, Microbic Cyanosis*)

A general lividity or cyanosis of the skin and mucous membranes is caused in rare cases by the conversion of the oxyhæmoglobin of the corpuscles into methæmoglobin and sulphæmoglobin.

Methæmoglobinæmia. This has happened from the use of certain drugs, especially acetanilide, phenacetin, antipyrin, veronal, and from the inhalation of poisonous fumes in workers dealing with coal-tar products, nitrobenzol, etc., and also from the absorption of nitrites in some intestinal lesions when diarrhœa is a prominent symptom, and when the production of nitrites may be due to organisms, as, *e.g.* the *Bacillus coli.* In some cases polycythæmia has been present, and sometimes enlargement of the spleen and clubbing of the fingers and toes. The patients have a ghastly chocolate colour. The blood shows no hæmolysis, but the corpuscles are very dark. There is usually no respiratory distress, because a marked colour is produced with a relatively small amount of hæmoglobin converted. The urine is generally normal. The **Treatment** is to remove the cause. Emetics and lavage may be required in poisoning by drugs. Since death is caused by deficient oxygen-carrying power of the blood, continuous oxygen administration, preferably with a tent, should be employed. After some hours the blood becomes normal spontaneously.

Sulphæmoglobinæmia. These patients, who are constipated, suffer from attacks of cyanosis, sometimes leading on to unconsciousness. Other symptoms in the attacks are headache, nausea and vomiting, and abdominal pain. The hæmoglobin in the corpuscles is partly converted into sulphæmoglobin. This substance resembles methæmoglobin in its absorption spectrum, a band being seen in the red. However, in the case of methæmoglobin this band disappears on adding a drop of 1 per cent. potassium cyanide, whereas in the case of sulphæmoglobin it remains unaltered. Another test is to pass acid-free CO through the mixture. All the bands of sulphæmoglobin are shifted towards the blue end of the spectrum. The bands of methæmoglobin are unaltered.

Like methæmoglobinæmia, the condition is due to poisoning with aniline derivatives, *e.g.* acetanilide and phenacetine, possibly associated with the formation of sulphur compounds in the gut due to constipation; but it may be a true enterogenous cyanosis, due entirely to poisons manufactured spontaneously in the gut, though this has been denied. It disappears much more slowly than methæmoglobinæmia, taking weeks or months. On this account if cyanosis follows medicinal doses of coal-tar drugs, it is almost certain to be sulphæmoglobin rather than methæmoglobin that is the cause. The simultaneous presence of both sulph- and methæmoglobinæmia in one patient has been described (**23**).

Prognosis. The disease is not fatal.

Treatment. Purges should be given for the constipation. Carious teeth should be removed. Oxygen should be administered continuously during the attack, especially if the patient is unconscious.

PURPURA

(*Hæmorrhagic Diathesis*)

This term is applied to a diseased condition in which a number of hæmorrhages occur under the skin or mucous membranes, so as to produce blotches of a less purple colour. It has been already seen that there are similar hæmorrhages in a number of diseases, for instance in scarlatina, measles, variola, typhus, cerebro-spinal fever, and plague; in cirrhosis, acute yellow atrophy of the liver, and leukæmia, aplastic anæmia, and malignant sarcomatous growths (*sarcoma-*

tosis) ; in malignant endocarditis, and other diseases of the heart ; and in some nervous diseases, *e.g.* tabes dorsalis. Hæmorrhages will be again mentioned in connection with hæmophilia, Hodgkin's disease, Bright's disease, and scurvy. As a direct result of poisoning from without, purpura arises from overdosing with potassium iodide, and from the commercial use (handling and inhalation) of benzol or its chief constituent, benzene. In all these cases it is clearly recognised that a cause for the hæmorrhage exists, and this cause is often an infective toxin or other poison.

Primary or idiopathic *purpura* has been divided clinically into different varieties : (*a*) *P. simplex, hæmorrhagica, fulminans ;* (*b*) *Henoch's purpura and Purpura rheumatica* (*Peliosis rheumatica* or *Schönlein's disease*), in which there is urticaria as well as purpura, and often the urticaria is more pronounced than the purpura (**39**) ; the term *anaphylactoid* purpura is sometimes used for this group.

Pathology. In severe cases of purpura a hæmolytic streptococcus can usually be isolated from the blood during the febrile period, and in fatal cases it can be cultivated from the heart's blood. The endothelium of the aorta is often stained with hæmoglobin pigment. These facts point to this organism as the cause of the disease ; its toxin may act by increasing the permeability of the capillaries so as to allow escape of plasma and diapedesis of red corpuscles into the tissues. Some purpuras result from *allergic* shock.

The blood shows the characters of a secondary anæmia if hæmorrhage is severe. The coagulation time of the first drop of blood taken from a prick is normal, but the coagulation time of subsequent drops is increased, being over a minute (**2**). It is possibly on account of this that the " bleeding time " (*see* p. 423) is increased. After the blood has clotted outside the body the clot does not retract and allow serum to ooze out (**26, 29**). The bone marrow does not show any characteristic changes ; if the demands on it are excessive and the nutrition is impaired by anæmia, it may become aplastic.

In the majority of purpuras of all kinds the blood platelets are absent or greatly diminished (*i.e.* under 100,000 per cubic millimetre (normal 200,000 to 500,000))—a condition known as *thrombocytopenia.* This might at first sight be considered enough to account for the purpura. However, thrombocytopenia by itself is not sufficient, for in scurvy, where there are bleedings, and in Henoch's purpura, the platelets and bleeding times are both normal. The explanation probably is that the endothelial damage is the essential factor in all purpuras, and this may take place without diminution of platelets, but that since platelets and endothelial cells are closely related genetically the poison—whether it be anti-platelet serum, benzol, etc.—usually destroys the platelets before attacking the endothelium (**22**). If only enough anti-platelet serum to destroy the platelets is injected, no purpura follows, so that the thrombocytopenia cannot be the essential feature of the disease. Another suggestion, which, however, is not supported by experimental evidence, is that the platelets disappear because by agglutination they fill up the gaps in the bleeding vessels. Platelets are formed by the marrow and they are absent when the marrow is aplastic ; they are destroyed by the spleen, and its removal increases the number for a time, but only for a time.

Symptoms. In its mildest forms (*P. simplex*) purpura consists in the appearance of spots of a dull red, deep red, or bluish-purple colour in different parts of the body. They are circular, vary in diameter from a millimetre to ⅛ inch, do not disappear on pressure, and are generally, when of this small size, not raised above the surface. They are scattered indiscriminately over the body. Each spot fades after a time, becoming brown or yellow in tint, and the larger patches go obviously through the changes characteristic of a bruise. Very little constitutional disturbance accompanies the eruption ; the patient may be pale, and loses appetite. Recovery generally takes place in from ten to twenty days.

In severe cases the hæmorrhages are more extensive, the skin may be raised by

large masses of blood beneath it, and bleeding takes place from the various mucous membranes (*P. hæmorrhagica*). The nose, mouth, stomach, and intestines, the kidneys, the female genital organs, and occasionally the bronchial mucous membrane may thus be the source of the blood. The gums are never swollen as in scurvy, but sometimes a spot of hæmorrhage is seen in their substance. In the severer cases there may be some rise of temperature, and a stage of prostration ensues which terminates in death. Post-mortem examination may reveal other ecchymoses in nearly all the mucous membranes, in the pelvis of the kidney, in the pleura, pericardium, peritoneum, in the meninges, and even in the lungs and the medulla of the bones. A cerebral hæmorrhage may be the cause of death. Sloughing and ulceration of the intestinal mucous membrane have also been found, leading to perforation and peritonitis. *Purpura fulminans* is the name given to some cases which are fatal in from five hours to three days. Many of these cases have occurred after scarlatina.

In *Henoch's purpura* the lesion of the skin, which may be erythematous or urticarial swellings, often of large extent, associated with but little hæmorrhage, is accompanied by joint pains and swellings, attacks of abdominal pain, vomiting and hæmorrhage from the bowel and hæmaturia. The spleen may just be palpable. It occurs in children, and recurs frequently during weeks or months. The sequence of symptoms in these cases varies a good deal, and the purpuric eruption is often late in its appearance, and not always very extensive; this fact may explain why there is no anæmia or thrombocytopenia. On the other hand, the early occurrence of the joint pains may give rise to a diagnosis of acute rheumatism, and in many instances the abdominal symptoms are the most prominent. Thus abdominal pain, vomiting, and distension sometimes suggest intestinal obstruction or appendicitis; or the same symptoms with hæmorrhage from the bowel and a palpable tumour occurring in a child lead to a diagnosis of intussusception. Laparotomy has been performed when the abdominal symptoms are present alone and the supposed intussusception has proved to be a portion of bowel infiltrated with effused blood. The urine may contain much albumin, with or without blood or casts, or pure blood. Many cases are fatal; others recover, but in them the albuminuria may persist for months. In *Purpura rheumatica*, which is probably a milder form of Henoch's purpura, the acute arthritis is prominent, associated with purpuric erythema and urticaria, and there may be endocarditis and pericarditis.

Diagnosis. In making the diagnosis, all the possible causes of a petechial eruption mentioned in the first paragraph must be excluded. *Scurvy* is distinguished by the spongy condition of the gums, the subcutaneous or fascial hæmorrhages. *Malignant sarcomatous* growths may present some resemblance to *P. hæmorrhagica*. It is well also to remember that the children of the poor sometimes present extensive petechial eruption as the result of *flea bites*, about the size of a pin's head. The sphygmomanometer provides a valuable test for the hæmorrhagic diathesis; a pressure just enough to obliterate the pulse is exerted on the arm for two minutes; if positive, purpura, often extensive, will appear on the forearm.

Treatment. Septic foci should be eradicated. In milder cases, rest in bed, tonic medicines, and good simple food will often rapidly effect a cure. When the purpura affects the lower extremities chiefly, it often disappears directly the patient takes to bed, and returns if walking about is too hastily resumed. Iron, arsenic, and quinine may be given in the usual doses. Intramuscular injections of calcium chloride (1 grain in 100 minims of water) or 3 c.c. calcium gluconate once a day may be of value; also an injection of 10 c.c. serum, preferably human, may be given, and this may be repeated. Liver treatment in thrombocytopenia, as given for pernicious anæmia, has been advocated (**40**).

In severe cases blood transfusion may be of value, and the spleen has been removed with beneficial results on the supposition that it is destroying the blood

platelets (**27**). It has recently been claimed that all cases do well with injections of ascorbic acid (*see* Scurvy), and if further experience bears this out it will be necessary to revise the views held as to the cause of purpura.

HÆMOPHILIA

Hæmophilia is a disease almost entirely restricted to the male sex, and characterised by a tendency to bleeding, either spontaneous or traumatic. It is hereditary. The disease is transmitted through the female, who is herself entirely free from it, and it only affects the male who is known as a " bleeder " ; in this it resembles pseudo-hypertrophic muscular paralysis.

Pathology. There is delayed coagulation time of the blood, which may be increased to forty minutes or more. Consequently there is nothing to stop any small hæmorrhage that may occur accidentally. There is a very slow formation of pro-thrombin, although the platelets which form pro-thrombin are present in normal numbers and their agglutination is also normal. Thrombokinase, the other precursor of fibrin ferment, is also present in sufficient quantity (**2**), but the conversion of pro-thrombin into fibrin ferment is also very slow. If a state of anaphylaxis is induced the coagulation time is much shortened, and this has been made use of in treatment. The fatty degeneration of the heart and of the arteries found in some cases is probably the result of secondary anæmia. Certain other conditions must be distinguished from hæmophilia—an acquired form connected with syphilis, shortage of fibrinogen, hæmophilia calcipriva with a low blood calcium and essential thrombocytopenia (**42**). These conditions may account for the female " bleeders " which are occasionally met with (**24**).

Symptoms. These generally appear within the first year of life, though they are sometimes delayed till the seventh or eighth year. In the most severe degree, spontaneous hæmorrhages occur from the nose, the gums, and the mouth, and less commonly from the stomach, the lungs, or the genitalia ; they are sometimes preceded by a feeling of fulness. Alarming and even fatal hæmorrhages may occur after the most trivial operation, such as vaccination, the extraction of a tooth, incision of an abscess, or after a cut finger. Besides these losses, hæmorrhage takes place readily under the skin from slight blows, producing bruises or blood tumours. Hæmorrhage also takes place into the synovial cavity of the joints, especially the knee joint ; this occurs most commonly between the ages of seven and fourteen, and results from blows, or from exposure to cold or to damp. The swelling and pain closely resemble those of rheumatism or synovitis, for which, indeed, the symptom has been mistaken. This condition of the joint is accompanied by fever ; it may recover, but returns again and again. Eventually the joint may become ankylosed or fixed by periarticular adhesions. A rheumatic affection of the muscles and the occurrence of trigeminal neuralgia are described as occasional complications of hæmophilia.

In the intervals between the bleedings the subjects of hæmophilia may appear to be in perfectly good health, but the loss of blood may cause anæmia. They may die from loss of blood before they are eight years of age ; and though the chances of survival are greater after this period, even in middle age death may occur in the same way.

Diagnosis. This depends on finding an increased coagulation time of the blood.

Treatment. For a surface hæmorrhage the best treatment is to apply to the bleeding spot, cotton wool soaked in some fresh human blood after useless clots have been wiped away ; but fresh animal tissue may also be used. The most certain method is to ~~give an injection of~~ snake venom, ~~but~~ a transfusion of citrated blood lowers the coagulation time for a period of five to seven days. It has, in fact, been stated that every hæmophilic should be tested against five or six possible donors, so that one of them at least would always be available in a

sudden emergency. It is not necessary to use much blood. Alternately citrated human plasma should be transfused: in this case blood grouping is not necessary. In case an operation becomes necessary a preliminary transfusion should be carried out, and this preparation is advisable before even the smallest operation, *e.g.* the extraction of a tooth. An injection of 10 c.c. horse serum ten days previously to produce anaphylaxis is much less certain (**41**). Some shortening of the coagulation time may be brought about by giving a diet of liver as for pernicious anæmia (**42**). When the albumin globulin ratio of the plasma is low (normal 4 to 1) injections of ascorbic acid (*see* Scurvy), 200 mg. for an adult, 100 mg. for a child, have been successful (**43**).

For the stiff joints hot-air baths and gentle massage may be employed: breaking down the adhesions under an anæsthetic is generally avoided, from fear of starting a fresh hæmorrhage, but it has been done without this accident following. Considering the serious nature of this disease and the manner in which transmission takes place through the female sex, it is clear that women who belong to bleeder families, even though themselves not the subjects of hæmophilia, should not marry.

BLOOD TRANSFUSION

By this term is meant the taking of blood from a healthy person ("the donor") and injecting it into the circulation of a patient ("the recipient") for therapeutic reasons. The indications for this treatment in medicine are—(1) simple hæmorrhage, *e.g.* in gastric and duodenal ulcer, dysentery, typhoid, ectopic gestation, melæna neonatorum; (2) diseases of the blood, *e.g.* severe purpura, hæmophilia, anæmia, leukæmia; (3) severe infections, *e.g.* infective endocarditis; (4) possibly certain intoxications, such as threatening uræmia.

Methods which necessitate cutting down on the artery or vein of the donor are undesirable, owing to the slight, but definite, risk to the donor from sepsis. The donor runs no risk if the blood is taken through a wide, hollow needle plunged directly into the median basilic vein; the point of the needle should be sharpened on an Arkansas stone and examined with a lens or low power of the microscope. In the "citrate method" the blood is run from the needle through a short piece of rubber tubing into a sterile measuring vessel containing 160 c.c. 3·8 per cent. sodium citrate solution (made with freshly distilled water) to 700 c.c. of the blood. The rate of flow is increased by means of pressure round the arm above. The blood must be kept warm all the time. A sterile cylindrical funnel, containing a little saline, and fitted with a rubber tube and clip and needle, is used for the infusion. A short piece of glass tube is inserted close to the needle to act as a window, and to make sure that the needle is in position the funnel is momentarily lowered until blood enters the glass tube; it is then raised and filled with the citrated blood. A sterile bottle may also be used so that the blood can be removed from the donor by suction and administered under slight pressure to the patient. If the donor becomes faint or pale or sweats, or if the pulse falls below sixty, the withdrawal of blood must be stopped. Favourable results have been obtained, especially in infections, by the use of defibrinated blood, which appears to retain its antitoxic or antibacterial properties to a greater extent than citrated blood. Instead of adding citrate the blood is agitated as it flows into the bottle and the fibrin becomes deposited on a bent glass tube which passes down from the stopper to the bottom of the bottle, and up again. Before injecting the blood it must be filtered through sterile gauze to remove small tags of fibrin. In "immuno-transfusion" the donor is immunised beforehand, or the blood is immunised *in vitro*.

Certain precautions must be taken. The Wassermann reaction of the donor should be investigated, and the "compatibility" of the bloods of donor and recipient must be determined.

Compatibility. It is sufficient if the donor's cells are not agglutinated by the recipient's serum. The reverse condition need not hold, because the donor's serum rapidly becomes diluted in the circulation of the recipient. To test compatibility a drop of blood from the donor's finger is allowed to fall into 1 c.c. of 1·5 per cent. sodium citrate solution, and one drop of the resulting suspension is mixed on a microscope slide with one drop of the recipient's serum and covered with a cover slip. After the lapse of a few minutes the slide is examined macroscopically for agglutination. Individuals are arranged in four groups, thus :—

		Serum			
		Gr. I.	Gr. II.	Gr. III.	Gr. IV.
Cells	Gr. I.	—	+	+	+
	Gr. II.	—	—	+	+
	Gr. III.	—	+	—	+
	Gr. IV.	—	—	—	—

It will thus be seen that, if the sera of groups II. and III. are kept in stock, the cells of any given individual can be assigned to their group. The cells of group IV. are agglutinated by no one, and, therefore, the members of group IV. can always act as donors, but it is generally safer to have both donor and recipient of the same group. It has been pointed out that a time control test is advisable ; the recipient's serum is mixed with cells from a blood of known incompatibility, and the time taken for agglutination is noted ; this has been as long as half an hour and the test with the donor's cells must be watched for the same length of time ; by this means the death-rate, 1–2 per 1,000 transfusions with apparently compatible blood may be lowered (**44**).

REACTION OF THE BLOOD AND ACIDOSIS

The reaction of any solution depends on its concentration of hydrogen ions (C_H) and hydroxyl ions (C_{OH}). When the reaction is neutral, the concentration of hydrogen and hydroxyl ions is equal ; when it is acid, the C_H is increased and the C_{OH} is diminished ; when it is alkaline, the C_H is diminished and the C_{OH} increased. The product of the two is always constant. At the neutral point and at body temperature the C_H, expressed in grams of hydrogen per litre, is $1{\cdot}83 \times 10^{-7}$, which is the same as $10^{-6{\cdot}74}$. The C_H of the arterial blood is about $10^{-7{\cdot}40}$, which, being smaller than $10^{-6{\cdot}74}$, is slightly on the alkaline side of neutrality. The method usually adopted of expressing these facts is to say that at the neutral point p_H (the logarithm of C_H) is 6·74, leaving out the minus sign for the sake of simplicity.

The C_H of blood is given by the equation

$$C_H = \text{constant} \times \frac{CO_2 \text{ pressure}}{\text{bicarbonate concentration}},$$

the CO_2 pressure being proportional to the CO_2 dissolved in the blood. In normal people the CO_2 pressure of the arterial blood is just below the CO_2 pressure in the alveoli of the lungs. The variations in this equation can best be seen from the following table : (**45**)—

TABLE I.—*Types of Disturbance of Acid-base Balance*

(1) *Affecting* CO_2	(2) *Affecting Bicarbonate Concentration*
(*a*) *Increase.* Increased formation — violent exercise. Impaired elimination. Depression of respiratory centre by narcotics, and sleep. Interference with respiration (disease of heart or lungs). Breathing CO_2.	(*a*) *Decrease.* Excessive ingestion of acids, or potential acids (NH_4Cl or $CaCl_2$). Excessive formation of acids—lactic acid in exercise. Failure of oxidation of acids—especially aceto-acetic acid. Failure of excretion of acids in nephritis. Loss of base.
(*b*) *Decrease.* Overbreathing—voluntary, in hysteria, emotional tetany, as a result of peripheral stimuli, in fevers, at high altitudes, in pure cardiac dyspnœa.	(*b*) *Increase.* Excessive ingestion of bases ($NaHCO_3$) or potential bases (*e.g.* sodium citrate). Loss of acid, *e.g.* gastro-colic fistula.

If the CO_2 pressure rises out of proportion to the bicarbonate, the C_H will be increased; in other words, the blood will be abnormally acid; this results from the conditions in 1 (*a*), and is known as *acidæmia.* The same thing results from a decrease in the bicarbonate concentration as shown in 2 (*a*). The term *alkalæmia* is used for the opposite condition, when the C_H is abnormally diminished; this occurs from a diminution in the CO_2 as shown in 1 (*b*) or an increase in the bicarbonate as shown in 2 (*b*). There is mild alkalæmia at high altitudes, and after washing out CO_2 from the body by forced breathing (acapnia) (1, *b*) and it is sometimes associated with tetany (*see* p. 488); it occurs after taking large doses of alkali (2, *b*) which also causes a lowered sugar tolerance and ketosis.

While the concentration of CO_2 depends on the respiration, the concentration of the bicarbonate ion is the resultant of all the non-volatile acid and basic substances of the blood. Among the acid substances of importance are oxyhæmoglobin and various acids which are produced in metabolism, such as chloride, phosphate, sulphate and abnormal acids like β-oxybutyric and aceto-acetic acids, while the basic substances are oxides of sodium, potassium, calcium and magnesium. The bicarbonate, the resultant of these acids and bases, is measured by the amount of CO_2 in the blood at a fixed pressure of CO_2, viz., 40 mm. This is defined as the *alkali reserve* of the blood, the *fixed* CO_2, or the *blood bicarbonate.* The normal value lies between 40 and 54 c.c. per 100 c.c. of blood at 38° C.

The term *acidosis* was first of all introduced to indicate the production of aceto-acetic and β-oxybutyric acids in the body and their excretion in the urine in diabetes, the condition which is now called *ketosis.* More lately *acidosis* has been used as equivalent to diminution in alkali reserve or blood bicarbonate, in whatever way this has been brought about. Other authors, however, have used the term to mean increase in the C_H of the blood, a totally different thing. Owing to this confusion in terminology, it is best to use the term *acidosis* to indicate the process of acid production in the body and *alkalosis* to indicate the process of alkali production.

The foregoing remarks are important when the cause of certain common types of dyspnœa is considered. In emphysema, asthma and bronchitis, and bronchial obstructions due to growths, when these conditions are associated with dyspnœa, there is marked acidæmia, owing to accumulation of CO_2 in the blood (1, *a*, in the table). In such cases, owing to the condition of the lungs, the CO_2 fails to escape in spite of the increased breathing. Want of oxygen may also play a part in the dyspnœa of some of these cases. The alkali reserve of the blood may remain about normal, though it is often raised considerably by the diffusion of bases into the blood from the tissues.

In the dyspnœa of mitral disease, the CO_2 is lowered from increased respiration

and there is alkalæmia (1, *b*). The alkali reserve is normal, provided there is no very extensive generalised œdema. In the latter case it may be diminished.

Acidæmia may be present in other conditions of clinical importance: ketosis, chronic or "asthenic" uræmia, and eclampsia. In ketosis the accumulation of aceto-acetic and β-oxybutyric acids in the blood is the primary cause of the acidæmia. They stimulate the respiratory centre, so that the respiration is increased and CO_2 is washed out of the blood, with lowering of the alkali reserve; but the CO_2 is not diminished in proportion, so that some rise in the C_H can be measured quite in the early stages. In the later stages, towards the onset of coma, a very considerable degree of acidæmia may occur (2, *a*). Ketosis will be considered further in the section on diabetes. The acidæmia of uræmia, œdematous nephritis, nephritis and eclampsia is also due to accumulation of fixed acids—the phosphate and sulphate ions in particular. In a case of uræmic coma (2, *a*) the p_H was 7·27 shortly before death. In a case of emphysema with CO_2 retention (1, *a*) the p_H was 7·24 some weeks before death, when the patient was walking about perfectly conscious. It is thus very doubtful whether the acidæmia by itself is the cause of uræmic coma, since the blood of the emphysematous patient was more acid. Coma is more probably due to the poisonous character of the acid substances retained in the blood. The same theory may apply in ketosis, for in this condition there is good evidence from the structure of its molecule that aceto-acetic acid is itself a poison (Hurtley and Trevan). In normal pregnancy and in secondary contracted kidney long before uræmia supervenes, there is a measurable lowering of the alkali reserve. In polycythæmia and in gas gangrene the alkali reserve is also lowered, and probably also in various febrile conditions.

The alkali reserve is increased and there is alkalæmia if hydrochloric acid is lost from the stomach by vomiting or through gastro-colic fistula (2, *b*); in some cases there is a secondary ketosis as there is after ingestion of alkalies and in spite of the alkalæmia the urine remains acid (37) owing to loss of salt (47).

There are various mechanisms for keeping the C_H of the blood within comparatively narrow limits. Acid is excreted by the kidney in two ways: (*a*) the urine is made more acid than the blood by the predominance of acid over basic phosphate; (*b*) ammonia is formed, and this combines with the acids to form neutral salts, which are excreted. The ammonia of the urine is thus increased. (*c*) Alkali is also excreted through the kidney; this takes place in pure cardiac dyspnœa or at high altitudes, when the CO_2 pressure is reduced by over-breathing (1, *b*); the loss of alkali by the kidneys then reduces the alkalæmia by lowering the alkali reserve. (*d*) The "buffer" action of the alkali reserve in preventing changes of C_H is helped by the tissues which have the power of taking up or giving out fixed acids and bases or even of manufacturing fixed acids, *e.g.* ketone bodies after alkali ingestion.

Diagnosis. Breathlessness is a valuable indication of acidæmia; but this may be due to (*a*) want of oxygen, (*b*) reflex action, as is possibly the case in primary heart disease, where the respiratory pump helps the circulation, (*c*) local irritation of the respiratory centre, (*d*) acidæmia, increase of CO_2 or fixed acid in the blood. (*a*) The patient will probably show lividity or cyanosis. (*b*) The respiration is rapid, and there will be evidence of heart disease. (*c*) There will be evidence of intra-cranial disease, such as cerebral hæmorrhage, and the patient will probably be unconscious. (*d*) Where there is no primary lung lesion, which causes acidæmia by increase of CO_2, the increased respiration will probably be due to increase of fixed acid in the blood. The respirations are often slow and deep. The most accurate measure of the amount of fixed acid is to determine the alkali reserve directly, but this is hardly a clinical method. Three other methods may be used: (1) The ratio of the ammonia nitrogen to the total nitrogen in a specimen of urine may be estimated. Normally this is 3 to 5 per cent. In severe cases of acidæmia values of 20 to 40 per cent. may be obtained.

(2) The alveolar CO_2 may be measured by some apparatus, *e.g.* Fridericia's CO_2 tensimeter, a determination taking about ten minutes. (3) The amount of sodium bicarbonate which is required, when given by mouth, to make the urine alkaline to litmus, may be determined. Five grammes are enough for this in normal people. When the alkali reserve is diminished a larger amount will be necessary, and gradually increasing doses at three or four hourly intervals may be given to test this (Sellards).

It is very necessary to make a sharp distinction between ketosis where the nature of the fixed acids is known and other conditions of lowered alkali reserve and acidæmia. Ketosis can readily be diagnosed by the mahogany brown colour of the urine when ferric chloride is added to it and the purple colour with Rothera's or Legal's tests, and by the smell of acetone in the breath. The presence of ketosis is not always due to lack of available carbohydrate in the body, tending to acidæmia. It is produced by giving large doses of sodium bicarbonate, which tends to alkalæmia.

Treatment. It has already been stated that it is doubtful how far acidæmia itself is a cause of death; but when it is present accompanied by a lowered alkali reserve, it is reasonable, in the present state of our knowledge, to counteract it. For this purpose sodium bicarbonate or sodium citrate may be given in drachm doses by the mouth every two hours. In acute cases an intravenous injection of 2 per cent. sterilised sodium bicarbonate may be given.

Where it is believed that the clinical condition is due to poisons in the blood the formation of the latter must be arrested (*see* under Ketosis), and their excretion must be facilitated. (*See* Treatment of Diabetic Coma.)

DISEASES OF THE SPLEEN

The spleen lies in the upper part of the abdomen on the left side, and is entirely concealed by the ribs. In health its position and size can only be estimated by percussion. There is dulness in the left infra-axillary region over the ninth, tenth, and eleventh ribs, and the included spaces. In front, this dulness is limited by a line drawn from the left nipple to the tip of the eleventh rib; behind, it reaches nearly to a line continuous with the anterior margin of the latissimus dorsi. If the spleen becomes enlarged, it extends downwards and forwards, and if the fingers be placed under the ninth and tenth costal cartilages while the patient takes a deep breath, the margin of the spleen can be felt to impinge against them. With greater enlargement, it comes distinctly below the ribs at this point, so that it can be readily felt, and occupies more or less of the left upper quarter of the abdomen. In extreme cases the spleen reaches down to Poupart's ligament and crosses the middle line below the umbilicus, though it may remain on the left side above. An enlarged spleen is always dull when percussed through the anterior abdominal wall; it comes from immediately behind the lower ribs, remaining in contact with the anterior abdominal wall. Its edge is sometimes felt projecting from under the ribs, further back in the loin. The anterior margin often presents one or two distinct notches. If the enlargement is very considerable there may be a dragging sensation or feeling of weight in the left side. Pain may be present from the formation of infarcts, and from the resulting perisplenitis, but is not a marked feature in the enlargements which accompany fevers. For X-ray examination of the spleen, *see* p. 383.

Histologically, the spleen has a lobular arrangement, and its arterial supply passes either to (1) the Malpighian corpuscles, which are merely small lymph glands, or (2) to venous sinuses, and so on to the veins, or (3) the pulp, and then through pores in the walls directly into the veins; before entering the venous sinuses or the pulp the blood passes through *ellipsoids*, bodies situated on the arterioles, which probably have the function, among others, of acting as valves

preventing blood from passing back into the arterial system from the pulp or venous sinuses. The pulp consists of a reticulated network on which lie branching multipolar cells and large amœboid phagocytic cells; these three elements constitute the *reticulo-endothelial* system.

Important functions of the spleen are the phagocytosis of foreign substances in the blood and the destruction of worn-out blood corpuscles, but the spleen also acts as a regulator of the blood volume, turning out blood from the pulp into the splenic veins and so into the circulation as occasion requires. Thus it may shrink to one-fourth or one-sixth of its normal size during hæmorrhage, or during exercise or exposure to heat, when extra blood is required in the skin for cooling purposes or during asphyxia (**25**). In disease the size of the spleen is very variable, probably owing to this regulating function.

The pathological changes to which the spleen is liable will now be summarised; their symptomatology and treatment are dealt with elsewhere.

Active Congestion. The spleen is enlarged in many acute infectious processes, and this is most prominently the case in enteric fever, in relapsing fever, in ague and other malarial fevers, in pneumonia, pyæmia, malignant endocarditis, purpura, phthisis, and acute tuberculosis, and less so in puerperal fever, erysipelas and syphilis. The capillaries and veins are distended with blood. The splenic pulp is swollen, and the capsule of the organ is distended. After death the spleen is found to be of dark red or purple colour, and very soft; and the pulp is readily washed away by a current of water. The histological changes resulting from infective processes in the spleen are, according to Muir, as follows: great phagocytic activity of the cells of the pulp, especially non-granular hyaline cells and endothelial cells, which may be seen to contain numerous red cells, and neutrophil leucocytes; the presence of myelocytes in the pulp; apparent enlargement of the Malpighian corpuscles due to proliferation of cells around them.

Splenitis and Perisplenitis. In some of these infective conditions the process goes beyond the stage of hyperæmia into one of acute inflammation, as shown, according to Ziegler, by the excessive quantity of white cells found within the vessels and pulp. Abscess is a very rare result of general splenitis. Accompanying the splenitis there may be inflammation of the capsule, *capsulitis*, or *perisplenitis*, with resulting adhesions to adjacent organs, or to the abdominal parietes. Acute or chronic capsulitis is very frequently found at post-mortem examinations; and its occurrence can often be traced, especially in the acute form, to infective processes.

Embolic Infarcts. These are the results of the impaction of fibrinous particles, detached from the valves of the heart or from thrombi in its cavities. The infarcts form wedge-shaped or conical masses, which may reach a large size, and occupy one-half or two-thirds of the organ; these are a cause of splenomegaly. They go through the changes of colour elsewhere described (*see* p. 313), and in septic cases they may become purulent. Infarcts also occur in the spleens of leukæmia and splenic anæmia.

Tubercle. This appears in the spleen as a part of general tuberculosis, in the form of grey or often bright yellow nodules, which may reach the size of small peas, scattered throughout the substance and on the surface. Sometimes large yellow caseous masses up to an inch in diameter are found, and these may cause splenomegaly.

Other Causes of Chronic Enlargement. A moderate enlargement is seen in malaria, rickets, congenital syphilis, Hodgkin's disease, erythræmia and lardaceous disease (*see* p 399); *Syphilitic* gumma is rare, but the greatest size is reached in leukæmia, especially the Gaucher variety, in infantile pseudo-leukæmic anæmia, in splenomegalic cirrhosis, in Kala-azar and in Egyptian splenomegaly, in all of which the organ may occupy a large part of the abdomen. Hydatid cyst and old blood cysts resulting from hæmorrhage occasionally cause splenomegaly. Finally there is a varied group of large spleens, associated with

involving those of the axilla and the groin. The glands form irregular and nodulated masses of different sizes, as large as a pigeon's or hen's egg, and are usually firm, painless, and at first freely movable upon one another under the skin. Subsequently they may become adherent, but rarely suppurate. The mediastinal glands are affected as shown by X-rays, and sometimes a broadening of the mediastinal shadow is the first evidence of the disease (Plate 15B, p. 308.) The mesenteric and retro-peritoneal glands are also affected. In many of these regions the growth of the glands may be such as to cause serious pressure on the neighbouring parts. These are—in the neck, the larynx, trachea, and œsophagus; in the thorax, the large veins and the recurrent laryngeal nerves. Occasionally the bones are invaded, but they do not fracture as they are liable to do when they are invaded by carcinoma; paraplegia may follow from pressure on the cord, or without obvious cause.

The *spleen* is, as a rule, only moderately enlarged; it projects a little below the left costal margin, or occupies the left upper quarter of the abdomen; it rarely attains the same size as that seen in myelocytic leukæmia. Secondary *anæmia* is a comparatively early prominent symptom; and in severe cases poikilocytes and nucleated red cells are seen. The leucocytes are increased in number, and when the glands are softer than usual amount to as many as 15,000 or 20,000 per cubic millimetre. But usually the increase is but slight. It is due to an increase in the polymorphs, which are commonly above 5,000 per c.mm. (*see* p. 427), and this is a valuable diagnostic point; but there is sometimes a leucopenia. *Pigmentation of the skin* sometimes occurs, and may be due to interference with the function of the adrenal cortex; occasionally there is intense *pruritus*, with prurigo, and this may suggest the diagnosis, also *herpes* and *lymphadenomatous* infiltration of the skin.

Pyrexia. When the deep glands are involved there may be a relapsing pyrexia (*see* Fig. 55), which differs from other "relapsing" fevers in the greater length of the span, which in 85 per cent. of cases lies between fifteen and twenty-five days, and is fairly constant for each individual case (**28** (*Pel-Ebstein's disease*)). There may also be continuous pyrexia.

A certain amount of weakness is soon observed, and as the disease progresses the effects of the anæmia become more pronounced. There may be dyspnœa. In time, also, œdema of the lower extremities takes place with, perhaps, ascites, pericardial effusion or hydrothorax; and hæmorrhage from the nose or gums, or under the skin, may occur as in other severe blood diseases. The deposits may ulcerate through the skin. Finally, death is caused by exhaustion, suffocation, hæmorrhage, coma or convulsions, or by pneumonia, pleurisy, or œdema of the lungs.

Diagnosis. It may be difficult to distinguish the early stage of Hodgkin's disease of the glands from tuberculous enlargement, especially when the growth is confined to one set of glands. However, tuberculous glands tend to be matted together; in Hodgkin's disease the glands are usually discrete. Tubercle usually affects one group of glands; in Hodgkin's disease the changes are eventually widespread. The glandular enlargement from neoplasm and glandular fever must be distinguished; in the latter there is a mononucleosis, and in Hodgkin's disease, as already stated, a polymorphonuclear leucocytosis. X-ray examination of the chest and Gordon's biological test have also been mentioned. A relapsing temperature of the kind described is a strong point in favour of Hodgkin's disease.

Prognosis and Treatment. Arsenic has been of great benefit in some cases; it should be given in increasing doses until as much as 15 minims of the liquor arsenicalis three times daily is being taken. Arsenobenzol and novarsenobenzol are also valuable. Good results have been obtained by means of deep X-ray therapy; the immediate results are good and deposits disappear to begin with. Whereas patients lived a few months previously, they now live for a few years. Vaccine therapy with Gordon's virus is still in the experimental stage.

REFERENCES

1	O. S. Gibbs	1924	*Quart. Journ. Med.*, **17**, p. 312.
2	R. V. Christie, G. Lovell Gulland and Others	1927	*Q.J.M.*, **20**, pp. 471–510.
3	J. M. H. Campbell	1922	*Brit. Journ. Exp. Path.*, **3**, p. 217.
4	C. Price-Jones	1922	*Journ. Path. and Bact.*, **25**, p. 487.
5	C. C. Ungley and G. V. James	1934	*Quart. Journ. Med.*, **3**, p. 523.
6	A. Goodall	1932	*Lancet*, **ii.**, p. 781.
7	E. Starkenstein	1928	*Klin. Woch.*, **7**, pp. 217, 267.
8	E. Bulmer	1933	*Lancet*, **i.**, p. 1119.
9	N. H. Fairley and H. H. Scott	1933	*Lancet*, **i.**, p. 75.
10	S. J. Hartfall	1934	*Lancet*, **i.**, p. 620.
11	F. W. Madison and T. L. Squier	1934	Quoted *Brit. Med. Journ.*, **ii.**, p. 29.
12	A. C. Hampson	1929	Personal Communications.
13	K. Faber	1927	*Lancet*, **ii.**, p. 901.
14	L. J. Witts (Goulstonian Lectures)	1932	*Lancet*, **i.**, p. 495, 549, 653.
15	L. G. Parsons	1933	*Brit. Med. Journ.*, **ii.**, p. 631.
16	A. C. Hampson and E. C. Warner	1930	*Arch. Dis. in Childhood*, **5**, p. 299.
17	J. F. Wilkinson and W. Brockbank	1930–31	*Quart. Journ. Med.*, **24**, p. 219.
18	R. D. Passey	1924	*Guy's Hosp. Rep.*, **74**, p. 329.
19	A. F. Hurst	1924	*Brit. Med. Journ*, **i.**, p. 93.
20	Review on Diseases of Blood	1923	*Med. Sci.*, **8**, p. 476.
21	S. C. Dyke	1924	*Lancet*, **i.**, p. 1048.
22	S. P. Bedson	1929	Personal Communication.
23	R. L. Waterfield	1928	*Guy's Hosp. Rep.*, **78**, p. 265.
24	Mildred Warde	1923	*Brit. Med. Journ.*, **ii.**, p. 599.
25	J. Barcroft	1925	*Lancet*, **i.**, p. 319.
26	Review on Blood Circulation, etc.	1922	*Med. Sci.*, **5**, p. 496.
27	G. A. Sutherland and B. Williamson	1925	*Lancet*, **i.**, p. 323.
28	A. J. Hall and J. S. C. Douglas	1922	*Quart. Journ. Med.*, **16**, p. 22.
29	H. C. Gram (quoted from)	1921	*Med. Sci.*, **3**, p. 369.
30	J. W. McNee	1929	*Glasgow Med. Journ.*, **111**, p. 65.
31	J. Fawcett and A. G. Gibson	1928	*Lancet*, **i.**, p. 1171.
32	H. D. Rolleston	1925	*Lancet*, **ii.**, p. 1209.
33	L. J. Witts	1930	*Guy's Hosp. Rep.*, **80**, p. 253.
34	R. S. Harrison	1931	*Guy's Hosp. Rep.*, **81**, p. 215.
35	F. A. Knott and W. L. Watt	1930	*Brit. Med. Journ.*, **ii.**, p. 991.
36	J. Bamforth and J. L. Edwards	1933	*Lancet*, **i.**, p. 857.
37	M. Maizels and C. B. Arthur	1929-30	*Quart. Journ. Med.*, **23**, p. 171.
38	F. Parkes Weber	1933	*Lancet*, **i.**, p. 800.
39	H. L. Tidy	1930	*Brit. Med. Journ.*, **ii.**, p. 1073.
40	W. Cramer	1929	*Lancet*, **ii.**, p. 1332.
41	W. W. Payne and R. E. Steen	1929	*Brit. Med. Journ.*, **ii.**, p. 1150.
42	J. W. Pickering	1929	*Lancet*, **ii.**, p. 1239.
43	A. Szent-Gyorgi	1934	Personal Communication.
44	J. Venables	1934	*Lancet*, **i.**, p. 108.
45	J. R. Marrack (Modified)	1929	*Lancet*, **ii.**, p. 512.
46	M. H. Gordon	1934	*Proc. Roy. Soc. Med.*, **27**, p. 1035.
47	R. A. McCance	1936	Goulstonian Lectures.

is prevalent among the Jews. It may be hereditary, or may occur in brothers and sisters of the same family. Hereditary diabetes may be very mild, but often shows a tendency to become more serious and to begin at an earlier age in successive generations. Diabetes often attacks fat people who eat plenty and take little exercise. Hence it is especially a disease of the well-to-do. This fact may be explained by the increased metabolism that follows excessive eating, which makes greater demands on the pancreas and other organs. The association of diabetes with gout is also probably explained by both diseases occurring in overfed people. In the Central Empires war diet had a profound influence on the disease, causing the glycosuria of fat elderly people to disappear. This fact had been observed by Bouchardat during the siege of Paris. Probably the most important factor was the reduction of the meat ration. There is a very general impression that diabetes is apt to occur in people who eat sugar and sweets to excess, but this lacks statistical proof. The great prevalence of a mild form of diabetes in India is probably associated with obesity, to which the excessive carbohydrate diet and the lack of exercise contribute. A strenuous life, nervous strain and emotional shock may play a pronounced part in the onset of the disease. This is of special interest owing to Cannon's observations that emotion in animals caused hyperglycæmia from excitation of the suprarenals, and that students who were up for examinations, or about to undergo some important physical test, such as playing for their college, often had glycosuria. Graham found in his own case that the blood sugar rose to 0·15 per cent. thirty minutes after taking 100 grammes of dextrose, but that when the same test was carried out after a period of hard work, when he was in need of a holiday, the value was 0·185 per cent., and this persisted for half an hour. True diabetes has followed exophthalmic goitre. Acute infection is a predisposing cause, whether this is general or localised particularly to the neighbourhood of the pancreas, giving rise to a pancreatitis. The diminished sugar tolerance and glycosuria found in septic conditions, sometimes called *saprœmic* glycosuria, must also be mentioned. The glycosuria disappears with relief of the condition. Syphilis is also a possible cause. Diabetes of a mild kind is common in the later decades of life. It is possible that atheroma or senile arterial changes or diffuse hyperplastic sclerosis may lead to some defect in the islands of Langerhans, similar to the slight defect in excretory power that may accompany arterio-sclerotic kidney. In diabetic gangrene both the diabetes and the gangrene may have a primary vascular cause; but the gangrene undoubtedly increases the glycosuria, which often clears up after operation. The reverse also holds, since the gangrene may clear up with insulin. Diabetes has followed trauma, not only over the site of the pancreas, but in places far removed, *e.g.* a fractured limb. Head injuries may cause glycosuria; these are probably analogous to Claude Bernard's "puncture diabetes" (*see* later).

Physiology of Carbohydrate Metabolism. The carbohydrate reserves of the body are stored in the form of *glycogen*, which is about equally divided between the liver on the one hand and the muscles on the other. Glycogen is formed from the carbohydrates and proteins of the food. The latter are absorbed from the intestine in the form of amino-acids, which may be used to synthesise the proteins proper to the organism, or after deamination may be oxidised at once, or built up into glycogen. Carbohydrates are also broken down by digestion, and may be absorbed in the form of *dextrins* and of comparatively simple substances like *dextrose* and *lævulose*. These bodies all pass to the liver by the portal vein. The dextrins and lævulose are entirely taken up by the liver and formed into glycogen there. If very large amounts of lævulose are eaten some of it manages to get through the liver into the general circulation, and is then promptly excreted by the kidney, producing *lævulosuria*. This condition also occurs in disease of the liver, which under these circumstances is unable to hold back the amount of lævulose, which normally can be dealt with quite readily.

Dextrose *may* be partly kept back by the liver, but some of it certainly gets through into the general circulation, because the amount of sugar in the blood of a healthy person shows an increase immediately after a meal (*see* Fig. 57). The systemic blood is thus supplied with dextrose from two sources: (1) the food, which forms a variable supply; (2) the glycogen of the liver, which probably forms a fairly constant supply, the glycogen being broken down by an amylolytic ferment there. Before breakfast the concentration of dextrose in the blood usually lies between about 0·08 and 0·10 per cent. This constancy is preserved by means of a steady production of dextrose from the liver on the one hand, and its disappearance into the tissues on the other hand, where it is either oxidised to form CO_2 and water, or elaborated into more complicated compounds, one of these being the glycogen of the muscles.

Insulin, which is the hormone secreted by the islands of Langerhans, plays an essential part in these processes, though its action is complicated. It is best regarded from two points of view: (1) In the *periphery* insulin causes the disappearance of dextrose from the blood stream, since if administered to a diabetic the percentage of sugar in the venous blood of the arm is found to be less than the percentage in the arterial blood, whereas before administration the two values are nearly the same (**5**). The sugar that disappears is partly oxidised by the muscles, skeletal and cardiac, and partly built up into glycogen in the muscles (**6**) and probably changed towards fat. (2) Its *central* or *visceral* action is manifested on the liver in two ways: (*a*) In acute diabetes there is lipæmia and increase of fat in the liver, probably because, in default of carbohydrate, fat is mobilised from the depôts and assembled in the liver to be utilised (**7**). Here it is probably converted into carbohydrate, which explains the low respiratory quotient found in severe cases, and this conversion involves the production of aceto-acetic and β-oxybutyric acid (*ketosis*) (**8**). Insulin arrests this process, the ketosis and lipæmia vanish, and the fat disappears from the liver, and the respiratory quotient rises. (*b*) The diabetic liver contains less glycogen than normal, since this is discharged into the blood and causes the well-known hyperglycæmia. It is not uncommon to find a concentration of 0·4 or 0·6 per cent. dextrose in the blood in severe diabetes. Insulin causes in the liver a retention of glycogen, which increases *pari passu* with the diminution in the liver fat. This result is possibly obtained because the insulin inhibits the action of the amylolytic ferment of the liver, which becomes excessive in its absence. The sudden fall in blood sugar, which is the most striking clinical effect of insulin, is thus due partly—probably only slightly—to oxidation and partly to storage in the muscles and to the fact that the excessive supply of sugar from the liver is stopped. At the same time any carbohydrate that is taken as food is partly stored in the liver as glycogen and probably partly converted into fat; the reason for the latter statement is that several observers have found a rise in respiratory quotient without any marked increase of combustion, which would occur if most of the sugar taken had been burnt. The following observation shows that storage of sugar by means of insulin may be only a temporary matter. A patient was given by mistake the enormous single dose of 100 units of insulin, and to counteract this was given by mouth immediately 110 grammes of carbohydrate in the form of dextrose and bread. This was retained in the tissues for two days and then largely excreted in the urine after the effect of the insulin had worn off (**9**).

The early stage of pancreatic deficiency, in which dextrins and amylolytic ferment enter the blood from the liver, is mentioned elsewhere (*see* p. 409). Three other ductless glands, the suprarenals, thyroid and pituitary act in the opposite direction to the islands of Langerhans, since their excitation increases the sugar in the blood. The suprarenals pour adrenin into the circulation, and this travels to the liver and causes the breakdown of glycogen into dextrose. For this action to occur it appears to be essential for the hepatic plexus to be intact. The thyroid probably acts by exciting the suprarenals. Claude

changes; in healthy persons after taking large doses of sodium bicarbonate; and in diabetes mellitus. When the aceto-acetic acid reaches a high concentration in the blood it may cause death by producing coma. This may occur in severe diabetes or after prolonged vomiting (*see* p. 341). In a very prolonged case of severe diabetes the body fat largely disappears as the patient wastes, and the ketosis may almost vanish, while the patient dies of inanition.

Clinical Tests for Ketosis. There is no colour test for β-oxybutyric acid in the urine. Gerhardt's test, which is used for aceto-acetic acid, consists in adding ferric chloride to the urine when a port-wine colour is obtained. It disappears on heating. It is not a very sensitive test. It must be distinguished from a similar reaction after taking salicylates, but in this case the colour is not discharged by heat. Two tests with sodium nitroprusside are given both by aceto-acetic acid and acetone, but they are about twenty times as sensitive for the former as the latter. In Legal's test a small crystal of sodium nitroprusside or a few drops of a freshly prepared solution of it are dropped into the urine, and then a little caustic soda. A cherry-red colour is developed which soon fades; an excess of acetic acid now added produces a carmine-red or deeper purple colour. In Rothera's test solid ammonium sulphate is added to the urine with a crystal of sodium nitroprusside and ammonia in excess. A purple colour gradually develops. This is much the most sensitive test there is for aceto-acetic acid.

These tests are excellent for indicating the presence of ketosis; but they are not of much use in indicating its amount, in order to be able to determine whether a diabetic patient is on the verge of coma or not. One reason is that when coma approaches the excretory power of the kidneys begins to fail with fall of blood pressure, so that the amount of these substances in the urine is diminished, and inversely they accumulate in the blood. It is this accumulation that gives the measure of the danger. Three methods are available (*see* p. 452). The determination of the ratio of ammonia nitrogen to total nitrogen and the test of giving 5 grammes of sodium bicarbonate by the mouth have already been sufficiently described. The alveolar CO_2 method depends on the fact that the normal CO_2 values lie between 4·5 and 6·2 per cent., being rather lower in women than in men. In diabetes a value of 2 per cent. means that coma may supervene within twenty-four hours, if no improvement takes place. A patient may go on living for many days or even some weeks with the alveolar CO_2 between 3 and 4 per cent. In the worst event coma will not supervene before three or four days. It has already been stated that the lowering of the CO_2 which is caused by increased respiration is a mechanism compensating for the increase of fixed acid in the blood, and this prevents the hydrogen ion concentration of the blood rising too much.

Symptoms. The onset of diabetes is often insidious; the patient only gradually notices that he drinks more fluids and passes more urine than normal; or he may complain of debility and loss of flesh rather than of any alteration in his urine. In some cases the onset is acute, the patient being able to remember the exact day when he first noticed he was thirsty.

In the more severe type of case, which may come on acutely or develop from a milder type, the characteristic symptoms, in the absence of treatment, soon become unmistakable—namely, frequent and abundant micturition, great thirst, generally a very large appetite, physical weakness, and loss of flesh. The appetite is sometimes enormous, but in other cases it is but little affected, and often fails towards the end. The mouth and lips are dry, the tongue red, raw, and "beefy"; and there is generally a sweet taste in the mouth. The digestion is, as a rule, good, and patients may have no difficulty in disposing of large quantities of food. The bowels are generally confined. The skin is harsh and dry. At the same time, nutrition is profoundly affected; the patient rapidly loses flesh, and becomes excessively weak; he is indisposed to make any mental effort, and is depressed and irritable. The teeth become loose from pyorrhœa alveolaris. There is often loss of virility in men, and in women the menses may cease.

The urine is increased to 5 or 10 litres in the day, the amount of sugar passed being over 500 grammes and the concentration up to 8 per cent. Owing to the presence of so much sugar, the specific gravity is raised to 1,040 or 1,045. The urine is generally pale yellow, or almost like water; it has a sweetish odour like hay and a sweet taste. The reaction is acid. It contains acetone, aceto-acetic and β-oxybutyric acids.

Mild cases of diabetes are sometimes described as " alimentary glycosuria "; but blood sugar tolerance curves show that this is a type of true diabetes, although the glycosuria may be found only after a heavy meal containing much starch. There is no thirst, and the amount of sugar passed in the day may be under 50 grammes. There may be no symptoms, but often the patients notice that the volume of urine is increased. They may suffer from various complications. This type occurs in elderly people particularly.

Complications. In the course of diabetes a number of complications are liable to occur. The irritation of the saccharine urine may excite in women a troublesome *pruritus* of the vulva, and in men *balanitis*. There may be a general pruritus of the skin. *Carbuncles* and *boils* are liable to occur in various parts of the body, and the former may be the cause of death. A form of *xanthoma* has also been seen in diabetes. There is sometimes *gangrene* of the toes or of an entire limb, but this is associated with atheromatous arteries. *Albuminuria* may be present, indicating coincident renal changes. The Achilles jerks and knee jerks are commonly absent in diabetes; this may be due either to *peripheral neuritis* or to degeneration in the fibres of the *posterior nerve roots* between the pia mater and grey matter, which leads to changes in the posterior columns of the cord (**11**). *Neuralgia* may be severe, especially sciatic, occipital and trigeminal. There may be cramps. Œdema of the feet and legs may be seen in very wasted individuals (*cachectic œdema*), and it can be readily produced by administering too large doses of sodium bicarbonate. *Phthisis*, *pneumonia* and other infectious diseases do not occur more commonly among diabetics than among the general population; but the outlook is worse, although it has improved with modern methods of treatment.

Vision is affected in diabetes in several ways. Rapid alterations in focussing power and amblyopia may be due to weakness of the ciliary muscle or to changes in the refractive index of the media presumably from the presence of sugar. Diabetic *cataract* is usually of the senile variety; but in young persons a posterior polar cataract due to diabetes may be found, though it is very rare. A retinitis similar to arteriosclerotic retinitis is common in elderly patients; possibly both the diabetes and the retinitis are secondary to arterial disease, and there is no direct connection between the two. Other changes are iritis, retrobulbar neuritis causing optic atrophy, hæmorrhages in the retina and vitreous, and *lipæmia retinalis* already mentioned in severe untreated cases.

Diabetic Coma. This name has been given to a group of symptoms due to the accumulation in the blood of aceto-acetic acid, which acts as a poison both on the circulatory and on the central nervous systems, and with a fatal result. Deficiency of CO_2 in the blood may also play a part in the causation of this symptom complex. The causes predisposing to coma are: (*a*) a diet rich in protein and fat; (*b*) excitement or emotional shock; (*c*) general anæsthesia: probably gas with oxygen is the least harmful, but it is very important that the patient should not get blue; (*d*) acute infections; (*e*) impaired function of the kidneys, so that aceto-acetic acid is imperfectly excreted; (*f*) constipation; (*g*) failure to continue the use of insulin in a young patient, who has put on fat by its help. The onset is often gradual, but may be indicated by loss of appetite, by a rapid fall in the quantity of urine and of sugar passed in the day, by the presence of albumin and casts in the urine, and by obstinate constipation. Sometimes there is severe abdominal pain. The patient then rather rapidly falls into a condition of collapse and coma. The pulse is quick and

feeble, the intraocular tension lowered, the surface cold, the features pinched, and the extremities livid. He lies with the eyes half open, taking no notice of his surroundings; and though he can be roused by a question, he answers, if at all, in a dazed manner, as if only half comprehending it. The breathing in these cases is peculiar; it is slow, deep, and sighing in character; the movements of the chest are very extensive; the respirations become rather more frequent towards the end. At the same time, examination of the chest reveals nothing abnormal. This form of breathing has been called *air hunger*. In many cases a sweetish, fragrant, or ethereal odour, likened to the smell of apples by some, may be noticed about the bed of the patient; it has been attributed to acetone. This condition may last from one to three days, when the pulse gets more and more feeble, though the heart may be beating forcibly, the patient more apathetic, and finally quite comatose; and death ends the scene. Occasionally there is a little muttering delirium. In some cases the symptoms are much more rapid; without any warning the patient becomes collapsed, with a quick, feeble pulse and livid extremities; air hunger develops, and he dies in coma after twenty-four or thirty-six hours.

Renal Glycosuria. *Benign Glycosuria* (*Diabetes Innocens*). These terms are applied to a condition where the patients pass sugar continuously for years, but remain in perfect health and have none of the symptoms of diabetes. The output of sugar is small, being usually not more than 30 grammes in the day. A dose of carbohydrate makes little difference to the output. In some cases it is difficult to get rid of the sugar by treatment, in others it disappears rapidly with starvation. The blood sugar tolerance curve is normal (*see* p. 464). The blood sugar on an empty stomach is normal, and yet sugar is passed, showing that the threshold of the kidney is low. The ætiology of the condition is unknown, but occasionally it is congenital. No treatment is required. Glycosuria associated with a low renal threshold occurs experimentally when an animal is poisoned by phloridzin.

Diagnosis. The presence of sugar in the urine as determined by one of the reduction tests, when there is also a present or past history of either thirst, polyuria or muscular weakness, makes the diagnosis of diabetes mellitus certain. If the urine is not tested, the presence of the disease may be overlooked, and the patient may be treated for a vague weakness and "debility"; or the possibility of diabetes underlying one of its complications, such as carbuncles, pruritus, or coma, may be forgotten. It must be borne in mind that coma may occur as a result of diabetes in persons not known to be diabetic; and that in diabetics abdominal pain, severe enough to suggest that a laparotomy is needed, may be the first symptom of the onset of coma. The chief difficulty is when a patient's urine gives a slight reduction on several occasions and there are no symptoms. The fallacies connected with the clinical tests have already been considered; but even if the presence of dextrose is proved by the fermentation and phenylhydrazine tests, it is still necessary to find out if the patient is suffering from true diabetes mellitus. If the blood sugar is above 0·16 the diagnosis will be very probable, but if lower than this it will be best to carry out a sugar tolerance test with analyses of the blood after a dose of dextrose, and this will also assist the prognosis.

Prognosis. Diabetes mellitus is a very serious disease, tending to run a more rapid and unfavourable course in young than in elderly subjects. At the same time the prognosis has improved with the introduction of insulin and careful dietetic treatment. In some cases the sugar tolerance increases as the result of treatment; but a cure must be very rare—in the sense that the patient is able to live without insulin on an unrestricted diet and yet keep a normal blood sugar. Without treatment the prognosis is uniformly unfavourable in young subjects, as the disease tends to progress. It may progress in spite of treatment, especially if the patient becomes infected. The prognosis is the more unfavour-

able the later in the disease that treatment is instituted. In elderly subjects with so-called "alimentary glycosuria," a fatal result need not occur in the absence of treatment; but there is always the possibility of complications such as carbuncle, cataract and retinitis, so that adequate treatment should always be instituted to prevent these occurring.

Prevention. Since early treatment is so important, the periodic examination of the urine has been recommended. This should certainly be carried out in the case of the healthy members when diabetes runs in a family. The best way of avoiding diabetes is to live a healthy life with plenty of regular exercise and to avoid obesity and focal sepsis.

Treatment. The first treatment of diabetes on rational lines was carried out by Rollo, who prescribed a diet of animal food containing no starch and sugar. This plan was very generally adopted up to 1915, enormous amounts of protein and fat being allowed. It was comparatively rare for the urine of a diabetic to become sugar-free on such a diet. Experiments carried out on depancreatised dogs by F. M. Allen and clinical observations at different times by Von Noorden, Guelpa and Graham showed the importance of undernutrition in treatment. The plan usually adopted consisted in first of all making the urine sugar-free by fasting and then in giving food in gradually increasing amounts, in severely restricting the carbohydrate intake, and in permanently underfeeding the patient, so as to keep him thin. In an underfed person the basal metabolism is low, so that there is less call on the island tissue, and this is of great advantage where the islands are deficient as in diabetes, because they steadily deteriorate if they are overworked. A high protein diet causes a high metabolism; this has been called the *specific dynamic action* of protein. The treatment of diabetes has been revolutionised by the discovery of insulin; but although fasting is now no longer necessary, an arranged diet is still usually necessary, particularly in the more severe cases.

At the beginning of treatment possible focal sepsis which may be due to dental apical infection, septic tonsils, gall bladder, or appendix should be eradicated. The aim of treatment is to administer insulin in such quantities and at such times that the blood sugar remains within normal limits during the twenty-four hours.

The principles of treatment can be deduced from Dr. W. W. Payne's determinations of the blood sugar of a patient shown in Fig. 59. Curve B is on the average higher than curve A, because carbohydrate was substituted for some of the protein. Otherwise the diet was the same in A and B. The effect of giving insulin twice a day at twelve hours' intervals before breakfast and supper, is, broadly speaking, to produce a double curve, a rise immediately after the meal followed by a fall. In this case, with rather a smaller dose of insulin, the morning rise was much higher than the evening rise; in curve A the rise certainly began before breakfast, and may be explained by the increased metabolic activity which suddenly occurs on waking. In other cases, with equal doses of insulin, the evening rise may be the higher, and when three doses of insulin are given at 6 a.m., 12 noon, and 9 p.m., *i.e. after* supper, a triple curve is obtained which may be just as high at night as in the day, presumably because protein metabolism takes place more slowly than carbohydrate metabolism, and so is delayed till night-time (**12**).

When treatment is first begun, injections of 4 or 5 units are given half an hour before breakfast and supper. The dose is increased by 4 or 5 units every two or three days. The sugar in the urine becomes less and eventually disappears. At this stage the renal threshold may be determined by estimating the sugar in the blood after emptying the bladder, and testing for sugar the urine which is secreted during the next 15 minutes. If the threshold is normal (0·16–0·18 per cent.) the absence of sugar in the urine passed at frequent intervals in the twenty-four hours will indicate that the blood sugar has never been too high;

The patient sits on the floor with his back pressed firmly against the wall and his knees bent. The body length is measured from the floor to the top of the head in inches and compared with the body weight without clothes in pounds. If the patient is too fat or too thin owing to disease, then his predicted metabolism would be best obtained by using in Plate 37 the average weight corresponding to his body length and not his actual weight. Table 3 is of general use to indicate at any time whether a patient is too fat or too thin.

Diabetic patients are nowadays treated more generously as regards carbohydrate than formerly, and provided the total calorie value of the diet is not excessive the insulin requirement is not higher than with low carbohydrate diets. In fact, the high carbohydrate low fat diet with a ratio of 6 to 1 often succeeds in bringing down the blood sugar to normal in an obese patient without insulin being used at all; but if such a diet is used for any length of time vitamins A and D must be supplied extra. In order to facilitate the prescribing of diets the author has calculated a number of diet formulas, some of which are given in the table. Each formula contains a definite number of carbohydrate rations of 20 grams each, of fat rations of 10 grams, and of protein in grams. Additional formulas may be calculated by adding and subtracting the top line which corresponds to 200 calories. In making out these ratios no account is taken of protein as a source of carbohydrate or fat; such calculations are too hypothetical, and with higher carbohydrate diets the glycerol of fat is unimportant as a source of carbohydrate. A carbohydrate to fat ratio of 2 to 1 will be found most generally useful though children may prefer 4 to 1, while a higher carbohydrate diet may be of special value in arteriosclerosis, angina pectoris, sepsis and phthisis. The old-fashioned diet corresponds to 1 to 1. The carbohydrate and fat rations are obtained from Lists A, B and C, which give the amount of each foodstuff corresponding to a whole and a half carbohydrate or fat ration, while in List D there are foods containing carbohydrate, fat and protein including a few recipes for ordinary household use. A diabetic may eat any food that the normal subject customarily takes provided its composition is known, and this scheme of diets enables him to take part in the ordinary meals of the family. A much more detailed list containing 200 recipes, is being published elsewhere (**54**). Dishes containing sugar should usually only be taken shortly after insulin, *i.e.* at breakfast and supper; but many physicians forbid it altogether. An allowance is made for vegetables, but apart from potatoes, butter beans and peas, weighing is not necessary. Clear broth can be taken freely. There is not the same object in giving alcohol as in the old days and it is better avoided. Beers contain from 4 to 8 per cent. carbohydrate. Saccharine may be used as a sweetening agent. These diet tables take account mainly of carbohydrate and fat; a variation in the protein is not of much consequence as the calorie value is low compared with fat. It is much more convenient to weigh the food in grams and so avoid the awkwardness of fractions which come in when ounces are used; both measures are given in the tables. Most of the carbohydrate should be given at breakfast and supper, shortly after the insulin; but some may be given at the midday meal and even at tea-time in milder cases. With large doses of carbohydrate it is often advisable to give the insulin three-quarters of an hour or even one hour or more before the meal so that it will produce its maximum effect from one to two hours after the meal when the blood sugar rise is at its maximum; but if the insulin is advanced too much there will be a reaction before or during the meal.

Choice of Case for Insulin Treatment. Insulin treatment must not be used for renal glycosuria. The glycosuria of pregnancy is frequently of this nature; but where pregnancy is complicated by true diabetes the woman should be given the choice as to whether the pregnancy should be terminated or not, and if not, insulin treatment should be instituted. The success of insulin in removing symptoms in practically all patients with glycosuria and hyperglycæmia indicates

List A.—20 grm. Carbohydrate Rations (C.R.).

20 grm. carbohydrate are contained in:	Grm.	or Oz.	These amounts also contain protein. Grm.
Barley, pearl	26	$\frac{7}{8}$	2
Beans, butter (as served)	139	5	8
Biscuits, water (H. & P.)	24	$\frac{7}{8}$	2
„ Thin Captain	25	$\frac{7}{8}$	3
Bread, white	38	$1\frac{3}{8}$	3·5
„ brown (Hovis)	49	$1\frac{3}{4}$	5
Currants, dried	34	$1\frac{1}{4}$	0
Flour	27	1	3
Force	26	$\frac{7}{8}$	3
†Golden syrup (Lyle's)	27	1	0
†Honey	25	$\frac{7}{8}$	0
Macaroni	27	1	3·5
†Marmalade, Cooper's, Oxford	35	$1\frac{1}{4}$	0
Oatmeal	30	1	5
Peas, fresh boiled	173	6	11·5
Potatoes, new, boiled	142	5	2
„ old, „	115	4	2
Rice, weighed (then washed)	28	1	2
Sago	26	$\frac{7}{8}$	2·5
†Sugar	21	$\frac{3}{4}$	0
Tapioca	23	$\frac{3}{4}$	0

List B.—Half Carbohydrate Rations ($\frac{1}{2}$ C.R.).

Fruit fresh and ripe unless otherwise stated, edible portion weighed.

10 grm. carbohydrate are contained in:	Grm.	Oz.	10 grm. carbohydrate are contained in:	Grm.	Oz.
Fruit.					
Apples	92	$3\frac{1}{4}$	Greengages	93	$3\frac{1}{4}$
Apricots, with skin, without stones	162	$5\frac{3}{4}$	Melon, yellow	218	$7\frac{3}{4}$
Banana	56	2	Oranges	127	$4\frac{1}{2}$
Blackberries	174	$6\frac{1}{8}$	Peaches	118	$4\frac{1}{8}$
Cherries	93	$3\frac{1}{4}$	Pears	104	$3\frac{5}{8}$
Currants, black	167	$5\frac{7}{8}$	Pineapple, tinned	31	1
„ red	255	9	Plums (Victoria)	113	4
Damsons	115	4	Prunes, stewed with stones	82	3
Gooseberries	120	$4\frac{1}{4}$	Raspberries	196	$6\frac{7}{8}$
Grapes	72	$2\frac{1}{2}$	Strawberries	177	$6\frac{1}{4}$

Protein negligible.

Vegetables.

Class 1.

An ordinary helping of:

Beetroot.	Onions.	Swedes.
Carrots.	Parsnips.	Half Small Grapefruit.

Class 2.

As much as may be desired of:

Jerusalem Artichokes.	Cucumber.	Radishes.
Asparagus.	French Beans.	Rhubarb.
Brussel Sprouts.	Lettuce.	Sea Kale.
Cabbage.	Marrow.	Spinach.
Cauliflower.	Mustard and Cress.	Tomatoes.
Celery.		Watercress.

List C.—Half Fat Rations ($\frac{1}{2}$ F.R.).

5 grm. fat are contained in:	Grm.	Oz.	These amounts also contain protein. Grm.
Butter	6	$\frac{1}{4}$	0
Cheese, Cheddar	15	$\frac{1}{2}$	4·5
„ Dutch	14	$\frac{1}{2}$	5
Egg, one	56	2	6

FISH, ETC.

5 grm. fat are contained in:	Edible portion cooked. Grm.	Oz.	These amounts also contain protein. Grm.
Bloaters, grilled	29	1	6
Eel, stewed	28	1	3
Herring, fried	26	1	6
Kippers, baked	44	1½	10
Mackerel, fried	44	1½	9
Sardines	22	¾	4·5
Sprats, smoked, grilled	21	¾	5·5
White fish, steamed *	70	2½	15
Crab, no shell	70	2½	15
Lobster, no shell *	70	2½	15
Prawns, no shell *	70	2½	15

* Add 4 grm. butter.

MEAT.

Bacon, collar, gammon	15	½	4
Lean ham	37	1¼	8·5
„ sirloin	40	1½	11
„ stewed steak (no fat)	58	2	18
„ veal fillet, roast	43	1½	13·5
„ other meat	30	1	8

ORGANS.

Heart, roast	34	1¼	8·5
Kidney, fried	55	2	15·5
Liver	32	1	10
Sweetbread, stewed	55	2	12·5
Tongue, stewed	21	¾	4
Tripe, stewed	83	3	15

POULTRY, ETC.

Chicken, roast	68	2¼	20
Duck, roast	21	¾	5
Goose	22	¾	6
Partridge	42	1½	15
Pheasant	54	2	16
Rabbit, stewed	33	2¼	17
Turkey, roast	33	2¼	19·5

LIST D.—FOOD CONTAINING CARBOHYDRATE, FAT AND PROTEIN.

The amount of food mentioned below in:	Grm.	Oz.	contains	C.R.	F.R.	P. Grm.
Milk measured in c.c.	200	7		½	½	7
	370	13		1	1½	13
	570	20		1½	2	20

BISCUITS.

Bath Oliver (3¼ large)	46	1½	1½	½	4·5
Breakfast (7), H. & P.	54	2	2	½	5·5
Cream Cracker (7), H. & P.	57	2	2	1	4·5
Petit Beurre (4½), P.F.	44	1½	1½	½	4·5
Shortbread (Grenock), 2½, P.F.	34	1¼	1	1	2·5
+ Chocolate (Bournville)	56	2	½	1½	10
+ „ breakfast (Cadbury)	26	1	1	—	15

NUTS.

Brazils	15	½	0	1	2·5
Chestnuts	75	2½	1	½	4·5
Filberts (add 15 grms. bread)	15	½	½	1	4
Walnuts	16	½	0	1	3

VARIOUS RECIPES.

The amount of food mentioned below in:	Grm.	Oz.	contains C.R.	F.R.	P. Grm.
†1.—Fruit cake	39	1⅓	1	½	2
†2.—Sponge cake	37	1⅓	1	½	3
3.—Cheese straws. Quarter of the amount given in recipe	53	1⅘	1	1	8·5
4.—Macaroni cheese. Half pudding	200	7	1½	1½	16·5
5.—Mashed potatoes. Half quantity	120	4⅕	1	½	2·5
6.—(*a*) Batter pudding, steamed. Half pudding	150	5¼	1½	1	11
(*b*) Batter pudding, baked. Half pudding	130	4½	1½	1	11
7.—Bread and butter pudding. Half pudding	170	6⅓	1½	1	10·5
8.—Savoury pudding. Half pudding	210	7	1	1½	11
9.—(*a*) Suet pudding, steamed. Half pudding	59	2	1	1	4
(*b*) Suet pudding, baked. Half pudding	47	1⅔	1	1	4
10.—Yorkshire pudding	113	4	1½	1	11
11.—Bread stuffing. Half quantity	28	1	½	½	2

† Foods thus marked contain more than 10–11 grm. soluble carbohydrate in the stated portion and should only be ordered by a physician.

RECIPES.

(1) *Fruit Cake.* ½ lb. flour, ½ lb. sultanas, ¼ lb. sugar, ¼ lb. butter, 2 eggs, 2½ oz. milk, 10 grm. Royal baking powder (a teaspoonful). In oven 1 hour.

(2) *Sponge Cake.* 6 oz. flour, ¼ lb. sugar, 2 oz. butter, 2½ oz. milk, 2 eggs, 5 grm. baking powder (a level teaspoonful). In oven 35 min.

(3) *Cheese Straws.* 70 grm. (2½ oz.) cheese (Parmesan), 113 grm. (4 oz.) flour, 62 grm. (2⅕ oz.) butter, yolk of 1 egg, ½ oz. water, salt, cayenne pepper. Sieve flour, rub in butter, add grated cheese and seasonings, bind with slightly beaten yolk of egg and water to form a stiff dough, knead lightly, roll out thinly and cut. Time in oven 15 min.

(4) *Macaroni Cheese.* 54 grm. (2 oz.) macaroni [or 53 grm. (1⅘ oz.) spaghetti], ingredients of Sauce No. 11, 62 grm. (2¼ oz.) Cheddar cheese. Soak macaroni in water for an hour, add salt and boil until tender, strain. Prepare hot sauce and add macaroni and most of the cheese, season well with mustard and salt, transfer to pudding dish, sprinkle remainder of cheese on top of pudding and brown in oven. Time, 45 min.

(5) *Mashed Potatoes.* Boil 200 grm. (7 oz.) peeled old potatoes until tender, pour off water, and steam slightly to finish cooking. Cooked like this there is no alteration of weight. Mash with 1 oz. milk, 12 grm. (⅔ oz.) butter, add pepper.

(6) *Batter Pudding.* (*a*) 70 grm. (2½ oz.) flour, 1 egg, 6 oz. milk; 12 grm. (⅔ oz.) butter for basin; mix, beat and cover, allow to stand, beat occasionally. Heat steaming bowl with butter thoroughly melted. Time, 1 hour. (*b*) It may be baked 40 min.

(7) *Bread and Butter Pudding.* 57 grm. (2 oz.) white bread, 6 grm. (⅕ oz.) butter, 1 egg, 10 oz. milk, 21 grm. (¾ oz.) sultanas. Time 2 hours.

(8) *Savoury Pudding.* 57 grm. (2 oz.) white breadcrumbs, 16 grm. (½ oz.) butter, 2 eggs, 7 oz. milk, 1 medium size onion, mixed herbs or chopped parsley, pepper and salt. Shred onion and boil in salted water until tender, beat eggs, mix ingredients together and season well with herbs, pepper and salt, butter dish and bake for 40 to 50 min.

(9) *Suet Pudding.* 49 grm. (1¾ oz.) flour, 22 grm. (⅘ oz.) shredded suet (Atora), 1½ oz. milk, 4 grm. Royal baking powder, salt. Sieve flour, baking powder and salt. Add suet mix in milk with knife. Use knife for arranging mixture on fruit as a "Cap" in No. 6. (*a*) It may be covered with greaseproof paper and steamed 80 minutes, or (*b*) baked in oven 30 minutes. (*c*) If dumplings in a Silverside stew are required, use 67 grm. (2⅓ oz.) flour in mixture and 10 grm. (⅓ oz.) flour for covering the dumplings.

(10) *Yorkshire Pudding.* Same mixture as No. 15, but use dripping for baking dish instead of butter. In oven 25 min.

(11) *White Sauce, Pouring.* 14 grm. (½ oz.) flour, 4 grm. (⅛ oz.) butter, 6½ oz. milk, salt and pepper. Melt butter and mix with flour, add milk by degrees, stir constantly and boil up after each addition. Boil for five minutes. Add seasonings.

(12) *Bread Stuffing or Force Meat.* 29 grm. (1 oz.) white breadcrumbs, 12 grm. (⅔ oz.) butter, margarine, or dripping, ¼ oz. milk, mixed herbs, pepper and salt. Rub butter into breadcrumbs, add seasoning, mix and moisten with milk. To be used for beef or veal olives or liver, in larger quantities for stuffing fowl, game, galantines or fish, or made up as balls to be stewed for 10 min. in boiling stock; 6 grm. (⅛ oz.) flour to be used in the cooking.

1,400 Calories. Ratio C. to F. = 2 to 1.
(6½ C.R., 6½ F.R. 64 grm. P.) 130 grm. C. 65 grm. F. 64 grm. P.

		Grm.	Oz.	C.R.	F.R.	Grm. P.
THROUGH THE DAY (1 C.R., ½ F.R.)	Milk, 7 oz. (⅓ pint)	—	—	½	½	7
	Vegetables (List B), including half small grapefruit	—	—	½	—	—

		Grm.	Oz.	C.R.	F.R.	Grm. P.
BREAKFAST	White bread	76	2⅝	2	—	7
(2 C.R., 1½ F.R.)	Bacon, collar or gammon, fried (List C, 2 portions)	30	1	—	1	8
	Butter (List C, 1 portion)	6	¼	—	½	0
	Tomato (List B)					
DINNER	Sirloin, roast (List C, 2 portions)	80	3	—	1	22
(1 C.R., 2 F.R.)	Boiled potatoes, old (List A, 1 portion)	115	4	1	—	2
	Butter (List C, 2 portions)	12	⅜	—	1	—
	Vegetables (List A)					
	Half small grapefruit					
TEA	Salad (List B)					
(½ C.R., 1 F.R.)	Bread (List A, ½ portion)	19	⅝	½	—	1·5
	Egg (1) or Sardines (List C, 1 portion)	22	¾	—	½	4·5
	Butter (List C, 1 portion)	6	¼	—	½	—
SUPPER	Cheddar cheese (List C, 2 portions)	30	1	—	1	9
(2 C.R., 1½ F.R.)	Butter (List C, 1 portion)	6	¼	—	½	—
	Bread	57	2	1½	—	5
	Fruit (List B, 1 portion)			½	—	—
				6½	6½	66

1,800 Calories. Ratio C. to F. = 2 to 1.
(8½ C.R. 8½ F.R. 77 grm. P.) 175 grm. C. 85 grm. F. 77 grm. P.

		Grm.	Oz.	C.R.	F.R.	Grm. P.
THROUGH THE DAY	Milk, 7 oz. (⅓ pint)	—	—	½	½	7
	Vegetables (List A), including half small grapefruit	—	—	½	—	—
BREAKFAST	Bread	114	4	3	—	10·5
(3 C.R., 2½ F.R.)	Bacon, collar or gammon, fried (List C, 2 portions)	30	1	—	1	8
	Tomato (List B)					
	Egg (1) (List C, 1 portion)	—	—	—	½	6
	Butter (List C, 2 portions)	12	⅜	—	1	—
DINNER	Lean meat (List C, 2 portions)	60	2⅛	—	1	16
(1 C.R., 2 F.R.)	Boiled potatoes, old (List A, 1 portion)	115	4	1	—	2
	Butter	12	⅜	—	1	—
	Vegetables (List A)					
	Half small grapefruit					
TEA	Salad (List A)					
(½ C.R., 1 F.R.)	Bread (List A, ½ portion)	19	⅝	½	—	1·5
	Butter	6	¼	—	½	—
	Sardines (List C, 1 portion)	22	¾	—	½	4·5
SUPPER	Cheddar cheese (List C, 3 portions)	45	1⅝	—	1½	13·5
(3 C.R., 2½ F.R.)	Butter	12	⅜	—	1	—
	Bread	95	3¼	2½	—	8·5
	Fruit (List B, 1 portion)	—	—	½	—	—
				8½	8½	77·5

2,200 Calories. Ratio C. to F. = 2 to 1.
(10½ C.R. 10½ F.R. 88 grm. P.) 210 grm. C. 105 grm. F. 88 grm. P.

		Grm.	Oz.	C.R.	F.R.	Grm. P.
THROUGH THE DAY	Milk, 7 oz. (⅓ pint)	—	—	½	½	7
(1 C.R., ½ F.R.)	Vegetables (List B), including half small grapefruit	—	—	½	—	—
BREAKFAST	Bread	114	4	3	—	14
(3½ C.R., 3 F.R.)	Bacon, collar or gammon, fried (List C, 2 portions)	30	1	—	1	8
	Tomato (List B)	—	—	—	1	—
	Eggs (2) (List C, 2 portions)				1	12
	Butter (List C, 2 portions)	12	⅜	—	1	—
	Fruit (List B, 1 portion)	—	—	½	—	—

		Grm.	Oz.	C.R.	F.R.	Grm. P.
DINNER	Eel, stewed (List C, 3 portions) .	84	3	—	1½	9
(1½ C.R., 3 F.R.)	Boiled potatoes (List A, 1 portion).	115	4	1	—	2
	Bread (List A, ½ portion) . .	19	⅝	½	—	1·5
	Butter (List C, 3 portions) . .	18	⅝	—	1½	—
TEA	Salad (List B)					
(1 C.R., 1 F.R.)	Bread (List A, 1 portion) . .	38	1⅜	1	—	3·5
	Sardines (List C, 1 portion) . .	22	¾	—	½	4·5
	Butter (List C, 1 portion) . .	6	¼	—	½	—
SUPPER	Cheddar cheese (List C, 3 portions)	45	1⅝	—	1½	13·5
(3½ C.R., 3 F.R.)	Bread (List A, 3 portions) . .	114	4	3	—	14
	Butter (List C, 3 portions) . .	18	⅝	—	1½	—
	Fruit (List B, 1 portion) . .	—	—	½	—	—
				10½	10½	89·0

that in all such cases the pancreas is primarily at fault, and it is reasonable to supply the deficiency by administering insulin, and this should certainly be done when complications are present such as gangrene, cataract, phthisis, angina pectoris, etc. In very mild *elderly* cases a diet with a C to F ratio of 1 to 1 of rather low calories will often be sufficient by itself to bring down the blood sugar to normal, though ketosis should be avoided. It is just in these cases that the high carbohydrate low fat diet may also be used with success, without insulin. In *young* subjects, however mild the case, insulin treatment should be instituted at once both to prevent the disease becoming worse and by resting the islands to produce some curative effect. Dextrose, say 2 ounces, should be given half an hour before a general anæsthetic, and 20 units of insulin half an hour before this.

After-Treatment. Patients must be taught to administer insulin to themselves, and should know how to test the urine for sugar. In elderly patients insulin may be discontinued at any time and no harm will result. Its administration may also become unnecessary. In the young the dose of insulin should be the maximum that the patient can tolerate without producing symptoms. With a normal threshold the urine should always be sugar free, and the Rothera's test for ketosis always negative. A positive Rothera's test often occurs when too little insulin is being used, so that the blood sugar remains above normal (**14**), but it is also due to there being too little carbohydrate or too much fat in the diet, and some modification should be made if this is the case. Patients should take less insulin if they are to take unaccustomed muscular exercise, since the latter tends to lower the blood sugar. A patient treated along the lines just laid down may find after a time that the dose of insulin to which he is accustomed is becoming too large, since he is experiencing hypoglycæmic reactions. This means that he is improving, and the dose must be diminished. If a cure with insulin is possible, it will certainly require some years before it is complete.

Infection. When the patient gets any acute infection such as tonsillitis, influenza, measles, pneumonia, gastro-enteritis, etc., the call by the body for insulin is increased.

(*a*) If the usual food is being taken, the ordinary dose of insulin is given. The urine should be tested every two or three hours, and if sugar appears a fresh dose of insulin should be administered before the midday meal, or at midnight (an extra feed being given). A gradual increase in the dose may also be necessary; but the insulin must, of course, be diminished as soon as the temperature falls and the urine remains sugar free.

(*b*) Suppose that no food is being taken (*e.g.* if there is vomiting). (1) If the urine contains sugar, the full dose of insulin should be given at the usual time, and the urine should be tested every two or three hours with fresh additions of insulin as has already been described. (2) If the urine does not contain sugar, half the usual dose of insulin should be given, and the urine tested every two or three hours, and fresh doses of insulin given if necessary. In both cases it would be better

to give glucose in 10 per cent. solution (a gramme per unit) half an hour after the insulin.

Diabetic Coma. At the beginning of diabetic coma a large dose of insulin, *e.g.* 60 units, should be given in part subcutaneously and in part intravenously with 60 grams of sugar by mouth in a pint of water, and the subcutaneous injection and sugar should be repeated every four hours, until the urine becomes free of ketone bodies; insulin and sugar are then continued in smaller doses at longer intervals. It is important to test every specimen of urine for sugar as it is passed, and to catheterize the patient in order to get a specimen, if there has been no urine to test for three or four hours. The reason for these precautions is that with the vigorous treatment necessary for diabetic coma, it is possible for the patient to pass into hypoglycæmic coma, without any intermediate return of consciousness, though this is unlikely if sugar is given as described.

An additional very important method of treatment is to give large amounts of fluid, containing the sugar and perhaps sodium bicarbonate. This will have the effect of keeping up the flow of urine and so will help to get rid of the poisonous aceto-acetic acid, which is probably the cause of diabetic coma. A stomach tube, Einhorn's tube, or a long nasal tube and funnel are essential for administering the fluid to an unconscious patient. The patient is made to lie on the right side, so that the fluid will gravitate at once towards the duodenum. A pint of warm sterile, isotonic solution is given every hour until a free flow of urine is established. On no account should this treatment be stopped if the patient vomits, but the actual duration of the administration should be prolonged so as to prevent distension of the stomach. Care must be taken by frequent examination to see that œdema of the lungs does not develop. From twenty-four to forty-eight hours of such treatment will be required before the patient becomes fully conscious after being in deep coma. When death occurs in spite of vigorous treatment, uræmia may be the cause, since in several cases the blood urea has been found to be high (**12, 13**). The patient must be kept flat to avoid heart failure.

Hypoglycæmia. The symptoms of hypoglycæmia have already been given. There is no danger of severe hypoglycæmia in the early stages of treatment, if the latter is carried out correctly. Later on, it may result from severe muscular exertion, especially if large doses of insulin are being taken in order that a high carbohydrate diet may be metabolised. Patients should carry some lumps of sugar with them to eat in case of emergency.

The symptoms of *hypoglycæmic coma* are to a certain extent the converse of diabetic coma. There is profuse sweating, the pulse is full and bounding, the veins stand out prominently. There may be some œdema of the lungs with cyanosis and fluid expectoration. The patient is convulsed, and there are no ketones in the urine. One patient complained of not being able to breathe. Hemiplegia has been reported. In a case of *hypoglycæmic coma* a subcutaneous injection of 15 to 20 minims of adrenalin (1 in 1,000), or failing this the same dose of pituitrin, may be given. This treatment will be of value if the liver contains a good store of glycogen. Plenty of sugar—4 to 8 ounces of cane sugar or dextrose—is given by mouth or by stomach tube. If the patient does not recover consciousness rapidly, an intravenous injection of a 5 or 6 per cent. solution of dextrose is given.

Spontaneous Hyperinsulinism. So far the hypoglycæmia of insulin administration has alone been dealt with. Spontaneous hyperinsulinism results from a tumour or hyperplasia of the cells of the islands of Langerhans. A number of cases of typical hypoglycæmic symptoms have now been described (*see* p. 471) with faintness or coma coming on if the patient went too long without food, and these have been relieved by giving sugar. Operation has sometimes disclosed the causal condition and the lesion has been successfully removed. Deep X-ray might be considered as an alternative method of treatment. In other cases a normal pancreas has been found and the problem as to the cause of

the symptoms has remained unsolved. Occasionally the liver may be responsible, though hypoglycæmia from liver disease usually means a very extensive involvement, and other signs of hepatic deficiency would be expected. There is the following possibility, though proof has so far been lacking.

Anterior Pituitary Deficiency. One of the many functions of the anterior lobe of the pituitary is to act as an antagonist to insulin. The diabetes of acromegaly is well known. Experimentally, it has been found that if in a depancreatised dog the pituitary is also removed, the animal loses his diabetes and the blood sugar may change from above to below normal. If the pituitary is removed alone, the normal antagonist to insulin is missing and hypoglycæmia readily occurs after fasting or exercise, and this can be remedied by giving sugar. In such a case preparations of anterior pituitary might be tried. Hypoglycæmia has been observed in the so-called pituitary cachexia of Simmonds's disease (*q.v.*).

Other cases of hypoglycæmia are excessive muscular exercise as in marathon runners, and exhaustion of glycogen stores by thyroid feeding. See appendix on p. 504.

THE THYROID GLAND

The normal thyroid gland contains cells which secrete colloid from which an iodine-containing crystalline substance, called *thyroxin*, has been isolated.

The human body normally contains about 8 to 14 milligrams of this substance; it is constantly being slowly formed, probably through the stage of di-iodotyrosine (**48**), and destroyed. The colloid is stored in the vesicles of the gland, having been secreted by the cells lining the vesicles, and after storage these cells become flattened and quiescent. Active secreting cells are cubical or columnar; they are arranged in the form of acini and are richly supplied with dilated capillaries. The thyroxin secreted may either become discharged into these capillaries, and so into the general circulation, or it may be stored as colloid in the acini producing a vesicle; at this stage the secreting cells become quiescent. Activity of the thyroid is indicated by increased secretion and by discharge of the colloid, probably through clefts between the lining cells (**15**). Thyroxin acts by stimulating the sympathetic nervous system, possibly by stimulating the adrenal medulla; an increase of adrenin has been found in the blood. The thyroid-adrenal apparatus also stimulates the liver to form glycogen as already explained and to mobilise it as glucose in the blood stream; the respiratory exchange is increased and the body temperature tends to be raised. Exposure to external cold stimulates this apparatus to increased functional activity, while heat inhibits it, and it is possible that fever is due to the action of bacterial toxins on this apparatus. It has been suggested that whereas the action of the adrenal is quick and short, the action of thyroxin is slow and sustained. The action of the thyroid on calcium metabolism is described under exophthalmic goitre.

The term goitre means an enlarged thyroid gland. It occurs in the following forms: (1) Hypertrophy, with the vesicles and secreting acini scattered diffusely through the gland. This is the goitre of puberty, pregnancy and the menopause, and it may follow oöphorectomy or ovarian disease; (2) Colloid goitre; (3) encapsuled adenoma, which may be solid or cystic (these three enlargements constitute forms of endemic or sporadic goitre); (4) primary exophthalmic goitre; (5) secondary Graves' disease or toxic adenoma; (6) malignant disease.

ENDEMIC OR SPORADIC GOITRE

Ætiology. Goitre is frequent in certain localities. In England it occurs in Derbyshire and in the West and South-west of England and Wales (**16**); it is commoner in the country than in the town. On the Continent it is frequent in the mountainous regions of Savoy, Switzerland, Northern Italy, the Tyrol, and

Styria. It is not, however, confined to the hills, but spreads down into the villages on the plains beneath. Endemic goitre may result from lack of iodine and tends to occur among people who live far away from the sea. It also results from an increased requirement for iodine, which is unsatisfied. Various factors may contribute to this increased requirement: contamination of drinking water with some organic material in the soil, possibly fæcal; infection, since acute goitre sometimes occurs in epidemics (**17**); unidentified substances (possibly cyanins, which inhibit tissue oxidation) in cabbage and certain other vegetable foods; excessive ingestion of fat; puberty and pregnancy; lack of vitamins A and C may cause goitre in experimental animals in spite of there being plenty of iodine present (**47**). Goitre is commonest in females and in young people. Sporadic goitres occurring in non-goitrous districts are to be explained along these same lines. Endemic goitre is often found to be associated with *myxœdema* and *cretinism*.

Pathology. A deficiency of iodine stimulates activity on the part of the gland as already described, with proliferation of secreting cells, increase of fibrous stroma and blood supply, and absence of colloid. At any stage in the process there may be involution with complete recovery. On the other hand, this active stage may be followed after some years by degeneration of two kinds: (*a*) atrophy of the cells and their replacement by fibroblasts, leading on to fibrosis and cyst formation, or (*b*) great enlargement with increase in the colloid of the gland—"colloid goitre," which represents a resting stage of the gland with accumulation of colloid and iodine after the period of previous activity, due to want of iodine. Adenomas of the thyroid probably arise from cell rests which grow under the same stimulus that produces colloid goitre. The differentiation of adenomas from colloid goitres is not absolutely clear cut, and intermediate types are common. Adenomas may pass through the same stages of involution, atrophy, cyst formation, or colloid formation, as affect the whole gland. As a rule adenomas are multiple and develop about the age of puberty. The size of a goitre varies from a moderate prominence of the neck on either side to a mass as large as the fist or a fœtal head, which hangs down in front of the upper part of the sternum, such as those which have been so common in Switzerland and Savoy. In the lymphadenoid goitre, there is epithelial keratinisation with aggregation of lymphocytes in the gland and ultimate fibrosis; vitamin A deficiency is a cause.

Symptoms. Enlargement of the neck and a feeling of fulness are often the only symptoms. If the goitre is very large, there may be dysphagia from pressure on the œsophagus, or dyspnœa from compression of the trachea, or of the recurrent laryngeal nerves. If there are any symptoms other than the local effects of the enlarged gland, they are indicative of diminution of the thyroid function, or hypothyroidism (*see* Myxœdema). The basal metabolism is normal or slightly reduced in colloid goitre.

Carcinoma occurs generally after middle age, and forms a hard, rapidly growing tumour, which infiltrates and presses upon surrounding parts. The functions of the gland are generally carried on; and if in such a case there are secondary growths in internal organs, the total removal of the thyroid does not cause myxœdema.

Diagnosis The thyroid nature of any enlargement is proved by its movement up and down with the larynx during the act of swallowing.

Treatment. Prophylaxis in areas of endemic goitre consists in administering 0·1 gramme of sodium or potassium iodide once a day for ten days in the spring and autumn. In the canton of Appenzell, in Switzerland, 0·25 to 0·5 gramme of potassium iodide has been added to each kilogram of salt, so that all the inhabitants cannot fail to get some. Abnormalities in the diet, as described in the ætiology, must be corrected. Congenital goitre can be prevented by treating the mother during pregnancy. In the treatment of the earliest stage of goitre, when

adenomas are not present iodine may be given internally as tincture in doses of 2 or 3 minims thrice daily. The administration of iodine has caused adenomatous goitres to overact, and hyperthyroidism may continue for years without further administration of iodine. Iodine does not intensify the hyperthyroidism of true exophthalmic goitre. Iodine treatment is not so successful in a developed colloid goitre, and thyroid extract may be tried. Surgical measures may be necessary in very hard or very large goitres and in malignant disease, if recognised sufficiently early; they are the enucleation of an encapsuled tumour and the removal of the greater part of the gland. The Röntgen rays may also be employed.

EXOPHTHALMIC GOITRE

(*Graves' Disease, Basedow's Disease*)

This disease, occurring more frequently in women than men in the proportion of 3 to 1 (**18**), was first described by the Dublin physician Graves in 1835, and by a German physician, Basedow, in 1840. The prominent symptoms are: protrusion of the eyeballs, enlargement of the thyroid gland, frequent action of the heart, and tremor.

Ætiology. Broadly speaking cases fall into two groups; but there is no hard and fast line between the two groups and the distinction has been considered rather artificial.

(1) *Primary Exophthalmic Goitre.* The onset is sudden and there are frequent remissions and exacerbations. There are corresponding alterations in the respiratory exchange or basal metabolic rate (*see* p. 459). The latter is high when the disease is severe, and *vice versâ*. It occurs usually in young persons. Sometimes there has been a neurotic tendency, as shown in hysteria or epilepsy, or mental disease in the family. In a few cases it has followed rapidly upon some emotional or mental excitement, or even direct injury to the head. Hyperthyroidism was frequently noticed among soldiers during the war, and was due to the intense mental strain. A hereditary connection has sometimes been observed: it has been observed in mother and son or daughter; more often it attacks brothers and sisters in the same family. The fact that the incidence of exophthalmic goitre was diminished in Germany during the war suggests that abundant feeding may help in its causation (**19**). The distribution of exophthalmic goitre in England and Wales is rather similar to that of endemic goitre; the incidence is greater in rural districts than in towns (**16**).

(2) *Secondary Graves' Disease.* There is often a history of previous swelling of the thyroid, indicating that the gland has been for some time the site of chronic changes. Symptoms of over-activity often begin to develop about the age of thirty-five or forty years, and may result from the administration of iodine to a case of adenoma. The disease pursues a steady course over years with symptoms that gradually become more severe. There are no remissions. There is a slow, steady increase in the respiratory exchange. Exophthalmos is often not very marked. There is a special liability to cardiac irregularities, such as auricular fibrillation, and advice may first be sought on account of cardiac failure. When there is evidence of adenoma of the thyroid these cases are often called *toxic adenoma*.

Pathology. That the disease is due to hypertrophy of the thyroid producing an excess of thyroxin is shown by the resemblance of the symptoms to those which follow large doses of thyroid extract, by their contrast with those of myxœdema, and by the improvement which has occurred after partial excision of the hypertrophied gland. Discussion has, however, taken place as to whether the disease is merely due to an over-production of normal thyroxin or whether the thyroxin is altered in some way, for instance, by containing less iodine in the molecule than normal—whether there is a true hyperthyroidism or a thyrotoxicosis. The arguments in favour of the latter view are that the symp-

toms cannot be exactly reproduced by giving excess of thyroid to animals, *i.e.* there is no exophthalmos. Further, there are some cases in whom some symptoms of hyperthyroidism and myxœdema appear to co-exist; but this does not necessarily mean that the two diseases co-exist, because the hyperthyroidism symptoms may be a relic of a previous over-activity, which has now died down. On the whole, there is not sufficient evidence for the second view. It is probable that in some cases the activity of the thyroid may be due to stimulation by an excess of the thyro-tropic hormone from the anterior pituitary (*q.v.*).

The thyroid intoxication leads to stimulation of the sympathetic, increased mobilisation of glycogen by the liver and increased respiratory exchange. Patients are very tolerant to insulin, which antagonises thyroxin by inhibiting the mobilisation of glycogen. In fact, as far as their effect on the liver is concerned, diabetes mellitus and exophthalmic goitre resemble one another. But their effect on the muscles is very different, since in exophthalmic goitre the sugar is burnt there, but in diabetes this is largely prevented (**15**). The sympathetic stimulation may account for the exophthalmos, von Graefe's sign, tachycardia, and sweating. In Cannon's well-known experiment the phrenic nerve of the cat was sutured to the cervical sympathetic on the same side. The excitation of the sympathetic thus produced caused exophthalmos on the same side. The exophthalmos has been regarded as due to the stimulation of Müller's muscle, which lies in the membrane lining the orbit over the spheno-maxillary fissure; but in man the muscle is rudimentary, consisting of a few scattered fibres. Another possibility is that the eyeballs are pushed forward by œdema fluid, since œdema of the recti has been found, and then there follows a secondary deposit of fat.

The emaciation is due to the high respiratory exchange, combined with alimentary disturbances which hinder absorption. As the fat depôts become exhausted protein is drawn upon, so that there is also an abnormally high protein breakdown. In spite of the increased combustion, the body temperature is not raised, except occasionally, because, owing to profuse sweating, the loss of heat from the body is increased. There is a pronounced excretion of calcium not only in the urine but in the fæces too; in fact, depletion of calcium in a healthy subject is more readily brought about by thyroid extract than it is by parathormone or acids. In contrast to hyperparathyroidism (*q.v.*) there is no rise of blood calcium, in fact, this tends to be low (and yet thyroid extract *raises* the blood calcium in parathyroid tetany!); on X-ray examination the bones may show deficiency of calcium (**21**).

Morbid Anatomy. The vesicular and parenchymatous cells proliferate. The contents of the vesicles lose their colloid nature and become mucous and granular. In later stages the gland may become fibrous or cystic. In primary exophthalmic goitre these changes are diffused throughout the gland; in secondary Graves' disease some parts of the gland show activity; other parts show colloid storage, fibrosis and cyst formation; there may or may not be definite adenomatous changes present.

The thymus gland is often persistent and enlarged. A thyro-toxic myocarditis with necrosis and hyaline changes of muscle fibres occurs in long-standing cases (**20**).

Symptoms. The symptoms may come on suddenly, but generally they come on rather gradually, and, as a rule, the cardiac symptoms appear first, the protrusion of the eyeballs and the thyroid swelling not till some months later. Occasionally they may appear in a different order, or one or other of the three chief symptoms may be absent; but the circulatory trouble is the most constant. In the fully developed disease, the *heart* beats quickly and forcibly; the impulse is felt over an abnormally large area. The carotids and large arteries pulsate with great force, and the patient feels the violence both of the cardiac beat and the arterial throbbings. The pulse may reach 140. The electrocardiogram is often

normal; but auricular fibrillation or a prolonged P.-R. interval may be present, and the T. and P. waves may approximate in size to one another (**20**). Very occasionally heart block is observed, especially if digitalis has been given in large doses. The patient suffers from shortness of breath on exertion in proportion to the cardiac disturbance. In course of time the heart may become hypertrophied and later dilated. Variations in pulse rate are usually followed closely by corresponding variations in basal metabolism; but sometimes the pulse may still remain high, from damage to the heart, after the activity of the disease has died down, so that the basal metabolism gives a more certain picture of the activity of the gland.

The enlargement of the *thyroid body* is symmetrical, usually moderate in dimensions, and rarely equal to that of the larger endemic goitres. If the hand be placed over it, a thrill can be felt which is due to the movement of blood in its dilated vessels, and a systolic murmur can be heard with the stethoscope.

The *prominence of the eyeballs* (exophthalmos, proptosis) with widening of the palpebral fissure is the most striking characteristic of the disease, and gives to the patient an unpleasant, terrified, staring appearance. It affects both eyes, and may reach such a degree that the sclerotic is seen both above and below the cornea, and the eyelids are unable to meet. Even when the eyelids can be voluntarily closed, they may lie apart during sleep; and if the exophthalmos is extreme, there may be irritation and ulceration of the cornea as a result of exposure. There is infrequent blinking (Stellwag's sign). In association with the exophthalmos there is a want of uniformity in the movements of the eyeball and the upper lid, so that, when the patient lowers the eyeball to look down, the upper eyelid is not depressed to a corresponding extent (von Graefe's sign). This is not present in every case, although it has sometimes been noticed even before the protrusion. On the other hand, when present it is of importance, as it does not occur in other kinds of exophthalmos. Weakness of the convergent muscles may be also present (Möbius' sign), and in some cases diplopia or definite paralysis of some or all of the ocular muscles. The pupil and accommodation are unaffected, and the ophthalmoscope reveals little beyond overfull and tortuous retinal veins.

A fourth very constant symptom is a more or less continuous fine *tremor* of the limbs, and even of the whole body. Muscular weakness and pain are also very characteristic. The patient has difficulty in extending the knees, so that going upstairs can only be carried out by pressing on the bannisters with the arms; but the arms and trunk muscles may also be affected. There may be widespread paresis one evening and complete recovery the next morning after a night in bed. Is this associated with depletion of the body of calcium?

The sufferer may be irritable, restless, or hysterical, but not anæmic. In some cases melancholia, hallucinations and even mania have occurred; and tetany is an occasional event. The nervousness and cardiac action are increased by attention or by any excitement. The patient is generally thin, and may waste a good deal. A moderate degree of fever is occasionally present; and some patients show various pigmentary changes of the skin, such as moderate bronzing, chloasma or leucodermia. A subjective feeling of heat, flushing of the head and neck, sweating and intermittent albuminuria have been noticed in different cases. Patients are very subject to attacks of diarrhœa, sometimes with vomiting. Glycosuria sometimes occurs, owing to hyperglycæmia; that is, the patient cannot take the normal amount of sugar without its appearing in the urine. True diabetes mellitus sometimes follows, and patients with Graves' disease have sometimes died of diabetic coma. The fasting blood sugar is, however, usually normal; but the sugar tolerance curve is rather delayed. The symptoms are liable to aggravation from time to time.

Diagnosis. There is difficulty in diagnosis in the early stages, before exophthalmos or swelling of the thyroid is noticeable. The disease must be

distinguished from tuberculosis. A persistent tachycardia with a normal electrocardiogram is suggestive, especially if there is sweating as well. However, auricular fibrillation is common in secondary Graves' disease. The respiratory exchange should be measured (*see* p. 459), which also indicates the severity of the disease. A blood calcium of 9 mg. or under and a threshold excitability for muscular contraction under 2 milliamperes are also suggestive.

Prognosis. Campbell has followed up the histories of 127 cases treated medically at Guy's Hospital between 1908 and 1917. The results agreed very closely with a similar investigation carried out previously by Hale White. At the end of the period 8 per cent. were absolutely well; 30 per cent were almost well and able to do a full day's work, but one or two signs persisted slightly; 34 per cent. were much improved, being able to do light work; 13 per cent. were not improved or worse; 15 per cent. were dead from the disease. There is a very great improvement in the prognosis if treatment by means of operation or deep X-rays is carried out. In 60 per cent. of cases the patient will be able to do full work without difficulty (**49, 50**).

Treatment. A simple satisfying diet with plenty of carbohydrate should be employed. Alcohol and tobacco are likely to be prejudicial. Rest in bed for some weeks certainly has a beneficial effect on patients. In a series of fifty-one patients in which this was the only treatment, three-quarters had a basal metabolism under 18 per cent. within six months (**4**). When the patients get up very mild exercise should be allowed; but plenty of rest should be taken. Exophthalmic goitre cases are tolerant to insulin, and some benefit may be produced by giving 15 or 20 units twice a day on a normal diet, possibly combined with parathyroid $\frac{1}{10}$ grain three times a day by mouth (**23**). The application of ice to the thyroid is soothing.

There are two chief methods of reducing the activity of the thyroid, viz., (1) Deep X-rays; (2) removal of the gland by operation preceded sometimes by ligation of one or two thyroid arteries. X-rays are usually employed at the beginning of the disease and operation may be considered later if no improvement results. Prolonged X-ray treatment makes subsequent operative treatment more difficult. In true exophthalmic goitre great temporary benefit may be obtained by giving Lugol's solution (5 per cent. iodine in 7·5 per cent. potassium iodide solution), 15 drops once a day. The metabolism falls to normal in a week or two. A similar result may be obtained with iodine in 10 per cent. alcoholic solution. The dose is 15 minims a day, and this is reduced to 3 or 4 minims after a week or two (**22**). This treatment may be of great value as preoperative treatment, and it may also be used in combination with X-ray treatment.

MYXŒDEMA

(*Cachexia strumipriva*)

Myxœdema and cretinism are the results of disease of the thyroid gland, causing deficiency of its secretion—hypothyroidism; cretinism is congenital; myxœdema arises sometimes in childhood (juvenile myxœdema), but more commonly in later life.

Ætiology. Myxœdema is much more frequent in women than in men; and, in the majority of cases, the symptoms begin between the ages of thirty and fifty, though they have begun as early as eight and a half and as late as sixty-seven. Some indications of heredity have been observed, and it has been more often seen amongst the poorer classes. All types of hypothyroidism are common in districts where goitre is endemic.

Morbid Anatomy. The changes in the skin are some nuclear proliferation and development of connective tissue in the neighbourhood of the sweat glands, sebaceous glands, and hair follicles. Gelatinous and œdematous skin, to which

the name *myxœdema* was given by Ord, have only a few times been recorded. There is a fair amount of subcutaneous fat.

The thyroid body is usually reduced to one-half or one-third of its normal size ; it is pale, yellowish white or buff-coloured, tough or indurated, fibrous, or structureless. The gland consists mainly of fibrous tissue, with scattered groups of cells, the remains of the vesicles ; and, finally, nothing but dense fibrous tissue is left. The pituitary body has been enlarged, or enlarged and degenerated in some cases ; in a case of the writer's the suprarenals were atrophied. Arteriosclerosis and myocardial degeneration are common. There is a decreased output of calcium.

Symptoms. These are at first insidious, so that in most cases the disease has not been noticed till it has been well developed. The appearance is then characteristic ; the face is expressionless, not unlike paralysis agitans ; the nose, eyelids, and lips are puffy ; the skin of the face has a most characteristic fine wrinkling, the colour is markedly yellow with a rather bright red patch on each cheek, and almost livid lips. The skin of the body generally is thickened, and the legs and feet have the appearance of slight œdema, although in many cases, but not in all, pitting is entirely absent. The shape of the hand also undergoes changes : it becomes broader opposite the heads of the metacarpal bones, and the fingers become thick and uniform in shape ; this change has received the not very distinctive name of " spade-like." The feet are similarly affected. Perspiration is often deficient or absent, the skin dry and scaly, and the hair falls out, leaving only a thin covering on the head, or causing actual baldness of the scalp (" frontal alopecia " and " cassowary neck "), the outer third of the eyebrows (" eyebrow sign "), and eyelids. The nails are stunted and brittle. The mucous membranes show the same change ; at any rate, the uvula and soft palate are swollen, and the tongue is large and thick ; moreover, the teeth become carious or loose. The nervous system of the patient is the next thing that strikes one : she appears dull, apathetic, and slow in thought and movement, and is often deaf. She speaks languidly and deliberately, as if the thick tongue mechanically interfered with articulation, but the slow movements of the eyes and the muscles of expression accompanying speech indicate that the neuro-muscular apparatus is also faulty. The voice is low-pitched and husky, from swelling of the vocal cords. On the mental side, memory is defective ; the patient is often irritable, or suspicious, or dull and sleepy ; and hallucinations, delusions, and convulsions have been noticed in a certain proportion of cases. Complaint may be made of headache and rheumatic pains. Tetany sometimes occurs, as it does after the operative removal of the thyroid. The temperature is mostly subnormal, the patient suffers from cold very readily, and the hands and feet are often cold and blue.

The pulse is weak or slow ; in advanced cases there is cardio-vascular disease with absent or inverted T waves and a low voltage electrocardiogram and arteriosclerosis ; the urine often contains albumin. Examination of the blood shows a microcytic anæmia. The bowels are constipated. The tolerance for sugar is increased, so that large quantities, even up to 10 ounces in some cases, can be taken without any glucose appearing in the urine. In females menorrhagia is common ; more rarely there is amenorrhœa. Epistaxis, hæmorrhage from the gums and hæmorrhoids are not uncommon. On palpation the thyroid gland is usually small and the rings of the trachea are palpable below the cricoid, where the isthmus should be. The progress of the case is slow ; patients are known to have had the disease ten years or more without material change. Nevertheless, it undoubtedly shortens life ; the sufferers die from myocardial and arteriosclerotic changes or from intercurrent diseases, such as pneumonia and bronchitis, or sink from general or nervous exhaustion.

Diagnosis. Myxœdema is most often confused with Bright's disease, or myocardial degeneration ; but though there may be a little albuminuria, the

renal function is normal. The abnormalities in the electrocardiogram disappear with treatment, which is helpful in diagnosis. Conclusive evidence may be obtained from a basal metabolism test, which may be 40 per cent. too low in a very severe case.

Treatment. Thyroideum (B.P.) made from the dried gland in doses of 1 to 5 grains in cachet or pill may be given by mouth once or twice daily. Synthetic thyroxin may also be given by mouth, the smallest daily dose being 0·2 mgm. In very severe cases of myxœdema oral treatment is not always successful, possibly because absorption from the alimentary tract is so slow. Intravenous injection of a specially prepared solution of thyroxin may be tried, *i.e.* three 5 mgm. doses at weekly intervals. However, it is safer to begin with an injection of 1 or 2 mgm., since severe reactions may be met with twenty-four hours after the administration; the symptoms are rapid pulse, headache, tremors, nausea, vomiting or diarrhœa, and pains in the back and legs. 3 : 5 di-iodothyronine, a substance allied chemically to thyroxine, and more soluble, has been used with success (**51**). The treatment should be controlled with the basal metabolism test. When the store of thyroxin in the body has once been increased to the right amount by this means, administration may be continued by mouth. In whatever way thyroid is administered it is advisable to begin with small doses; otherwise anginal symptoms may be precipitated.

CRETINISM

Cretinism is seen as an *endemic* disease in the mountainous parts of Europe (Switzerland, North Italy, and Savoy) and in Northern India (Chitral and Gilgit), where goitre also is extremely prevalent. The two conditions are often associated in the same individual; indeed, many of these cretins are goitrous; of 208 cretins in India, McCarrison found eighty-eight to be goitrous.

Sporadic cretinism occurs in other parts, *e.g.* in England; in the subjects of it the thyroid is deficient, or there is a slight goitre.

Pathology. The association of endemic cretinism with goitre in the individual and in the community, the absence of the thyroid in some cases, and the resemblance to myxœdema, show the relations of the disease to the thyroid gland. When endemic cretinism and goitre appear in the same individual, the former precedes the latter, and so is not due to it. The cretinism is due to the goitrous condition of one or both parents, and the defective thyroid function in the mother acts prejudicially in the fœtus. The lesion involves the parathyroid as well as the thyroid bodies.

Symptoms. Cretinism is characterised by stunted growth, a large, broad head, thick features, wide separation of the eyes, flat nose, large mouth, much wrinkling of the coarse and rough skin even in early life, a narrow chest, full abdomen, usually an umbilical hernia, crooked legs, and considerable mental deficiency, amounting to idiocy.

The characteristic features are generally noticed in the latter half of the first year of life; walking is acquired very late, and the arrest of growth may be such that an adult cretin is not taller than a child of five or six. Puberty is long delayed, or the sexual functions are entirely absent. Speech is acquired very slowly or not at all, and some are deaf mutes and idiots. Nystagmus, strabismus and spastic rigidity of the legs occur in some cases. Above the clavicles are often found subcutaneous tumours formed of masses of fat. Remarkable defects are present in the osseous system; the basi-occipital and basi-sphenoid are prematurely ossified; the long bones are permanently shorter than normal, the legs are bowed, and fibrous tissue from the periosteum grows in between the epiphysis and the shaft of the bone. The centres of ossification of the bones of the foot and wrist appear very late. Radiographic examination of these structures affords a valuable means of diagnosis.

Treatment. In cretinism, as in myxœdema, thyroid extract has been

used with much success. Under its influence children have grown rapidly, have lost the œdematous infiltration of the tissues, and have become more intelligent. It must, however, be admitted that the child improves physically more readily than he improves mentally, especially when treatment is begun late.

THE PARATHYROID GLANDS

The parathyroid glands are small bodies, generally four in number, situated near or within the substance of the thyroid, and consisting of groups of epithelioid cells in a fibrous meshwork, but without the vesicular arrangement and colloid contents of the thyroid; each measures 6 or 7 mm. by 3 or 4 mm. by 1½ or 2 mm., and weighs about ½ grain. *Parathormone*, the active principle of the glands, can be obtained commercially. Injection at first causes an increased output of phosphorus in the urine with a fall in the inorganic phosphorus of the plasma; then there is an increase of calcium in the blood, *hyper-calcæmia*; at a certain critical level of serum calcium the blood phosphorus suddenly rises, presumably due to altered renal function, as the non-protein nitrogen of the blood rises as well. Severe hyper-calcæmia causes definite symptoms in dogs; but man is not so sensitive. Parathyroid has been used in many varieties of ill health, infections, etc., in which the amount of ionised calcium in the serum has been found low (*see* Chorea). Unfortunately the action of parathormone is variable and immunity to the drug often develops, so that it is no longer effective (**21**).

Changes in the parathyroids—hyperplasia, fatty degeneration, fibrosis, cyst and colloid formation—may occur.

Hyperparathyroidism. Hyperplasia of a gland may form a tumour in the neck palpable on swallowing. The serum calcium is raised up to 16–17 mgm. per cent., the plasma phosphatase is high and calcium is lost in the urine daily; the blood phosphate is always low. The calcium comes from the bones, and gives rise to the disease known as *generalised osteitis fibrosa of von Recklinghansen.* This disease is twice as common in women as men.

Symptoms. There is pain in the bones and X-ray examination shows a mottled appearance due to spaces (*osteoclastoma*) diffusely spread through the bones, which may give rise to spontaneous fractures; there may be thirst, polyuria, renal calculi with colic, hypotonicity of the muscles, nausea, vomiting and wasting, which is common in severe cases. Improvement sets in after excision of the tumour; but tetany very commonly results from a rapid fall of blood calcium. This may be relieved by parathormone, which should always be kept available for use (**21**). Deep X-rays might be an alternative to operation. In the commoner *focal osteitis fibrosa* there is no abnormality in the calcium metabolism.

TETANY

Tetany may arise from disease of the parathyroids, in *spontaneous hypoparathyroidism*, but this is rare. Post-operative tetany after removal of the parathyroids in thyroid operations is well known; but there are many other causes of clinical tetany.

Ætiology. It occurs at all ages, but is especially frequent in infants and young adults. In children males are more often attacked than females; in older people the reverse holds good. In children rickets and diarrhœa are the commonest predisposing causes; in adults the causes are pregnancy and lactation, recovery from febrile diseases, the existence of dilatation of the stomach and intestinal obstruction and, in the case of the writer's, gastro-colic fistula with oss of free HCl in the stools. It has occurred after the operative removal of the thyroid body when the parathyroids have been removed as well. McCarrison says it is common in women in the high valleys of Gilgit (Northern India), and that all such sufferers are goitrous. In these cases it may be due to associated parathyroid disease. Similar paroxysms have been seen as the result of ergotism

and in association with osteomalacia, and from poisoning with sodium bicarbonate. Tetany is sometimes present in certain nervous diseases, particularly in epilepsy. Tetany also occurs in epidemics among workmen at certain seasons of the year, in particular European cities (Vienna, Heidelberg). It may be produced artificially by continued forced breathing, with washing out of CO_2 from the body (*acapnia*).

Pathology. The essential characteristic of the disease is over-excitability of the peripheral motor neuron, and it has been suggested that want of oxygen is the primary cause and that a number of agencies may bring this about (**26**); thus, *alkalæmia*, due to injections of sodium bicarbonate, or to forced breathing (which washes out CO_2 from the body), may act by rendering more difficult the dissociation of oxygen from oxy-hæmoglobin (pleonexy), so that the tissue oxygen tension falls; the latter also occurs with guanidine and histamine poisoning, both causes of tetany. Parathyroidectomy does not itself cause a lowered O_2 tension, though it is possible that owing to the low blood calcium the oxygen supply to the cells is interfered with. Such interference is known to occur in cyanide poisoning. Another way of producing experimental tetany is by repeatedly washing out the stomach of a dog whose pylorus has been obstructed. The tetany can be stopped by administering sodium chloride intravenously. It is thus possible to group together the tetany of dilated stomach, intestinal obstruction, and gastro-colic fistula as due to a loss of chloride from the body, and in these cases the plasma chloride has been found to be low and the plasma bicarbonate raised, and there is also an increase of urea in the blood. The tetany is not due to alkalæmia in these cases (**33**), and here again it may be due to a low ionic calcium (**24**); *i.e.* in hysterical hyperpnœa a low calcium has been found in the cerebro-spinal fluid.

Symptoms. There may be some discomfort or malaise, or stiffness in the arms, or tingling for some hours or days before the attack. Sometimes the paroxysm comes on suddenly without warning. The hands are then bent on the wrist; the fingers are flexed at the metacarpo-phalangeal joints, extended at the phalangeal joints, and pressed closely together with the thumbs bent into the palm of the hands, so that the fingers form a cone ("*main d'accoucheur*"). The elbows are slightly flexed, and the arms are adducted to the sides. Sometimes the four fingers are flexed into the hand, the wrists extended, and the elbows fully flexed. In the lower extremities, the foot is extended on the leg, the tarsus arched, and the toes flexed and crowded together. These are the characteristic contractions, and in most cases these alone occur. In very severe cases spasm affects the muscles of the abdomen, chest, face and tongue, as well as those of the back, causing slight opisthotonus, and of the eyes, causing strabismus. There may be some cramp-like pain in the parts affected; the back of the hands may be tumid, and the veins swollen. There may be sweating, flushing, and slight rise of temperature. The spasm ceases in from five to fifteen minutes, or it lasts one, two or more hours; it gradually subsides, and recurs after an interval of some hours or days.

In the intervals the nerves and muscles show an increased susceptibility to mechanical irritation (Chvostek). Percussion of the nerves causes contractions in the corresponding muscles, and this is well shown in the face by percussing midway between the zygoma and the angle of the mouth. Stroking the face from above downwards causes contraction of the muscles one after the other. Trousseau first showed that in the intervals a fresh paroxysm could be brought on in a few minutes by firmly grasping the arms, or by pressure on the nerves and arteries. The motor nerves also are unduly susceptible to faradism, and still more to galvanism (Erb). Hyperexcitability, suggestive of tetany, exists if galvanic currents below 2 milliamperes produce a contraction on cathodal closing or anodal opening (*see* p. 628). The normal range is between 2·5 and 3·0 milliamperes.

But there is not always an interval between the paroxysms. In infants a continuous spasm is more common, and in adults the spasm may not entirely relax, so that this form is called *remittent*, while the form with complete intervals is called *intermittent*. In *latent* tetany, which is fairly common, there are no spontaneous attacks of spasm.

In rachitic children the undue excitability of the nervous system is represented not only by tetany, but also by laryngismus stridulus, and by convulsions.

In parathyroid tetany lens opacities, which in the earlier stages may be demonstrated by the slit lamp, brittleness and ridging of the nails, transverse ridging of the teeth from defective enamel, and loss of hair may occur (**21**).

The disease lasts from a few days to a few weeks, and recovery is the rule. Occasionally some weakness of the legs remains for a short time after recovery, and muscular atrophy and fibrillary tremors have been seen. But death may occur from exhaustion when the paroxysms are severe, or from pneumonia as a result of interference with respiration, or in infants from the diarrhœa which caused the disease.

Diagnosis. The distribution of the spasms—namely, their occurrence chiefly in the hands and arms—distinguishes it from *tetanus*. *Hysterical* contractions may assume the form of tetany; they are generally unilateral, and are associated with other hysterical conditions. Latent tetany can be diagnosed by Chvostek's and Trousseau's signs, and by the presence of certain symptoms commonly associated with it, viz., defects in the enamel of the teeth, perinuclear cataracts, dystrophies of the hair and nails and recurring conjunctivitis.

Treatment. Parathormone may be given subcutaneously, intramuscularly or intravenously in doses of 10 to 30 units a day; vomiting is the first symptom of an overdose. Calcium chloride (15–20 grains, in the case of infants) is given by mouth every four hours (**25**). The chlorine passes into the circulation to supply the deficiency of chloride, while the calcium is excreted by the bowels. Ammonium chloride in large doses may also be tried. The ammonia is converted into urea, so that here also the hydrochloric acid may be utilised. These drugs may also be given per rectum. The predisposing condition of the patient should be as far as possible removed. Thus gastric dilatation should be treated by surgical operation (gastro-jejunostomy); in children, diarrhœa should be treated, and rickets met by cod-liver oil, iron, suitable diet, etc.; women should give up nursing their children, and should take iron and other tonics.

THE THYMUS GLAND

The thymus gland weighs about ½ per cent. of the body weight from birth to 1 year, and diminishes to ·085 per cent. of the weight between 11 and 16 years. Even in adult life, however, its remnant can be found if carefully sought, consisting of fibrous and fatty tissue, islets of lymphocytes, and a few Hassall's corpuscles (Dudgeon). In atrophy, which is associated with marasmus or tuberculous and other chronic wasting diseases in children, the organ is reduced in size. Enlargement of the thymus may occur in a number of diseases, of which the most important are leukæmia, especially the lymphatic form, Hodgkin's disease, exophthalmic goitre and myasthenia gravis. The gland may be converted into a fibro-caseous mass as a result of tubercle, and it may be the subject of new growth.

In the past importance has been attributed to the thymus as the cause of sudden death in the condition known as *status thymo-lymphaticus*. This diagnosis has been made to account for a death under an anæsthetic, particularly in a child, when the cause of death was not obvious. In these cases there is often a general hyperplasia of the lymphatic structures throughout the body, while the thymus has been considered large. On the other hand the lymphoid tissue is probably no larger in amount than is present in any normal child, though in a

child who has died of any wasting disease the lymphatic tissue shows in the atrophy. A recent investigation has now pointed to the thymus gland as also being within normal limits, so that the diagnosis of status thymo-lymphaticus or *status lymphaticus* has no foundation in fact, and in future such deaths must be attributed to the anæsthetic directly, or in other cases of sudden death to an unknown cause.

THE SUPRARENAL CAPSULES

The suprarenal capsules consist of two parts :—

1. The *cortex* (*interrenal system*) is derived from mesodermal cells closely related to the cells of the genital organs. It contains cholesterin esters and lecithin in large quantity, and its yellow colour is due to these. It is about 90 per cent. of the whole gland in weight, and becomes rather larger during pregnancy. The lipoids of the cortex disappear within a few days as the result of an acute febrile illness of an infective character, which is fatal. On the other hand, they are not discharged in cases of inanition, *e.g.* in malignant disease. In these respects they offer a marked contrast to the ordinary body fat. The cortex is related to sex. In rare cases, where the cortex is hypertrophied, there is precocious development of the sexual organs, with an increase of male characteristics. More commonly these symptoms are caused by carcinoma of the cortex (*q.v.*). Conversely, hypoplasia of the adrenals has sometimes been seen in cases of disappearance or original absence of hair from the genitals and hypoplasia of the genital organs. The cortex contains a reducing substance, hexuronic acid or ascorbic, identical with vitamin C (*q.v.*), which inhibits the *oxidases* of the body. When the reducing substance is absent, as in Addison's disease, the oxidases have full play in converting the hydroquinone groupings in the constituent molecules of the body into the darkly coloured quinone groupings and so pigment the body (**27**) ; it is by oxidation that a freshly sliced apple goes dark on exposure to air. Finally, the cortex contains a specific substance which prevents Addison's disease, known as suprarenal cortical extract, eschatin, eucortone or cortin.

2. The *medulla* is derived from the same cells as the ganglion cells of the sympathetic nervous system. It has a characteristic staining reaction with bichromate, and so is called a *chromaffine body*. It elaborates a substance, *adrenin* or *epinephrin*, which has been prepared synthetically, and is chemically ortho-dioxyphenyl-ethanol-methylamine. This substance is poured out into the circulation on stimulation of the splanchnic nerves. It has a powerful action on all sympathetic nerve endings. Under normal circumstances this liberation into the circulation occurs when the powerful emotions of excitement, pain, fear and rage are produced ; the processes associated with digestion and reproduction are inhibited ; the animal becomes prepared for battle or for flight. The pupils are dilated ; the skin becomes pale ; the hairs stand on end ; the heart is accelerated. The sugar in the blood is increased by action on the liver ; the skeletal muscles show increased power and are less readily fatigued. The coagulability of the blood is increased, which is of advantage in case the animal is wounded. There can be little doubt that the proverbial strength of the madman is due to the outpouring of adrenin, while his keepers, who experience his power, are not actuated by the same strong emotions. In dementia præcox it has been found that the medulla is deficient and shows histological changes (**28**).

It has been suggested that the regulation of the heat produced in the body is largely due to the supply of adrenin acting on the liver, and mobilising glycogen, and that fever results from the rapid liberation of adrenin. On this hypothesis the sudden hyperpyrexia associated with intense congestion of a hæmorrhage into the medulla is a symptom of acute *hyper-adrenalism* (**15**). Such hæmorrhages are not uncommonly due to specific fevers such as malaria, pneumonia, erysipelas, purpura, etc., where congestion of the medulla might be expected ; but hæmorrhage may also result from thrombosis of the adrenal veins ; and so in this case the

pyrexia is not due to infection at all, but to sympathetic stimulation; it is a "sympathetic fever."

In some of these cases the fever may subside, and be followed by a subnormal temperature, asthenia and collapse—symptoms of acute *hypo-adrenalism* because the medulla has been destroyed. In this connection it is to be noted that in persons dying slowly with general distress the adrenalin content of the medulla will be found to be from 0·2 milligramme to 2·3 milligrammes, whereas in cases of sudden death the amount is about 4·5 milligrammes. Other symptoms of acute hypo-adrenalism are sudden onset of epigastric pain and tenderness, followed by abdominal distension; convulsions, coma and delirium, or a typhoid stage.

ADDISON'S DISEASE

This disease was first described by Dr. Thomas Addison in 1855.

Ætiology. The disease may occur at all ages, and is commoner in males. Tuberculosis is the most frequent cause. In some cases the capsules become infected from pre-existing phthisis, or spinal caries or psoas abscess; but in many cases it is a primary tuberculous infection of the glands. On section they show a combination of translucent greyish or greenish-grey tissue and opaque yellow cheesy substance. Sometimes the caseous matter has softened down into a cavity containing pus. In 25 per cent. of cases the only change is atrophy of the cortex (**29**). In other instances the glands have been attacked by growth, or there has been thrombosis of vessels with extravasation of blood.

Pathology. Addison's disease is due to destruction of the cortex of the suprarenal, so that there is absence of ascorbic acid with resulting pigmentation as already explained. The absence of the specific cortical substance leads to a fall in the sodium chloride of the plasma, a rise in the potassium, and a renal retention of nitrogenous substances; the kidneys still excrete plenty of chloride and excess of water. These biochemical changes cause polycythæmia from concentration of the blood, the low blood pressure and general asthenia of the disease, and possibly the gastro-intestinal disturbances. The basal metabolism has been found below normal (**4**).

Symptoms. The cardinal symptoms are debility, low blood pressure, vomiting and pigmentation. The onset is generally insidious, and the patient gradually suffers from weakness, depression, languor and indisposition for exertion. There may be pain and tenderness in the loins, hypochondrium or epigastrium. The heart's action is very weak, and there are faintness and giddiness on rising in bed, or breathlessness and palpitation on exertion. The pulse beats from eighty to ninety in the minute, and is small and feeble; the blood pressure is very low, measuring as little as 80 or 60 mm. of mercury. Appetite is generally deficient, and nausea, retching and vomiting are important features of the disease. A crisis is marked by diuresis with concentration of the blood and so polycythæmia. Irritability and restlessness are sometimes very pronounced. A peculiar *discoloration of the skin* is the symptom which has attracted most attention. This symptom may be noticed coincidently with the above general symptoms; it may develop before them, or it may occur several months after they are pronounced. It is possible, in this last class of cases, that, if the general symptoms are very severe, they may be fatal before the skin is affected; and thus the occasional absence of pigmentation in Addison's disease of the suprarenal capsules is explained. The pigmentation or *bronzing* is, in its lighter shades, dusky or yellowish brown, sometimes of olive or greenish-brown hue. In its more pronounced form the skin has a rich brown colour, like that of a mulatto. The pigmentation usually affects, first, the parts of the skin which are naturally exposed, such as the face, neck and the backs of the hands and fingers, and not the scalp or the lip under the moustache; secondly, parts which are naturally more deeply pigmented than others, such as the axillæ, penis, scrotum and areolæ of the nipples; and thirdly, seats of pressure or slight injury, such as the marks of

garters and waistbands in women, and places where blisters and plasters have been applied. But the scars of wounds destroying the skin remain white, and are bordered by a deep layer of pigment. Sometimes there is darkening of the depressed lines in the palms. On the darkened parts of the skin may be seen small black specks, like moles or freckles. In advanced conditions the whole body may be covered by the pigmentation ; but, as a rule, one must be prepared to recognise the disease, and, indeed, many patients die before this stage is reached. The pigmentation is not limited to the skin. A bluish-black line may often be seen on the inner side of each lip running along the mucous membrane, parallel to the line of junction with the skin ; and other more irregular patches may occur on the mucous membrane of the cheek and on the side of the tongue. Some of these seem to be determined by the presence and consequent irritation of carious teeth. The temperature is, as a rule, normal ; the urine is normal. Although weak, the patient is not necessarily emaciated ; even a considerable layer of subcutaneous fat may persist to the end.

The course of the disease is very variable. It is often marked by exacerbations and remissions, periods of severe illness, which confine the patient to bed, alternating with times of comparative health ; but after each fresh aggravation of the disease the patient is left decidedly worse than he was before it. The duration varies from a few months to six or seven years. Death takes place mostly by asthenia, the patient getting gradually weaker and lapsing into a drowsy or semi-comatose condition, with increasing feebleness of pulse. Delirium and convulsions occasionally close the scene. In some cases the general symptoms and a very slight pigmentation have been noticed only for some months, when extreme prostration has ensued and carried off the patient in a few weeks.

Diagnosis. The mistakes most likely to be made are : (1) to take some other discoloration for that of Addison's disease ; (2) to fail in recognising the symptoms when the pigmentation is slight or absent. The discolorations likely to be mistaken for it are slight *jaundice*, or that of *pernicious anæmia* ; *phtheiriasis*, to be recognised by the scratches and the limitation of the colour to parts which can be reached by the finger nails, and the entire freedom of the face ; the sallow or earthy tints of *malaria* and of *phthisis* ; *chloasma uterinum* in women ; and *tinea versicolor*. In early stages, without much darkening, the apparently causeless weakness, with small, feeble pulse, and sickness, are the diagnostic features. The biochemical and therapeutic tests are the most certain. The symptoms will be aggravated by a salt-free diet (but this is not free from danger) and improved by giving salt and abolished by cortical extract ; the latter raises the plasma chloride and abolishes the other abnormal biochemical changes.

Treatment. This affords one of the striking recent advances in medicine. Salt in doses of 10 or 15 grams a day ameliorates the disease. Daily subcutaneous injections of cortin up to 10 c.c. completely remove the symptoms with disappearance of pigmentation. This expensive drug can be dispensed with to a large extent if salt is given ; the pigmentation disappears on giving ascorbic acid (*q.v.*).

TUMOURS OF THE SUPRARENAL CAPSULES

The tumours affecting these glands are adenoma, sarcoma, carcinoma and neuroblastoma. Sarcoma is very rare, and occurs only in adults. Neuroblastoma occurs in children, and arises from the medulla of the gland. It is a malignant growth, closely resembling a small-celled sarcoma, but it has rosettes, which are characteristic of neoplasms of the central nervous system. It readily gives rise to secondary deposits in the bones. It may form a large mass, which may be mistaken for a renal tumour ; it is likely to be fatal, unless it can be removed early. Carcinoma is rarely primary, but generally part of widespread secondary lesions. When primary, it is a small-celled carcinoma, which very readily gives rise to hæmorrhage and necrosis. The cells have a tubular or alveolar arrange-

ment, or are grouped radially round blood vessels ; and there is a general resemblance to the suprarenal cortex. Metastasis may occur in different parts of the body. When present, the growth gives rise to characteristic symptoms due to the activity of the tumour cells (hyper-interrenopathy). The same symptoms are observed with simple hypertrophy of the cortex. If the disorder begins in intrauterine life *female pseudo-hermaphroditism* is seen ; *i.e.* the individual is in reality female, as ovaries are present, but has external male characters. This condition is congenital, and is due usually to bilateral cortical hyperplasia. When the disease begins soon after birth, it produces the condition known as *premature puberty.* The children become obese. In male children there is precocious and excessive sexual development. Great muscular strength is developed, producing what is known as the *infantile Hercules* type ; there are hair on the face and increased sexual functions. Occasionally feminisation or homosexual precocity occurs. In girls there is usually masculinisation, or heterosexual precocity with hypertrophy of the clitoris, growth of hair and deepening of the voice ; but homosexual precocity has also been described, and there may be early menstruation. In later life hyper-interrenopathy leads to *adult hirsutism* or *virilism.* In women certain male characteristics are seen. Hair grows on the face, and the hair elsewhere on the body is increased ; there is absence of menstruation and of mammary development ; there is increased bodily strength and mental symptoms suggestive of masculinity, such as aggressiveness and egotism, appear. In the case of *progeria* or premature senility, shown in Plate 38, there are bilateral tumours in the suprarenal areas and no evidence of pituitary involvement as found in other cases ; the arteries are thickened, and blood pressure, blood urea and sugar raised and the patient is bright and fond of games with other children.

Certain other changes in the suprarenal capsules may be mentioned. Inflammation and *abscess* from proximity to suppurating foci, hæmorrhage from injury, *lardaceous* change in common with other organs, miliary tubercles in general tuberculosis, and rarely syphilitic gumma, are among the other pathological conditions which may be found.

THE PITUITARY GLAND

This gland, often called the hypophysis, consists of three parts :—(1) the *pars anterior* or *glandulosa,* derived from the buccal ectoderm and containing colloid cysts ; (2) the *pars posterior* or *nervosa,* consisting of neuroglia fibres and cells ; (3) the *pars intermedia,* glandular in structure, lying between the first two. The colloid from the pars anterior (anterior lobe) is discharged through the pars posterior (posterior lobe) into the third ventricle, and is found in the cerebro-spinal fluid.

Pathology. Experimentally, in rats it has been found that removal of the anterior lobe prevents both the general growth of the animal and the development of the sexual organs (*hypopituitarism*). Again, the injection of active extracts causes gigantism. In man over-activity of the anterior lobe (*hyper-pituitarism*) leads to *gigantism* in early life from overgrowth of the long bones, and in adult life to *acromegaly,* when the epiphyses of the long bones have finally become ossified. In both cases the overgrowth is associated with hyperplasia of the thyroid and parathyroid and of the adrenal cortex, and it not only involves the bones but all the structures in the body, so that *macrosomia* would be a better term to employ. Recent work has proved the importance of the anterior lobe as a regulator of all types of endocrine activity, as well as of carbohydrate metabolism (see hypoglycæmia). If the anterior lobe of the pituitary is destroyed, degenerative changes occur in the thyroid, ovaries, testes, pancreas, suprarenal cortex and possibly the parathyroids ; these can be prevented by the injection of anterior pituitary extracts, from which thyrotropic, gonadotropic (see Gonads)

and adrenotropic hormones have been prepared, as well as a hormone which stimulates the breast to secrete milk; these hormones are normally liberated from the anterior lobe into the body and control the other endocrine organs. For instance, the thyrotropic hormone stimulates the thyroid to secrete thyroxin and so raises the basal metabolism; but this rise does not last because, in spite of continued activity of the gland, the body produces some anti-thyrotropic substance (**40**). The endocrine relationships of the pituitary are thus complicated, and lesions may produce various pluriglandular syndromes depending on which particular hormone is missing. A scheme is shown below.

ANTERIOR PITUITARY HORMONES.

Thyrotropic, stimulates thyroid gland, raises basal metabolism.	Adrenotropic, stimulates adrenal cortex.	Gonadotropic, (*a*) a prolan-like substance, which stimulates ovary to produce (1) œstrin.
? to pancreas.	to breast, stimulates production of milk.	(2) progestin.
? parathyrotropic		(*b*) stimulates testis.

From the pars posterior is obtained an extract (pituitrin) which contains two hormones *vasopressin* (*pitressin*) and *oxytocin* (*pitocin*). It is possible that these are normally discharged with the colloid into the cerebrospinal fluid. Oxytocin has a direct action on the uterus. Vasopressin stimulates the intestinal muscle and also causes a rise of blood pressure with diuresis in the anæsthetised animal, and an increased flow of cerebrospinal fluid and milk; but in an unanæsthetised man the volume of urine is diminished. The pars posterior also provides a substance necessary for the growth of oxyntic cells in the stomach and of the marrow. Injection of large doses in rabbits causes hæmorrhagic gastritis, which begins in the oxyntic cells.

The adiposity often met with in pituitary disease is due to pressure on the hypothalamic region; diabetes insipidus is considered later.

Morbid Anatomy. Pituitary disease may be due to: (1) Lesions inside the sella turcica (*intrasellar*). Of these there are: (*a*) the *eosinophilic adenoma*, consisting of the proper secreting cells of the anterior lobe; this causes hyperpituitarism: (*b*) the actively growing *chromophobe adenoma*, the cells of which do not contain granules that stain with eosin; this tumour tends to destroy the anterior lobe and so causes hypopituitarism: (*c*) the *mixed adenoma* with both eosinophilic and chromophobe elements; this gives rise to *dyspituitarism*, a condition in which signs of both hyper- and hypo-pituitarism are present simultaneously; these adenomas do not usually occur in people under twenty years: (*d*) the rare *adeno-carcinoma*: (*e*) ischæmic necrosis from infarction: (*f*) the recently discovered basophil adenoma with its characteristic symptomatology. It is remarkable that while adenoma occurs in about 10 per cent. of autopsies, especially in later life, it is present in 50 per cent. of cases where there is a neoplasm in other parts of the body (**37**). (2) *Suprasellar* lesions, which are all destructive and so cause hypopituitarism. Of these the suprasellar cyst is the commonest; it is described under Cerebral Tumour. Other growths are meningioma, cholesteatoma, glioma, and sarcoma: (3) Intracranial lesions at a distance, which cause a secondary hydrocephalus and so cause pressure on the pituitary from above.

Symptoms. These depend on variations in the activity of the gland caused by the lesion (glandular symptoms) and on pressure on surrounding structures (neighbourhood symptoms). The latter are described under cerebral tumour.

Hypopituitarism may be associated with symptoms of a distant cerebral lesion.

Glandular Symptoms. *Acromegaly.* This is due to hyperpituitarism. The disease was described by Marie in 1880. It usually occurs in adolescence or early adult life. There is enlargement of the bones of the extremities (hands

and feet) and of the face (ἄκρον, an extremity; μέγας, large). The phalanges are thickened, and there are bony exostoses. The jaw is enlarged and is undershot (*mandibular prognathism*). The teeth become separated. The soft parts are also thickened; the papillæ of the skin are hypertrophied; the nails are broad, coarse and ribbed; the skin is thick and greasy; and the lips and nose and ears and tongue are coarse and large. The thickening of the fingers gives a characteristic appearance to the hand—*type en large* (Marie). The viscera, including the heart, are enlarged. There may also be kyphosis. Acromegaly with active hyperpituitarism is associated with an increased basal metabolism and a lowered sugar tolerance, so that there is hyperglycæmia and glycosuria if a sugar tolerance test is carried out. True diabetes may occur with ketosis, and in one such case the diabetes was greatly improved after removing the tumour (**31**). If dyspituitarism supervenes, the sugar tolerance is increased. There is often low intellectual development.

If hyperpituitarism occurs during childhood, the bones become longer than normal (*gigantism*). The fingers also become longer than normal, and the type of hand that results has been called the *type en long* by Marie.

Hypopituitarism. The purest examples are those rare cases where the anterior lobe has been destroyed by infarctions, the result of some septic process. If this occurs in childhood dwarfism results (pituitary *ateleiosis* or the Lorain type of infantilism). The whole body is small (microsomia or *hypophyseal nanism*) but well proportioned; the sexual organs are undeveloped and the secondary sexual characteristics absent. In the type called *Simmonds's* disease, the patient becomes apparently old with wrinkled skin and wasting of the subcutaneous tissues, asthenia, mandibular, dental and genital atrophy, amenorrhœa, anorexia, constipation and *lowered* body temperature, blood pressure, pulse frequency, blood sugar and basal metabolism. He may die in a somnolent state. This premature senility with atrophied viscera may come on in adult life if the anterior lobe is destroyed at this time. Pituitary dwarfism associated with premature senility may be found; this is one type of *progeria*. As may be imagined from the controlling effect of the pituitary on other endocrine glands, which has already been mentioned, when these glands are found to be atrophic, symptoms may be due to a multiple deficiency of hormones—a type of *pluriglandular syndrome*. Of course, neighbourhood symptoms are absent in these cases; but the pituitary fossa may be small in long-standing cases (*see* Plate 57, B).

The suprasellar tumours commonly produce a combination of adiposity and infantilism met with in children, and known as *Fröhlich's syndrome*, or *hypophyseal dystrophia adiposo-genitalis*, which is due to hypopituitarism. The fat is most noticeable on the abdomen, buttocks, and proximal portions of the extremities. Dwarfism may result. The genital organs remain in an infantile state, and the skin is pale, thin, soft, and smooth. The nails are small, without crescents, and the fingers are tapering. The epiphyses remain unclosed. Mental development is usually normal. The clinical picture due to these tumours is often not clear cut; there may be emaciation, polyuria and premature senility.

The chromophobe adenoma of the adult produces at an early stage depression of sexual functions, which is indicated in the female by amenorrhœa. The cutaneous changes may be seen as just described, and there is a tendency to adiposity and loss of hair and pigmentation. There may also be asthenia, drowsiness, increased sugar tolerance and subnormal temperature from lowered metabolism, and in some cases polyuria.

Basophil Adenoma of the Anterior Pituitary or Cushing's Syndrome. The constant symptoms of this syndrome are painful adiposity confined to the face, trunk and neck, rounded shoulders or kyphosis, loss of sexual function, including amenorrhœa, increase of hair on face and trunk in the female and young male, a *plethoric appearance* of the skin with dusky lineæ atrophicæ, vascular hypertension, polycythæmia, backache, abdominal pain and asthenia. The variable

symptoms are blueness and œdema of extremities, ecchymoses like bruises, various eye symptoms, dryness of the skin, thirst and polyuria, polymorphonuclear leucocytosis, glycosuria, osteoporosis and spontaneous fractures. At autopsy there may be chronic nephritis, colloid goitre, cortical hyperplasia of the suprarenals, atrophy of the gonads, so that the symptomatology evidently represents a pluriglandular syndrome, and it has in fact been found in cases of carcinoma of the suprarenal cortex

In adults cases of extreme obesity may be due to pituitary disease. *Adiposis dolorosa*, or *Dercum's disease* may probably be either due to pituitary disease or hypothyroidism (*see* p. 501). Epilepsy is also associated with hypopituitarism.

Diagnosis. This depends upon the recognition of neighbourhood and glandular symptoms, and is usually not difficult. However, it is important to distinguish between intrasellar and suprasellar lesions and intracranial lesions at a distance, which cause pituitary symptoms. The age incidence of adenoma and suprasellar cyst will be of value in distinguishing the first two, and there are also the characteristic X-ray appearances and the different symptomatology. The intracranial lesion at a distance, such as a cerebellar tumour, will also provide characteristic signs.

Prognosis. This is bad, since the tumour usually progresses, although slowly. The operative mortality of sellar decompression is about 7 per cent. (Cushing).

Treatment. In cases of hypopituitarism benefit has been obtained by administering the anterior lobe in tablets by the mouth, combined with thyroid. Pituitrin must be given subcutaneously, since it is destroyed by the alimentary canal. The progress of treatment can be estimated from the sugar tolerance. Operative treatment is considered under Cerebral Tumour.

DIABETES INSIPIDUS

Polyuria may be caused by disorders of the kidney, by increased blood pressure, by the presence of sugar in the urine in diabetes mellitus, in severe Addison's disease, and temporarily in some disorders of the brain, especially hysteria and migraine. Diabetes insipidus is a persistent polyuria not traceable to any of the above conditions.

Pathology. Diabetes insipidus may be due to injury or disease of the pituitary gland, probably the posterior lobe. Subcutaneous or intravenous injections of pituitrin (vasopressin) are specific for the disease, the urine being at once reduced to the normal volume, and the patients get complete relief from their symptoms. Motzfeld has shown that in the unanæsthetised animal the volume of urine is diminished, and this diminution is more striking if an artificial polyuria has been produced by previously filling the stomach with water. The action of the drug is stopped if the splanchnic or renal nerves are divided. The action of the extract is probably due to rather more than mere splanchnic vaso-constriction; its presence may be necessary for the reabsorption of water at the end of the tubules (*see* p. 518). Diabetes insipidus may also follow injury of the hypothalmic region of the brain, possibly because the normal outflow of the pituitrin is obstructed.

Morbid Anatomy. Radiograms of the sella turcica usually show no enlargement. Various lesions of the pituitary gland or its neighbourhood have been described: fractures of the base of the skull, cerebral tumour, syphilitic or tuberculous basal meningitis, caseation of the infundibulum. In one remarkable case a bullet was found pressing against the posterior lobe. Parkes Weber has described what he regards as a tuberculous infiltration of the posterior lobe of the gland.

Dilatation and hypertrophy of the bladder, dilatation of the ureters, and enlargement of the kidneys may be seen, and are attributable to the prolonged pressure of large quantities of urine.

Symptoms. These begin either insidiously or suddenly. The prominent symptoms are the enormous quantity of water passed and the great thirst by which the patient is led to replace the loss. The urine may reach 15, 20 or even 40 pints in the twenty-four hours. It is very pale, almost like water, of specific gravity 1,002 to 1,005, and faintly acid in reaction. The percentage of solid constituents is small. Occasionally there is glycosuria or an increased secretion of the salivary glands. The mouth, tongue and skin are dry, and the bowels constipated. Beyond this the patient may be in the enjoyment of very good health, and he finds the diabetes an annoyance rather than an illness. The symptoms of pituitary disease may also be present.

Spontaneous and idiopathic cases may last for years if untreated. They are rarely fatal, except from the intervention of other illnesses; occasionally glycosuria has supervened, and the case has become one of diabetes mellitus.

Diagnosis. The enormous quantity of pale urine, of low specific gravity without abnormal ingredient, and the accompanying thirst, are distinctive. But care must be taken to exclude other forms of polyuria, such as those from *Bright's disease* and *hysteria*. In the former there is generally at some time or other a distinct trace of albumin, the quantity of urine is not so considerable, and other indications are present, such as high arterial tension and cardiac hypertrophy. In hysteria the condition is but temporary.

Treatment. This consists in the administration of pituitary extract subcutaneously. One cubic centimetre (15 minims) is injected twice a day to begin with. The attempt is then made to control the volume of urine with as few injections as possible. Unfortunately treatment by the mouth is useless, as the active principle is destroyed in the alimentary canal; but the drug has been given by means of an intranasal spray or a nasal jelly containing pitressin, or best of all by dried pituitary insufflated into the nose as "pituitary snuff." Some cases are refractory to pitressin.

In syphilitic cases antisyphilitic treatment (*q.v.*) is indicated. In cases of gross cerebral disease (*e.g.* tumour, etc.) the question of operation will naturally arise. A few cases have been relieved by lumbar puncture, which suggests that a serous meningitis at the base of the brain was responsible for the disease (**32**).

THE PINEAL GLAND

The pineal body (epiphysis cerebri or conarium) is a glandular organ, weighing about 3½ grains, and consisting of epithelioid cells in loosely disposed trabeculæ, with blood sinuses between them. Like the thymus, its chief use appears to be in early life, and it undergoes a certain amount of involution later.

The lesions which have been recorded are hypertrophy and atrophy, tumours, cysts and abscess, hæmorrhage and syphilis.

In the cases of tumour which have shown changes in metabolism, indicating a disturbance of the internal secretion, the subjects have been boys up to eleven years, and the changes consisted, in different degrees in different cases, of mental precocity, unusually rapid growth of the body, enlargement of the penis and testes, precocious growth of pubic hair, and sometimes adiposity. These were sometimes associated with evidences of intracranial tumour, and the tumours present were in different cases sarcoma, cystic psammo-sarcoma, glioma or teratoma.

THE GONADS

A systematic description of the pathological changes found in the testicle and ovary will be found in text-books of surgery and gynæcology. The gonads will only be considered here from the point of view of their endocrine function.

Female Sexual Organs. At the beginning of the menstrual cycle, after hæmorrhage has ceased, the mucous membrane of the uterus consists of a single

layer, the basal mucous membrane. During the first half of the cycle it proliferates, becoming thicker under the influence of a hormone, which is called œstrin or the follicular hormone or folliculin; this, the female sex hormone responsible for secondary sexual characters, is produced by the Graafian follicle, which grows to maturity during the same period. After the bursting of this follicle with liberation of the ovum, the corpus luteum is formed and this produces a second ovarian hormone called progestin, which causes an increase in glandular activity of the uterine mucosa with convolution of the glands—the secretory phase—preparatory to the reception of a fertilised ovum. If conception does not take place the mucous membrane breaks down and becomes discharged from the uterus with hæmorrhage, thus ending the cycle. In castrated females the menstrual cycle can be initiated by giving large doses of dioxy-œstrin (2,500,000 units) in five doses on the first, fourth, seventh, eleventh and fourteenth out of twenty-eight days, followed by progestin (five rabbit units), *i.e.* one rabbit unit a day, beginning on the seventeenth day (**42**), so that amenorrhœa due to poor development of the sexual organs may be treated by this means. If too much œstrin is found in the body, or administered, the Graafian follicle continues to grow without bursting, and the mucous membrane also continues to grow and becomes cystic and may eventually break down with severe hæmorrhage. As the corpus luteum is not formed, there is no progestin to bring about the secretory stage, and this should be administered by injection during the stage of hæmorrhage; often quite small doses are sufficient—three to ten rabbit units spread over five days, though sixty to eighty may be necessary. Œstrin also produces changes in other sex organs, such as the vagina—cornification of the epithelium in the rat and mouse—to facilitate mating. Curiously enough the richest source of naturally occurring œstrin is the urine of the stallion, and the most active compound is obtained by adding two hydrogen atoms to the œstrin molecule, which is a sterol allied chemically to cholesterol and calciferol (vitamin D) as well as to the most active cancer-producing substance which has so far been prepared. Further, a number of different though closely allied substances possess œstrous-producing properties in varying degree, while one has the power of producing both œstrus when injected and carcinoma if painted on the skin (**43**). The development of the ovary and all that follows from it is controlled by the anterior lobe of the pituitary, by means of a hormone unnamed at present, which in small amount causes the development of the Graafian follicle with secretion of œstrin, and in large amounts causes full development of the corpus luteum which secretes progestin. During pregnancy there is present in the blood and urine a closely allied substance which probably arises from the placenta and is called prolan. This fact was first utilised by Ascheim and Zondek as a means of testing for pregnancy, since the injection into animals of urine containing prolan produces changes in the ovaries that can be recognised (**44**).

Male Sexual Organs. Removal of the testes causes non-development or atrophy of the accessory organs, seminal vesicles, prostate, Cowper's glands and penis. The influence exerted by the testes is due to the male sex hormone elaborated in the interstitial cells of the testis. Like the ovary, the development of the testis is also under hormonic control of the anterior pituitary. This gonado-tropic principle, which is present in urine during pregnancy, may be of value in treating undescended testicle, 500 rat units in the form of "pregnyl" being injected twice weekly (**45**).

Eunuchism. The symptoms depend on whether castration has been performed before or after puberty. In the former case the penis, prostate, vesiculæ seminales, remain small and the subjects do not develop libido or potentia. If the operation is performed after puberty, the penis need not atrophy much, but the prostate becomes smaller. Libido may persist, and even potentia, at least for a time. Prostatic secretion is ejaculated. Psychically, the normal aggressiveness of the

male disappears, but eunuchs may possess great intellectual powers and artistic ability. Physically, they are either (1) tall and thin, with long arms and legs, or (2) short and fat, with a distribution of fat similar to hypophyseal dystrophia genitalis. In both types the pelvis remains broad, the skin pale ; there is drooping of the lateral half of the eyelids with a sleepy appearance, and there is generally a deficient growth of hair. In the female, double oöphorectomy brings on a premature menopause with tendency to obesity, hot flushes, respiratory, cardiac, and digestive disturbances. Neurasthenia, psychasthenic or psychotic symptoms may appear.

Eunuchoidism. This term is applied to conditions resulting from loss of the gonads by disease. They are not uncommon in patients with undescended testicles (*cryptorchidism*). Like eunuchism, the condition may be noticeable at puberty (early eunuchoidism) or later during the normal period of active sexual life (late eunuchoidism). As in eunuchism, the patients may be tall or short and fat. Mentally, they are quiet and silent and there are disturbances in libido and potentia. The skin is pale and sometimes has large numbers of small wrinkles. Linear wrinkles radiating from the mouth make these patients look prematurely old. Female eunuchoids are tall, and fat is deposited on the lower abdomen, mons veneris, buttocks and outer sides of the thighs and the mammary glands. The uterus and vagina become hypoplastic.

Hyper and Hypogenitalism. While the terms eunuchism and eunuchoidism are reserved solely for results following primary disease or absence of the gonads, over- or under-activity of the latter may also result secondarily from disease of other ductless glands. Thus hypergenitalism which causes precocity or premature puberty may result from tumours of the testicle or ovary, from hyperfunction of the latter, or from tumours of the suprarenal cortex or pineal body already described. Delayed puberty, so commonly met with in both sexes, may similarly be due to hypofunction of the gonads primarily or may result from other organs acting on the gonads.

VARIED SYNDROMES

OBESITY

Obesity, corpulence, or excessive fatness is a condition which may amount to a disease, and sometimes calls for treatment. But it is often difficult to say where normal deposition of fat ends, and where obesity begins ; and the two conditions must be dealt with together.

Ætiology. There appear to be some differences in the tendency to obesity among the races of mankind. Heredity certainly has a share in its occurrence. There are some periods of life when fat is more likely to accumulate ; these are infancy, puberty, during pregnancy and at the climacteric in the female, and during middle age in the male. Females, on the whole, are more liable to be fat than males.

Pathology. In a normal individual whose body weight remains constant the energy supplied by the utilisation of the food must balance the energy given out in the form of heat and external muscular work. If he suddenly changes his habits by leading a more sedentary life, the energy output will be diminished, and less food will be oxidised, the excess being deposited in the body as fat. Both fats and carbohydrates are readily stored in this way ; but the constituents of protein are more easily oxidised, increasing the heat output. This is called the *specific dynamic action* of protein. Hence the important factors in many cases of obesity are bodily inactivity and over-eating.

There are, however, cases of great obesity which cannot be entirely explained in this way. Amongst healthy persons there are many very fat who eat comparatively little ; and, on the other hand, many big eaters are persistently thin.

These idiosyncrasies are explained by the rate of oxidation peculiar to the

INFANTILISM

By infantilism is meant the retention of the characters of childhood for a longer time than usual, or an abnormally slow development. Infantilism is not necessarily associated with dwarfism; but the childish form may be retained, and there may be delayed ossification and absence of sexual development. There need not necessarily be any delay in the child's mental progress.

Infantilism may be secondary to various chronic infections and other toxic causes, such as syphilis, tubercle, malaria, pellagra, scarlet fever, chronic diarrhœa, pancreatic deficiency and some inorganic poisons, such as lead and mercury; chronic interstitial nephritis in children may be associated with infantilism. A second group includes those cases which are due to disease of the endocrine organs, such as cretinism, Fröhlich's syndrome, pituitary ateleiosis, progeria, and diabetes insipidus. Other instances of infantilism are the delays in development which have been seen in association with achondroplasia, muscular atrophy, sclerodermia, cardiac and vascular lesions, microcephaly, hydrocephalus, amentia, hypertrophic cirrhosis of the liver, splenomegalic cirrhosis, and some other disorders. Finally, there is the sexual form of ateleiosis, which is of unknown origin and which differs from the pituitary form already described in that ultimately the sexual organs mature, the epiphyses unite, and the individual remains in some respects a child, in others a man or woman in miniature.

REFERENCES

1	T. W. Adams and E. P. Poulton	1935	*Guy's Hosp, Rep.*
2	E. W. Ainley Walker	1916	*Proc. Roy. Soc.*, B. 89, p. 157.
3	E. P. Poulton	1917	*Guy's Hosp. Gaz.*, N.S. 31, p. 50.
4	E. Dubois (Basal Metabolism in Health and Disease)	1924	Lea & Febiger, New York,
5	R. D. Lawrence	1924	*Brit. Med. Journ.*, i., p. 516.
6	J. H. Burn and H. H. Dale ..	1924	*Journ. Physiol.*, 59, p. 164.
7	J. J. R. Macleod	1924	*Brit. Med. Journ.*, i., p. 45.
8	E. P. Poulton (Goulstonian Lectures)	1918	*Lancet*, June 22.
9	Burgess, Campbell, Osman, Payne and Poulton	1923	*Lancet*, ii., p. 777.
10	C. von Noorden (Pathologie d. Stoffwechsels)	1906	Berlin, 1, p. 207.
11	R. T. Williamson (Diseases of the Spinal Cord)	1911	p. 371.
12	E. P. Poulton	1924	*Brit. Med. Journ.*, i., p. 261.
13	W. W. Payne and E. P. Poulton	1925	*Lancet*, ii., p. 638.
14	W. W. Payne	1924	*Guy's Hosp. Rep.*, p. 308.
15	W. Cramer (Fever, etc., and the Thyroid-adrenal Apparatus) ..	1923	London.
16	J. M. H. Campbell	1927	*Journ. of Hygiene*, 26, p. 1.
17	Adams and Crossley	1923	*Lancet*, ii., p. 501.
18	G. R. Murray	1922	*Brit. Med. Journ.*, ii., p. 908.
19	H. Curschmann	1922	*Klin. Wochenschrift*, June 24, p. 1296.
20	J. S. Goodall and L. Rogers ..	1927	*Lancet*, i., p. 486.
21	D. Hunter	1930–31	*Quart. J. Med.*, 24, p. 393.
22	F. R. Fraser	1925	*Brit. Med. Journ.*, i., p. 1.
23	R. D. Lawrence	1924	*Brit. Med. Journ.*, ii., p. 753.
	E. G. B. Calvert	1924	*Brit. Med. Journ.*, ii., p. 834.
24	Review on Biochemistry of Blood	1922	*Med. Sci.*, 6, p. 474.
25	S. Graham and G. H. Anderson..	1924	*Quart. Journ. Med.*, 18, p. 62.
26	J. Argyll Campbell	1926	*Lancet*, i., p. 72.
27	D. Gyorgi (Communication) ..	1929	Assocn. Physicians, Cambridge.
28	F. W. Mott and J. E. Hutton	1923	*Brit. Med. Journ.*, ii., p. 95.
29	P.M. Statistics, London Hospital.		

31	A. W. M. Ellis	1924	*Lancet*, i., p. 1200.
32	Tucker	1922	*Brit. Med. Journ.*, i., "*Epitome*," p. 25.
33	I. Greenwald	1922	*J. Biol. Chem.*, **54**, p. 285.
34	G. Graham	1917	*Quart. Journ. Med.*, **10**, p. 245.
35	F. Dickens, Dodds, and Wright	1925	*Bioch. Journ.*, **19**, p. 853.
36	R. A. McCance and R. D. Lawrence	1929	Med. Res. Council, Report on Carbohydrate Contents of Food.
	W. O. Atwater and A. P. Bryant	1906	Washington. The Chemical Composition of American Food Materials.
37	H. G. Close	1934	*Lancet*, i., p. 732
38	A. Walton	1929	*Eugenics Rev.*, **20**, p. 253.
39	W. W. Payne and E. P. Poulton	1928	*Guy's Hosp. Rep.*
40	E. M. Anderson and J. B. Collip	1934	*Lancet*, i., p. 784.
41	I. Snapper	1928	*Proc. Roy. Soc. Med.*, **21**, p. 1771.
42	C. Kaufmann	1934	*Proc. Roc. Soc. Med.*, **27**, p 849
43	E C. Dodds (Goulstonian Lectures)	1934	*Lancet*, i., pp. 931, 988, 1048.
44	P. M. F. Bishop	1933	*Guy's Hosp. Rep.*, **83**, p. 308
45	A. W. Spence and E. F. Scowen (Communicated)	1934	Therap. Section, *Roy. Soc. Med.*
46	E. P. Poulton and E. C. Warner	1931	*Proc. Roy. Soc. Med.*, Oct. 13, p. 347.
47	R. McCarrison	1933	*Brit. Med. Journ.*, ii., p. 671.
48	C. R. Harington	1933	*Proc. Roy. Soc. Med.*, **26**, p. 870.
49	F. R. Fraser	1931	*Brit. Med. Journ.*, i., p. 739.
50	E. P. Poulton and W. L. Watt ..	1934	*Lancet*, ii., p. 535.
51	A. B. Anderson, C. R. Harington, and D. M. Lyon	1933	*Lancet*, ii., p. 1081.
52	H. M. Turnbull and M. Young	1931	*Journ. Path. Bact.*, **34**, p. 213.
53	W. Hartston	1933	*Lancet*, ii., p. 1416.
54	E. P. Poulton	1936	Diet Tables and Recipes and the Treatment of Diabetes and Obesity.

APPENDIX

Glycogen Disease (*Hepato-megalia glycogenica of Von Gierke*). In this disease of children, often congenital, there is enlargement of the liver and sometimes of the kidneys, with increased storage of glycogen in these and other organs constituting the main feature. There is a tendency to infantilism and obesity. The fasting blood sugar is low with a delayed fall in the blood sugar tolerance curve; the blood sugar does not rise after injecting adrenaline. The blood glycogen and cholesterol are raised and there is acetonuria.

R. W. B. Ellis and W. W. Payne .. 1936 *Quart. J. Med.*, N.S. **5**, p. 31.

DISEASES OF THE URINARY ORGANS

EXAMINATION OF THE KIDNEY AND BLADDER

THE kidney normally extends from the lower border of the eleventh dorsal vertebra to the lower border of the second lumbar vertebra, its inner margin being, on an average, 3 inches from the middle line; and it is fixed in this position by its surrounding capsule of adipose tissue, by the layer of peritoneum in front of this, and by the renal vessels. The position of the kidneys corresponds on the anterior surface of the body to a rectangular figure, 8 inches by 4 inches, having its lower long side level with the umbilicus, and its short sides each 4 inches from the middle line.

The kidney cannot be felt, except in very emaciated persons, or when it is enlarged, or when it is more mobile than normal (*movable kidney*), or when it is pushed down by disease above. Each flank should be examined by the bimanual method, and the patient should be directed to take a deep breath; or in thin persons the flank may be grasped by one hand, the fingers behind and the thumb in front. An enlarged kidney forms a rounded swelling, which fills up the loin when it is palpated from behind, while in front the hand can be inserted between the upper part of the tumour and the costal margin; in these ways it differs from a large liver or large spleen, which also both have their characteristic shapes. Further, if the resonance of the colon is detected in front of the mass, it is not the spleen or the liver. An *ovarian* tumour grows up from below, whereas a renal tumour begins above and grows downward. *Mesenteric glands* lie nearer the middle line than the kidney, and form very nodular masses; isolated enlarged glands may give a clue to the nature of the larger mass.

Uro-Selectan B, an iodine pyridine compound, opaque to X-rays and excreted by the kidney, provides a valuable means of examination. Ampoules contain 15 grams of the dye in 20 c.c. of solution, for an adult, and this is injected intravenously (3); abrodil is an alternative preparation. Radiograms are taken before, and three, seven and fifteen minutes after intravenous injection; a lateral radiogram should also be taken. The whole area of each kidney is shown up as a faint shadow and in three minutes an opacity is already visible in the pelvis and by fifteen minutes the whole pelvis with calyces, ureter and bladder can be seen. Hence the shape, position, rate of excretion of the kidney—thus the dye is also a test of renal function—the size, shape and position of the pelvis and ureter, their relation to shadows suggesting calculi, deformation and filling defects due to growths, kinking and hydronephrosis can be determined. If a radiogram is taken in the vertical position the amount of dropping of the kidney can be determined. (Plate 39.)

With the aid of the cystoscope information may sometimes be obtained as to the condition of the kidneys. If one or other kidney is the subject of pyelitis, pyelo-nephritis, tuberculous disease, or similar lesion, and the ureter is involved, the orifice of the ureter in the bladder may be patent, with swollen lips and vascular adjacent mucous membrane. The ureters may be catheterised and the urine from them collected separately in order to find out if disease is localised in one of the kidneys. The relative volume of the urine from each kidney is

noted, and examination for blood, pus and albumin is carried out. In the diagnosis of certain congenital malformations of the kidney, hydronephrosis, kinking of the ureter, renal tumours projecting into the pelvis and renal calculus, *retrograde pyelography* may be of assistance. After catheterising the ureter and allowing urine to escape, a 20 per cent. solution of sodium bromide, which is opaque to the X-rays, is cautiously run in and a radiogram is then taken. The normal pelvis will allow 6 c.c. of the solution to enter. No anæsthetic is given and the injection is stopped if pain in the loin is experienced. Only one ureter is catheterised at a sitting. To show up the bladder 10 per cent. sodium bromide may be used, or 10 per cent. colloidal silver (1) (*see* Plate 40).

EXAMINATION OF THE URINE

Quantity. The water content of the body is a balance between that which is taken in by the mouth and that which is excreted from the kidneys as urine, from the skin as sweat, from the lungs, in the fæces, etc. The secretion of urine depends on the amount of blood flowing through the kidneys. Excessive secretion of urine is called *polyuria*, its suppression *anuria*, which must be distinguished from *retention*. The volume is increased by the ingestion of fluids and exposure of the body to cold, because in the latter case the secretion of sweat is diminished, while it is diminished by abstinence from drink, by free sweating, and the loss of fluid from the circulatory system. The average daily volume of urine is 1,500 c.c.

In disease, variations are seen in the following circumstances: The flow of urine is increased in secondary contracted kidney, in rare cases of cerebral disease, in diabetes insipidus, and in diabetes mellitus. A temporary increase is seen in hysterical attacks, as a result of mere nervous excitement (not infrequent during medical examination for life insurance), and from the administration of substances having a diuretic action, such as the acetates, citrates, and tartrates, and, perhaps most commonly, alcoholic drinks. The urine is scanty or suppressed in acute nephritis, hydræmic nephritis, in obstruction of the ureter unless the other kidney is equal to the task of secreting twice its normal amount, in all febrile processes, in cardiac failure, and after repeated vomiting, or profuse diarrhœa.

Specific Gravity. This varies directly as the amount of solids in the urine, inversely as the quantity of water—that is, of the urine itself. A hydrometer, called a *urinometer*, is used to determine it. If the quantity of urine is too small to float the urinometer, it may be diluted with one, two, or three volumes of water, as may be required, and the specific gravity will be obtained by multiplying the last two figures by the number which represents the dilution. The density varies with the temperature. For accurate record all observations should be made at 60° F., or corrections should be made by adding one degree of density for every 8° F. above 60° F. The urine in health usually has a specific gravity of 1,015 to 1,025. It is diminished by most of the causes of polyuria, so as to be 1,010, 1,006, 1,004, or less. It is increased by all the causes of scanty urine. In diabetes mellitus the specific gravity may be increased to 1,030, 1,040, or 1,050, although the quantity of urine is many times more than the normal; the unnatural excretion of large quantities of sugar accounts for this exceptional condition. Albumin occurs in urine of both low and high specific gravity.

The relative amounts of the various constituents of blood and urine and the average twenty-four hourly output are shown in the table on p. 422. A description of certain of them is given below.

Urea. This constitutes about one-half the total solids of the urine, and is the chief form in which the nitrogen of the body is excreted.

Quantitative Estimation. A convenient method of estimating the urea is to

decompose it by the addition of *sodium hypobromite* (or *hypochlorite*) into carbonic acid, water, and nitrogen—

$$CON_2H_4 + 3NaBrO = 3NaBr + CO_2 + 2H_2O + 2N$$

A measured quantity of urine (5 c.c.) is mixed with a quantity of the hypobromite solution in a bottle, and the nitrogen is collected in a graduated tube and measured. The bottle and tube are surrounded with water so as to keep the temperature constant. The hypobromite solution rather readily undergoes decomposition on keeping. The nitrogen is measured, and from that the amount of urea can be calculated from the fact that 1 gm. corresponds to 370 c.c. of gas measured over water at 15° and 760 mm.

The determination of the output of urea in the twenty-four hours is a rough measure of the amount of protein metabolism. A more accurate way of measuring the latter is to estimate the total nitrogen of the urine by Kjeldahl's method. Allowance must also be made for the loss of nitrogen in the fæces, sweat, etc. Under normal conditions the nitrogenous content of the body remains constant, so that the excretion of nitrogen exactly balances the amount contained in the protein of the food, and varies from day to day as the amount of protein in the food varies. In disease the nitrogenous content of the body may vary, and this will produce its effect on the nitrogen excreted in the urine. For instance, in fever there is a destruction of body proteins, whereas in Bright's disease there may be a retention of nitrogenous products. This will show itself by an increase or decrease in the urinary nitrogen relatively to the protein consumed in the food. Such changes can only be measured if the patient eats an absolutely constant diet over a period of days.

Chlorides. These are lessened in all acute febrile processes, and especially in pneumonia, where they may be entirely absent.

Sulphates. These result from protein catabolism. The ethereal sulphates are partly the result of putrefaction in the intestines, and are largely increased in disorders of the intestines (obstruction, peritonitis, constipation) leading to such changes. The sulphates may be absent in lysol or carbolic acid poisoning and intravenous sodium sulphate (5 ounces of a 10 per cent. solution made with crystalline sodium sulphate) should be given immediately.

Phosphates. The chief function of the phosphates in the urine is to play the part of what are known as " buffers." This means that a large amount of acid or alkali may be passed from the blood into the urine without altering very greatly the acidity (hydrogen ion concentration) of the latter. In this connection the two most important compounds are the monosodium dihydrogen phosphate (NaH_2PO_4) and the disodium monohydrogen phosphate (Na_2HPO_4). The result of excreting acid is to form more of the former compound, and of excreting alkali more of the latter. A rich protein diet increases the acidity of the urine. It may be made more alkaline from the ingestion of much vegetable matter or other food containing citrates, tartrates, or malates of potassium and sodium. These are converted into alkaline carbonates in the intestines, and absorbed as such into the blood, and hence diminish the acidity of the urine; the *p*H is 7 or greater. In these circumstances the less soluble phosphates preponderate, and those of the earthy salts, calcium and magnesium, may be precipitated in the urinary tract, a condition known as *phosphaturia* (*see* Treatment of Calculus, p. 550); the turbid, white deposit is soluble on adding a little acetic acid. But more commonly it is found that on heating a feebly acid or neutral urine a white deposit of phosphates appears, which closely resembles albumin, but is at once distinguished from it by being dissolved by a drop of acetic acid. The urine may become alkaline from the presence of ammonia, which is formed as the result of bacterial decomposition of urea, either within the bladder (cystitis) or after standing in a vessel exposed to the air. In this case ammonium magnesium phosphate is precipitated ($MgNH_4PO_4 + 6H_2O$). It forms triangular prisms, with bevelled ends.

Reaction of the Urine. The reaction of the urine (hydrogen ion concentration) is usually on the acid side of neutrality. Hasselbalch has shown that the p_H may vary from − 5·0 on a meat diet or during starvation to − 8·0 when a diet containing vegetables and free alkali is eaten, depending on the relative amounts of Na_2HPO_4 and NaH_2PO_4 present in the urine.

The kidney may be regarded as an organ which secretes a large amount of acid in the twenty-four hours, forming from the neutral blood a liquid, viz. urine, with an acid reaction, and this is another way of looking at the acidity of the urine. The amount of the acid excreted is determined by titrating the urine with decinormal soda back to the neutral point, *i.e.* the reaction of the blood, neutral red being used as an indicator. In health there are wide variations; but the average value for twenty-four hours on a rather high protein diet is about 600 c.c. decinormal acid (Folin).

The term *amphoteric reaction* is used when the urine turns blue litmus red, and red litmus blue; this is the safe zone where there is no precipitation in urinary lithiasis; if both these changes of colour occur readily the *p*H is 6·4. If the red paper only turns a very faint blue, the *p*H is 6, and if it does not turn blue at all the reaction is below 6, which favours uric acid precipitation. If the red paper turns blue easily and the red paper shows no change the *p*H is 7 or above, which is the zone of phosphate precipitation (**2**). Other indicators may be used, such as methyl red in spirit which is added a drop at a time—a pink colour means a *p*H under 6, a yellow colour means a *p*H over 7; series of tubes are sold showing the grading of colour of indicators with change of *p*H. (*See also* p. 538.)

When it is desired to render a patient's urine alkaline, the best means of doing so is to administer repeated drachm doses of the potassium or sodium salt of citric, tartaric, or malic acids, which act as below explained; but sodium bicarbonate is the most effective. The acidity of the urine is increased in fevers and diabetes. It may be artificially increased by administering acid sodium phosphate (30 grains) by the mouth three or four times a day, or calcium chloride or ammonium chloride in 15 grain doses, four or five times a day.

Calcium Oxalate. The quantity of calcium oxalate secreted daily is only about 15 to 20 milligrams a day, but it is sometimes seen as a deposit in the urine, or it forms calculi in the kidney. Under the microscope will be found the minute octahedra of calcium oxalate, looking often like square envelopes. In different positions they may seem to have a rhombic or hexagonal outline, and if the edges are not developed they may form square prisms, with pyramidal ends. A not uncommon variety is that of the "dumb-bell," which is really a disc, with a central depression on either face, lying on its side, and seen edgeways. Such formations no doubt result from slow precipitation in the presence of colloid matter.

Oxalic acid may result from the catabolism of proteins and the purin containing nucleo-proteins, and possibly even from carbohydrates and fats by oxidation. There are only four foods which contain enormous quantities of oxalic acid (**4**); these are cocoa 450 milligramme per cent., sorrel 360, spinach 320, and rhubarb 240. So far as published figures go, the next in order are dried figs 100, chocolate 90, and potatoes 40; this is a very different list to that ordinarily published. Oxaluria is frequently present without symptoms; when these occur they are pain and sometimes hæmaturia, rather similar to renal calculus, and occasionally severe attacks have simulated acute intestinal obstruction. A non-purin low protein diet is indicated, with avoidance of oxalate-containing foods.

Uric Acids and Urates. Although the daily excretion of urates is quite small, the free acid and its salts are not infrequently deposited from the urine. (*See also* Reaction of Urine, Treatment of Renal Calculus and Gout.)

Uric acid is precipitated in acid urine of *p*H 5·7 and below. The deposit is scanty and looks like Cayenne pepper. Under the microscope the crystals show

themselves as yellow fusiform or lozenge-shaped crystals, with sharp ends and rounded sides; or as shorter and thicker crystals, with blunt extremities and more barrel-shaped; but generally in some modification of the diamond shape. They are frequently grouped together in radiating clumps or star-like masses.

Urates are, as a rule, precipitated, in an amorphous form, as a thick pink or red sediment (*brick-dust* or *lateritious*). The causes of their deposition are (1) the cooling of the urine, because they are abundantly soluble at the body temperature, and very much less so at 50° or 60° F.; and (2) concentration of the urine. A gentle heat will at once dissolve the deposit; and if the urine is being tested for albumin, the urates dissolve, and leave the fluid clear before the albumin begins to appear. (3) Acidity of the urine also favours the deposition of the urates; and in some urines the addition of acetic acid prior to testing for albumin will cause a precipitate of urates, which will redissolve on heating.

Urinary Pigments. The urine varies in colour both in health and disease. In health it is sufficient to distinguish between pale urines of low specific gravity, normal-coloured urines, and high-coloured urines of high S.G.; while in disease we may observe, in addition, different shades of red, reddish-brown, and brownish-black from the admixture of blood, urobilin, or bile-pigment, and an opaque white colour in chyluria.

There are several pigments in the urine. Probably its colour is chiefly due, as shown by A. E. Garrod, to an iron-free pigment named *urochrome*. This pigment obscures the violet end of the spectrum, but gives no absorption bands. *Urobilin* exists in the normal urine in only small quantities, 1 to 2 grains in twenty-four hours; it gives a definite spectrum, with an absorption band at Frauenhofer's line F—that is, between the green and the blue. The chemical test of its presence is to render the urine strongly alkaline with ammonia solution, filter, and add a few drops of a 10 per cent. aqueous or alcoholic solution of zinc chloride: a green fluorescence occurs if urobilin is present. Urobilin is probably absorbed from the intestine, where it is originally derived from bilirubin. Urobilin is in excess in fevers, in some diseases of the liver, in cardiac failure, in excessive hæmolysis (*e.g.* in pernicious anæmia and in acholuric jaundice), and during absorption of extravasated blood. It is diminished when the formation of bile is checked (phosphorus poisoning, acute yellow atrophy) or the bile duct is occluded. *Hæmatoporphyrin* is derived from hæmoglobin; it occurs in minute quantities both in health and in disease, and more abundantly in the urine of rheumatic fever and some other disorders. It may not cause any appreciable difference in tint, and though it exists in quantity in some dark red urines passed after the administration of sulphonal, the dark colour is mainly due to other pigments. There is a rare in-born error of metabolism, in which hæmatoporphyrin is passed in the urine giving it a ruby-red colour. Porphyrins are present in the fæces and the skin is very sensitive to light, which causes a bullous eruption of hydroa æstivale (**2**). *Uroerythrin* is another pigment, which gives the colour to pink urates. Uric acid deposits are coloured by urochrome, and also sometimes by uroerythrin (Garrod).

The urine may also contain *chromogens*—that is, bodies which do not at the time colour the urine, but develop a colour either on standing, or on the addition of oxidising agents. The following are known: (1) the chromogen of urobilin, urobilinogen, shown to exist in febrile urine by the addition of nitric acid; (2) a chromogen found sometimes in the urine of anæmia, which, though quite pale when passed, may yield a deep red colour on the addition of nitric acid; (3) the chromogen of *melanin*, a black pigment which is developed on exposure, or on the addition of nitric acid, in the urine of patients suffering from melanotic sarcoma, although it is clear when passed; (4) indican, or potassium indoxyl-sulphate, the chromogen of indigo-blue. This is the result of the absorption from the intestinal canal of indol, which results from the bacterial decomposition

of proteids. It exists in normal urine to a very small extent, but is greatly increased in all conditions leading to retention of intestinal contents. Its presence is detected by the addition of an equal quantity of hydrochloric acid, and then a few drops of a saturated solution of calcium hypochlorite. Indigo is thus formed, and colours the mixture blue or violet. It can be separated by shaking with chloroform, which then forms a blue layer at the bottom of the test-tube. Sometimes the addition of nitric acid alone develops a blue, violet, or blackish colour, due to the separation of indigo.

In *alkaptonuria* the urine is of a natural colour when passed, but darkens on exposure, is darkened rapidly by alkalies when warmed, is turned deep blue by a dilute solution of ferric chloride, and is found to contain homogentisic acid, and sometimes uroleucic acid. The condition is rare, but in many of the cases it is congenital, and occurs in two or more members of the same family, and the children of parents who are blood-relatives. It causes no symptoms (*see* Ochronosis).

Several *medicinal and other chemical substances* colour the urine, or give colour-reactions with tests employed for other purposes. Rhubarb, which contains chrysophanic acid, makes the urine a deeper yellow; and santonin the same. The addition of an alkali will turn these urines red. Logwood gives a reddish tinge to the urine. Carbolic acid, taken internally, or absorbed from carbolic dressings, often causes the urine to become dark brown or greenish-black on exposure, though clear when passed, from the presence of pyrocatechin and hydroquinone. Creosote may have the same effect. Methylene blue, taken internally, renders the urine blue, or, if in small quantity, green. Eosin, used to colour toys or sweets, has caused a bright red urine in children. If potassium iodide or potassium bromide is being taken, nitric acid may darken the urine from the liberation of free iodine or bromine. Free iodine or bromine can be separated by shaking with chloroform.

ALBUMINURIA

The term *albuminuria* is commonly used to denote the presence both of serum albumin and globulin in the urine. The serum globulin is often in excess in the urine of lardaceous disease, and may be detected by pouring the urine into a large bulk of distilled water, when the globulin is precipitated, or by saturating the neutralised urine with magnesium sulphate. On the other hand, in chronic parenchymatous nephritis the globulin in the urine is much diminished relatively to the albumin, the ratio being 1 to 6. In cases of functional albuminuria this ratio is usually 1 to 2.

Albuminuria may be detected in various ways.

Heat. If clear acid urine containing albumin be heated in a test-tube, it will become opaque from the coagulation of this substance. According to its quantity there will be a mere opalescence, a decided turbidity, or a thick creamy deposit. The best way of applying the test is to fill a test-tube to one-half or two-thirds of its length, then add a few drops of dilute acetic acid, and, holding it by its lower end, warm the upper part of the urine. The heat is thus confined to that portion of the urine, and whatever slight change takes place in the clearness can be recognised by comparison with the cool urine below.

Some precautions are necessary. First, heat may precipitate substances which are not albumin, *i.e.* phosphates, which, however, are at once dissolved by a drop of nitric or acetic acid. Secondly, albumin, though present, may fail to be coagulated by heat. This occurs when the urine is not sufficiently acid, and the serum-albumin has been converted into alkali-albumin, which is not precipitated by heat; the fallacy can be guarded against by the addition of acetic acid to the urine after boiling, so as to render it acid. In any case the experiment must be performed upon a clear urine: if turbid from urates, a gentle

heat clears it; if from phosphates, a drop or two of acetic acid should be added; if from any other deposit, the urine should be filtered.

Nitric Acid. The test is best applied by placing a little nitric acid in the bottom of a test-tube and very gently pouring the suspected urine down the side of the tube, so that it flows on to the surface of the acid without mixing with it. At the line of junction a layer of albumin forms, of white colour if abundant, or a thin grey disc when the quantity is very small. In the former case also it forms at once; in the latter it may take several seconds, or two or three minutes, or even half an hour.

There are but few fallacies connected with this test. First, in urine containing an excess of urates, these are sometimes precipitated as a cloud or haze some distance above the nitric acid, instead of lying immediately upon it; the application of a gentle heat will at once dissolve them. Secondly, nucleo-protein (mucin) is precipitated as a haze in the same position. Thirdly, the urine of persons who are taking copaiba internally contains a resinous acid, copaivic acid, in combination with bases. If nitric acid be added to this the resinous body is thrown down, generally as a cloud, evenly diffused through the urine. This precipitate is also dissolved by heat. Fourthly, the addition of nitric acid may give rise after some time, when the mixture has become cold, to a crystalline deposit of nitrate of urea; but this has no resemblance to albumin, consisting, as it does, of lamellar crystals, radiating in various directions. Nitric acid also precipitates the albumoses, which are redissolved by heat.

Picric Acid. A test-tube should be more than half filled with urine, and a saturated solution of picric acid, which has a low specific gravity, should be poured on to it so that the liquids may mix as little as possible; at the line of junction a delicate white line, or a thicker white cloud, at once forms, which, if albumin, is not dissolved by heat. Besides albumin, picric acid also precipitates urates, alkaloids, and albumoses. These are said to disappear at once on warming the urine. Quinine is the only alkaloid that is likely to be taken in sufficient quantity to be precipitated by picric acid. Nucleo-protein is also precipitated by picric acid and is not dissolved by heat. If picric acid gives no precipitate albumin is certainly absent.

Salicyl-sulphonic Acid. A saturated solution of this acid is a delicate test for albumin: added to clear urine in a test-tube, it throws down an opalescent cloud of albumin. It is useful for confirming the results obtained by the heat test. Albumoses are also precipitated.

The following are *quantitative tests* for albumin:

Esbach's Test. This method is simple but uncertain and inaccurate. A test solution is prepared, consisting of one part of picric acid and two parts of air-dried citric acid in 100 parts of water. A graduated tube from 6 to 8 inches long and ½ inch in diameter is filled up to a certain level (2¼ inches) with urine, and then for a certain distance (1½ inches) with the picric solution. The precipitated albumin is allowed to settle for twenty-four hours, and the marks on the tube show the amount of albumin contained in 1,000 parts of the urine, *i.e.* grammes per litre.

Kerridge's Test. This is the best clinical method and should come into general use. 1 c.c. of urine (or cerebrospinal fluid) is shaken in a small standard test-tube with 0·1 c.c. of a carbon suspension and then with 0·1 c.c. of trichloracetic acid; the colour is compared with standard tubes (**6**).

The Causes of Albuminuria. In considering the reason why albumin appears in the urine in Bright's disease, we must remember that the occurrence of albuminuria is not limited to cases of nephritis, but accompanies a variety of other disorders. The different conditions in which albuminuria has been observed may be enumerated as follows:

I. Arising in the kidney—

1. Bright's disease in its varieties, as detailed later; acute fevers.

2. Pyelonephritis, including calculous pyelonephritis; and metastatic nephritis.
3. Tuberculous kidney.
4. Lardaceous disease.
5. Venous obstruction in diseases of the heart and lungs, and local disturbances of the circulation.
6. Cystic disease.
7. New growths, including leukæmia; and parasites.
8. Hydronephrosis and temporary obstruction of the ureters; pregnancy.
9. Functional albuminuria.
10. The presence of foreign proteins in the blood and Bence Jones albumosuria.

II. Arising in the urinary passages below the kidney—
1. Disease of the pelvis of the kidney and the ureters.
2. Cystitis.

In this last group, the albuminuria is always slight, since it is merely either a part of the pus that exudes directly from an ulcerated stratified mucous membrane, or blood that may be the result from rupture of vessels as in the case of calculus.

Other Proteins of the Urine. *Nucleo-protein, Euglobulin.* If a few drops of acetic acid be added to the cold urine, especially if diluted, a precipitate may form, which was once thought to be mucin, and more recently a nucleo-protein derived from the renal cells. Such precipitates have been considered by Mörner to be compounds of serum-albumin with chondroitin-sulphuric acid, with nucleic acid, and in cases of jaundice with taurocholic acid. On the other hand, they have been thought to be a mixture of euglobulin and fibrinogen (Oswald). The practical importance of this substance, euglobulin, or whatever else it turns out to be, is that it may be the substance that causes functional albuminuria in young persons (*see* p. 551). It is generally agreed that its presence in quantity definitely excludes the case from the category of true nephritis, so that the prognosis is good.

Specific *proteoses* occur in the urine in asthma and other allergic conditions (*q.v.*), in tuberculosis, influenza, and probably in most if not all infective febrile conditions. Proof has been obtained that the patients are sensitised to their own proteose by means of skin reactions, and in influenza and in one case of purpura tested the proteose was associated with a hæmolysin. To test for proteose, urine acidified with a few drops of 25 per cent. sulphuric acid is shaken with a quarter of its volume of ether, when the ether layer becomes opaque and viscous (**4**).

Bence Jones *protein*, which occurs in multiple myeloma of the bone-marrow (*myelopathic albumosuria*), and occasionally in myelogenous leukæmia, is coagulated by a lower temperature than albumin, that is 58° C. (137° F.), as compared with 75° C. (167° F.), and the coagulum is re-dissolved as the temperature is raised to boiling. It is precipitated by a saturated solution of ammonium sulphate. Strong hydrochloric and nitric acid throws down an abundant precipitate, which is only dissolved in very great excess of acid, but is soluble on boiling. In smaller quantity, an amount of the protein equal to 0·5 per 1,000 will give a white ring at the junction of the fluids, when the urine is floated on the acid (Bradshaw's test).

Peptones rarely, if ever, occur in the urine. They give the biuret reaction—a pink or rose colour when the urine is floated in a test-tube over a small quantity of Fehling's solution—but they are not precipitated by nitric acid, nor by saturation of the fluid with ammonium sulphate, which precipitates the other proteins. This and other salts may be used for the separation of the proteins, since ammonium sulphate precipitates all proteins, except peptones, sodium magnesium sulphate precipitates serum-albumin, and magnesium sulphate throws down serum-globulin.

HÆMATURIA

Blood may be present in the urine in obviously large amounts, forming clots, or in sufficient quantity to give the urine a bright red colour. When there is less present the urine often has a dirty-brown colour and turbid "smoky" appearance from the presence of methæmoglobin or hæmatin; generally with this there is a granular reddish-brown sediment. It must, of course, not be forgotten that the urine may be coloured red by hæmoglobin without the presence of actual blood, and by some other red pigments (*see* pp. 444, 510). The presence of blood is determined in several ways.

The Microscope. By this we can recognise red blood cells in cases where there is no suspicion, from the colour of the urine, that blood is present; if the urine is distinctly red, or brown and turbid, the discs will be there in abundance. From suspension in the urine they may have lost their bi-concave form, and are often shrivelled, and have crenated edges, or may present protrusions of their substance. They remain visible for the longest time in acid and dense urines, but may be quickly dissolved in ammoniacal urine, or in urine of low specific gravity.

The Spectroscope. The spectrum of urine containing oxyhæmoglobin shows two absorption bands in the yellow and green portions between Frauenhofer's lines D and E, the narrower, darker, better-defined band being nearer to D. Methæmoglobin gives three absorption bands, two in very nearly the same position as those of oxyhæmoglobin, and a third about half-way between C and D. Acid hæmatin shows a fourth band between E and F.

The Guaiacum Test. To the urine, in a test-tube, are added a few drops of tincture of guaiacum, and then about ½ drachm of ozonic ether or ozonic alcohol, which contain hydrogen peroxide. Quickly or slowly, according to the quantity of blood, a blue colour forms at the junction of the fluids, and diffuses itself through the ether which floats on the surface; its appearance may be hastened by gently shaking the mixture. The test is not absolutely trustworthy. The urine of patients taking potassium iodide will give a blue colour, but it appears only slowly unless the iodide is in very large amount.

Causes of Profuse Hæmaturia. For convenience these may be classified as (1) Surgical, though with medical bearings—renal calculus, tuberculosis. neoplasm, aberrant renal artery, enlarged prostate, papilloma of bladder, (2) Medical (roughly in order of frequency)—acute nephritis, tubal nephritis, and secondary and primary contracted kidney, hyperpiesia; heart disease, *e.g.* infective endocarditis, and mitral stenosis with infarction or congestion; urinary tract infection; purpura, anæmia, polycythæmia; irritation by drugs, such as hexamine, carbolic applications, and rhubarb; oxaluria and bilharziasis.

The recognition of the true cause of hæmaturia has frequently failed in the past, and so the term *Essential Hæmaturia* or *nephrostaxis* has often been used, and even now, occasionally, no cause can be assigned to a case; but it is wiser and simpler to plead ignorance than to perpetuate an unexplained pathology. No doubt some cases are due to minute nævi in the renal pelvis, and a number of cases of purpura of the urinary tract have been described.

Diagnosis. Cystoscopy, etc. should be used to determine from what part of the urinary tract the blood is coming; however, it is useful to remember that in urethral hæmorrhage the blood is discharged separately and is not mixed with the urine.

CASTS

These are solid bodies, which are detected by the microscope in the urine, and if sufficiently numerous form a sediment visible to the naked eye. Where they are too few to be easily detected, they may be found after centrifugalising the urine. They are cylindrical in shape and from 0·01 to 0·05 mm. in breadth; but they vary still more in their length, which may reach 1 or even 2 mm., so as to

stretch right across the field of the microscope, but is more often from five to ten times the breadth. Their connection with the kidney is proved by finding them after death, *in situ*, usually in the junctional tubules. They are probably formed in the loop of Henle, since the lumen of the tube is much narrower here than elsewhere, so that the material becomes squeezed as it passes through. The following varieties are distinguished :—

Hyaline Casts. These are transparent colourless cylinders, with refractive properties so like those of the fluid in which they lie, that they are discovered with great difficulty, unless they are stained by the addition of carmine or iodine, or one of the aniline dyes, such as gentian-violet. They are homogeneous, soft, and flexible, straight or curved, and varying in length. Occasionally they have other deposits adherent to, or embedded in, them, such as red blood corpuscles, leucocytes, epithelial cells, granular masses, fatty granular globules, crystals of urates or oxalates, or particles of hæmatoidin.

Some of the varieties of casts described below probably have the same hyaline material as a basis, which is then completely covered by, or mixed up with, the other elements.

Hyaline casts are often spoken of as " fibrinous," but it appears that they are not pure fibrin. Most probably they are formed from an albuminous coagulate, which has transuded through damaged epithelium from the blood. More rarely they are formed from tubular epithelium, which has undergone hyaline degeneration.

They occur in the different forms of nephritis, and in the congestion produced by heart disease ; they are nearly always associated with the albuminuria of renal origin, but may precede for a few hours or days the appearance of the albumin, and may continue for a time after its disappearance.

Epithelial Casts. These consist of cells of the renal epithelium held together by, or embedded in, the coagulable material which makes up the hyaline casts. The epithelial cells may be more or less distinct ; they may come from the convoluted tubule or the loop of Henle.

Granular Casts. These are not so transparent as hyaline casts, being sometimes like ground glass, sometimes darker and much more opaque. They are formed by the degeneration of epithelial cells, and in many cases it is possible to see the outlines of the epithelial cells in the cast.

Fatty Casts. These are either hyaline casts in which globules and granules of fat are embedded, probably from the disintegration of epithelium in a state of fatty degeneration ; or they actually consist of such fatty epithelial cells themselves. *Lipoid* casts show double refraction, when examined with the polarising microscope.

Blood Casts. These result from the coagulation of blood which has been effused into the renal tubules ; they are easily recognised by their colour, and by the size and close aggregation of the blood corpuscles composing them. Their presence in a case of hæmaturia proves that the blood comes from the kidney itself.

Waxy Casts. These are large and highly refractive casts, which are sometimes found in cases of lardaceous disease, but also in other chronic forms of Bright's disease. They are brittle, and break irregularly, which gives them rather the appearance of wax. They often do not give the reactions of lardaceous material, and their nature is doubtful, but it is possible that they are a later stage of the granular cast.

Though the character of the casts found in the urine must be determined to some extent by the condition of the kidney, conclusions on this last point must not be too hastily drawn from them. Frequently two or more forms are found in the same urine, and we must be guided by the predominance of one or the other. Hyaline and granular casts are found in all forms of nephritis, acute or chronic. Blood casts and epithelial casts are most common in acute cases ;

fatty casts are most frequent in cases of chronic nephritis, in which fatty degeneration has supervened.

Leucocyte Casts. This is the name given to casts in which pus cells are embedded.

Cylindroids. These are large hyaline bodies with tapering or branching ends, a wavy outline, and longitudinal striation : they are probably threads of mucus, the undissolved residue of nucleo-proteid, and not really casts. They have no significance.

THE ESTIMATION OF THE RENAL FUNCTIONS

Water Output Test. To test the ability of the kidneys to excrete water, 1,200 c.c. water are taken in the early morning without breakfast. At least 900 c.c. urine should be excreted during the following five hours, and the specific gravity should be 1,003.

The Concentration or Specific Gravity Test. No fluids are allowed for twelve or sixteen hours, and a high-protein supper with salt is given at 6 p.m. Three specimens are collected, on waking, and at hourly intervals. The maximum specific gravity should be at least 1,026 ; otherwise the concentrating power is deficient.

Estimation of Urea in Blood. The simplest and shortest method is Yvon's. Ten cubic centimetres of blood from a vein are mixed with 5 c.c. trichloracetic acid to precipitate the proteins and made up to 25 c.c. in a small measuring flask. The mixture is filtered into a measuring glass and the volume of the filtrate noted. This is made alkaline with caustic soda, phenolphthalein being used as an indicator. The measuring apparatus consists of a small funnel connected below by a stopcock with a short burette. On the lower end of the burette a rubber bag is fixed containing some glass beads. The bag is squeezed, and the apparatus is filled with the alkaline filtrate, which is carefully washed in, all the air being expelled from the bag and burette, and the stopcock is then closed. Some sodium hypobromite is poured into the funnel, and is allowed to enter the burette. The contents of the latter are mixed by inverting it several times. The nitrogen liberated is collected at the top of the burette, and is measured by transferring the burette to a cylinder of water and removing the bag. The calculation follows from the fact that 1 gramme urea corresponds to 370 c.c. of gas measured over water at 15° C. and 760 mm.

Normally the blood contains 30 milligrammes per cent. Figures of ten times this amount are found in uræmic coma. Cerebro-spinal fluid may also be used. In this case it is unnecessary to remove the proteins with trichloracetic acid.

Urea Concentration Test. The patient abstains from fluid for fifteen hours ; on waking in the morning, he empties his bladder, and immediately drinks 100 c.c. of a solution containing 15 grammes urea flavoured with tincture of orange. One hour later he passes urine, and again after a second and third hour. The percentage of urea is determined in the two specimens. If the percentage is above 2, the excretory power is satisfactory. It has been found that this test is only accurate if the volume of urine passed is about 100 c.c. (**9**). So the writer advocates returning to the principle of McCaskey's original method as follows :—

The Rate of Urea Output Test. The procedure of the urea concentration is followed ; but there is no necessity to restrict the fluid unduly beforehand. From the hourly volumes and the urea percentages the maximum amount of urea passed during one of the three hours is calculated. The minimum amount of urea which healthy kidneys excrete varies a little with the volume of urine as below :—

Hourly volume, c.c.	50	60	70	80	100	120	150	200	250
Urea output (gms. per hr.)	1·81	1·92	2·0	2·05	2·08	2·09	2·10	2·10	2·2

If the maximum hourly urea output of a patient falls below the minimum figures in the second line of the above table, the excretory power of the kidneys is to be regarded as deficient.

Blood Urea Clearance Test. As this test was originally described, the patient at 6 a.m., without breakfast, drinks slowly 1000 c.c. of water (35 ozs.) containing 30 grammes of urea. If the urea concentration in the blood is already high, *i.e.* 60 milligrammes per cent., no urea need be taken. At 7 a.m. and every hour afterwards until 11 a.m. the patient drinks slowly two glasses of water (about 16 ozs.). The amount of urea passed in the urine during each hour between 9 a.m. and 12 noon is determined and samples of blood for blood urea estimations are taken at 9·30, 10·30 and 11·30 am. Then the ratio of the amount of urea passed per unit time to the concentration of urea in the blood is a constant —in other words, as the urea in the blood rises, so the amount passed in the urine increases. To avoid taking such a large quantity of urea the writer gives a dose of 15 grammes at 8 a.m.

The amount of urea (u) passed per minute in a volume of urine (v) may be looked upon as coming from a volume of blood (V), which contained an amount (U) of urea before the kidney had completely cleared it out, so that the UV = uv. Therefore $V = \frac{uv}{U}$, a fraction which is the same as the ratio above. Hence this constant represents a hypothetical volume of blood which in the space of a minute has been cleared of its urea—hypothetical because no portion of blood is ever cleared of its urea completely. The constant is called the *maximum clearance*, because during the test the kidney is working up to its maximum capacity to get rid of water and urea. It is a measure of the amount of functional renal tissue present in the body, and it provides the best test of renal function at present available. In an adult the maximum clearance varies within a range of 60 to 94 c.c. per minute, average 75 c.c. In the case of children and of individuals varying considerably from the normal in size (*e.g.* wt. 10 stone and ht. 5 ft. 7 in.), the value obtained must be multiplied by $\frac{1{\cdot}73}{\text{the body surface in sq. metres}}$ before it is comparable to the normal figures just mentioned (*see also* p. 460). The body surface is calculated from the height and weight as explained on p. 460 (**10**). This test may be looked on as an extension of the last test since blood urea comes in as a factor additional to concentration and volume ; in fact, rate of urea output is only satisfactory, because, when the blood urea is normal beforehand, it usually rises to a constant level after giving 15 grammes urea.

Example : the figures obtained from an adult male for each of the two last hours of the test were as follows : Urine vol., 483, 466 c.c. ; urea percentage, 0·47, 0·48 ; blood (milligrammes per cent.), 0·48 and 0·45. The maximum clearances per minute were $\frac{470}{48} \times 8{\cdot}05$, $\frac{480}{45} \times 7{\cdot}75$, and multiplying out 79, 83. Mean = 81—a normal figure.

It is claimed that reliable results are obtained even when the volume of urine is as low as 120 c.c. per hour, but below this figure the clearance fraction, which is no longer now a maximum, is not constant. This is a disadvantage, because the diuresis of hydræmic nephritis will often not even reach this figure. But a fair approximation may be arrived at by using $\sqrt{v}$, in the case of children $\sqrt{\frac{v \times 1{\cdot}73}{\text{Body Surface}}}$, instead of v in the above equation. This is the *standard clearance* and the normal range is 41–67 c.c. ; and the mean 54 c.c. (**11**). This modified formula may be used when the blood and urine are analysed over hourly periods without giving either urea or water ; but the maximum clearance test is probably best. A similar test with creatinine has been described (**12**).

Estimation of Diastase in the Urine. This test has been described on

(*b*) *Theories of Renal Œdema.* There is normally a balance between the blood in the capillaries and the tissue fluids, which prevents any excessive exudation of fluid from the capillaries. The osmotic pressure of the blood proteins plays a part in this balance. The loss of the smaller protein molecules means that the osmotic pressure in the plasma due to the proteins is greatly diminished and the equilibrium between the blood and tissue fluids is upset, and so fluid and salts escape into the tissues, which become œdematous, the protein content of the dropsical fluid being very low. This is Epstein's theory of œdema. Now it is an undoubted fact that the osmotic pressure of the plasma is lowered in renal œdema, and the serum albumin with its smaller molecules is also diminished relatively to the serum globulin; but there are, in the writer's opinion, three objections to these changes being regarded as the cause of renal œdema: (*a*) a lowered osmotic pressure would mean a greater filtration pressure through the glomeruli, so that the agency that drove the fluid out into the tissues would also increase the flow of urine; a balance would result; (*b*) the transfusion of 500 c.c. blood in one case did not cause a diuresis; it only increased the albuminuria (**39**); (*c*) in one case of the writer's the œdema rapidly subsided, while the protein in the serum still remained at the same low value. Two other theories have been advanced to account for renal œdema: (1) It has been suggested that the systemic capillaries are injured through some intoxication and so become more permeable to the fluid parts of the blood; but it is difficult to see why a toxin should get into the blood in just those cases of renal disease, where the excretion of protein catabolites is not greatly interfered with, while many cases with very seriously impaired renal efficiency, *i.e.* secondary contracted kidney, do not suffer from œdema at all. (2) It has been suggested that the œdema follows because the kidneys cannot excrete chloride, and if salt is retained water must also be retained so as to preserve the isotonicity of the body fluids, and œdema results. But it has been shown that excess of water by itself leads to œdema (**20**). However, if salt is added as well, the tendency to œdema is still further increased. The latter was shown by a case of the writer's, where, in spite of a low blood chloride, the administration of salt and water for a special therapeutic purpose not only caused an increase of body weight, from œdema, but also diminished the flow of urine, which remained low for some time. In the writer's opinion, the simplest and most probable theory is that œdema is due to the blocking of the tubules, so that the glomerular filtrate from normal glomeruli trickles through so slowly that a larger proportion of chloride than normal is absorbed with its quota of water. Œdema follows when excess of water or of chloride and water are taken; if water is deficient owing to vomiting, for instance, there is retention of salt without œdema, the "dry retention" of French authors.

2. *Excretory Functions of the Kidneys.* (*a*) If there were complete obstruction of glomeruli or tubules, no fluid or salts could get through the kidney at all; there would be suppression of urine and accumulation of all the excretory products in the blood, in the same way as when both ureters are obstructed by calculus. If there was a partial obstruction, there would be a resistance to the excretion of water and salts, so that œdema might follow if the patient took plenty of fluid. If the tubal epithelium were not much interfered with, the excretion of urea might not be much below par, and unless too high a protein diet were eaten the urea would not accumulate in the blood. This is the case in one form of acute nephritis (nephritis mitis), where the tubules are obstructed. If there was glomerular destruction and this took place slowly, the resistance might be entirely compensated for by an increased pressure exerted on the glomeruli, and here again it is interesting to note that certain cases of war and civilian nephritis have recovered completely as far as the excretory powers of the kidney are concerned; but a permanent hyperpiesia has been the result (**17**).

(*b*) If the tubules were seriously affected alone the glomerular filtrate would be produced normally and there would be no high blood pressure. However, the con-

centration of urea would be seriously interfered with ; urea, sulphates, phosphates, etc., would be retained in the blood and the patient might die of uræmia without any circulatory symptoms, a condition which has also resulted from war nephritis. If the lower part of the tubules were alone affected the patient would merely pass an extremely dilute urine, but the excretory power of the kidney would be unaffected. It has been suggested that such a condition occurs in diabetes insipidus owing to the absence of posterior pituitary extract (**7**).

(*c*) If both glomeruli and tubules were simultaneously and gradually affected the condition described in secondary contracted kidney would be expected. A high blood pressure and hypertrophied heart would follow from the relative impermeability of the glomeruli. The functions of the tubules would be disturbed, so that urea, etc., would accumulate in the blood, and the destruction of the lower part of the tubules would prevent reabsorption of water, so that the patient would continually pass a very dilute urine of low specific gravity. This failure to reabsorb water would tend to prevent œdema. The same reasoning holds for those cases of nephritis repens in which large portions of the glomerulo-tubal systems are completely destroyed, leaving too small a number for the work of excretion.

ACUTE GLOMERULO-TUBAL (TOXIC) NEPHRITIS

Ætiology. This disease, commonly called *acute nephritis*, is a *diffuse* nephritis. The actual cause is at present unknown. There is, however, a general consensus of opinion that the disease is due to infection, though whether the kidneys are themselves the place where the organisms are growing or are solely affected by toxins which arise from micro-organisms in quite a different part of the body is an open question. In many of these cases the tonsils are septic, and it is quite common for an acute nephritis to be preceded by an acute tonsillitis, points which suggest that focal sepsis may be a primary cause ; in these cases the micro-organism implicated will be the streptococcus. Scarlet fever is a well-known cause of the condition, and in this case children are more often the subjects than adults. As a rule, the symptoms are first observed during convalescence, and the nephritis is presumably due to streptococcal invasion ; sometimes it commences before convalescence is established. However, of cases met with in a general hospital, acute tonsillitis is eight times as common as scarlet fever as the predisposing cause (**17**). Several other febrile diseases are sometimes the precursors of acute nephritis. They are coryza, acute rheumatism, measles, variola, cholera, varicella, typhus, enteric fever, pneumonia, relapsing fever, diphtheria, Henoch's purpura, tubercle, syphilis, and septic conditions, including empyema and wounds of the skin and scalp. The micro-organisms of some of these infections have been found in the urine, *e.g.* pneumococci and typhoid bacilli.

Exposure to cold and damp, particularly if the patient is under the influence of alcohol, is sometimes regarded as a predisposing cause. A very good example of the type of nephritis arising apparently spontaneously is the so-called "trench nephritis," which occurred among soldiers in the recent war ; it was not confined to soldiers in the trenches. Similar outbreaks have occurred in other campaigns, notably the American civil war. There is no essential difference between trench nephritis and the acute nephritis of civilian practice. Pregnancy is not infrequently the cause of nephritis, which may be of the most severe type, with uræmia and retinal changes.

Morbid Anatomy. In some cases the kidney may be of normal size and of normal appearance to the naked eye—a remarkable fact considering that the patient has died very often from virtual suppression of urine. This has been noted in cases of trench nephritis and scarlatinal nephritis when death has occurred rapidly. In other cases the kidney is more or less swollen ; it has a rounded form, is tense and elastic, the capsule strips readily, and

the surface is paler than normal. On section, the cortex is considerably swollen, and of greyish-red colour, while the pyramids are dark red from congestion. Here and there are bright red spots: some of them are congested glomeruli, others are small hæmorrhages. In yet other cases the kidneys are intensely congested, dark red or chocolate in colour, dripping with blood, and showing on section a still more extreme congestion of the pyramids.

Microscopically, when the inflammatory reaction is intense (nephritis acris), the glomerular tufts are swollen with a proliferative glomerulitis, and they contain many polymorphonuclear leucocytes. The cells of the tubal epithelium show a swollen granular protoplasm with disappearance of nuclei, cloudy swelling or albuminous degeneration, and they may contain hyaline droplets (hyaline droplet degeneration); dropsical, fatty and lipoid degeneration may also be present, and there are hyaline and granular casts. The presence of doubly refracting lipoid droplets constitutes lipoid degeneration. The interstitial tissue is frequently œdematous, and there is periglomerular infiltration with polymorphonuclear leucocytes. When the inflammatory reaction is of low grade (nephritis mitis), the stroma of the glomeruli is œdematous. The endothelium of the capillaries of the tuft is swollen; there is cloudy swelling and lipoid degeneration of the epithelium of Bowman's capsule, and very marked lipoid degeneration of the epithelium of the renal tubules, while the nuclei of these cells are degenerated. Cellular and albuminous *débris* are frequently present in the capsular spaces, and the tubules contain hyaline and granular casts (**24**).

Pathology. There is interference with most of the renal functions during an attack of acute nephritis, but there is much variation from case to case. Owing to failure to excrete non-protein nitrogenous substances, there is a corresponding retention of them in the blood; this is shown by the rise in the urea content of the blood, which is considerable in some cases (180 milligrammes per cent.), though it is slight in others. The œdema may be due to the inability of the kidneys to excrete water and salts owing to deficient glomerular function. There may or may not be some deficiency in the excretion of diastase. A rise of blood pressure, both systolic and diastolic, accompanies the œdema in acute nephritis. Its effect is to increase the circulation of blood through the kidneys, and so help to keep up the flow of urine. It rapidly falls to normal when the œdema subsides and the volume of urine is increased.

Symptoms. The onset of symptoms is often insidious. Very often œdema is the first symptom noticed by the patient or his friends. The face looks puffy, the fluid collecting beneath the eyes in particular, when the patient rises in the morning. It may subside in the course of the day, but if the feet be examined at night there is œdema just below the ankles. There is, indeed, a small quantity of effusion into the subcutaneous tissue, which always seeks, by force of gravity, the most dependent part. During the daytime it reaches the feet; in the recumbent position of sleep it diffuses itself generally, but is most pronounced in the loose tissues of the eyelids. If the patient takes to his bed, it will leave both the face and the feet, and accumulate in the tissue over the sacrum, which has now become the most dependent part. The puffiness of the face is in marked contrast to the onset of œdema in cardiac failure, which gravitates downwards, becoming first of all visible in the legs. The duration of the œdema of acute nephritis varies greatly. In mild cases it may disappear in a day or two. On the other hand, it may continue, and the case eventually becomes one of large white kidney. Associated with the œdema there is diminution in the volume of urine and albuminuria. In the worst cases only a few ounces of urine of high specific gravity may be passed during the day, and it may become solid on boiling owing to the high concentration of albumin. In milder cases the volume of urine is greater, and it may be turbid and have a colour which is due to the presence of fresh or altered blood, and is dusky brown, deep brown, "porter-coloured," pink, or distinctly red, according to the quantity and condition of the

blood. In some cases hæmaturia may be present with no more albuminuria than would be accounted for by the blood (*Hæmorrhagic Nephritis*). The volume of urine is often not diminished in such cases.

Quite early the pulse becomes hard, and the blood pressure is raised, sometimes up to 180 mm. The rise is greater at night than in the morning. The heart sounds are modified. The first sound (systolic) increases in intensity, and the second sound (over the base of the heart) is also accentuated or "ringing" in character.

The patient may feel unwell; there may be some rise of temperature; there is anorexia and usually vomiting. Headache is complained of. There may be pain over the epigastrium associated with vomiting; but the writer considers that the pain described occasionally in the loins, means acute pyelonephritis (*q.v.*) and not acute nephritis. Anæmia may be present. Dyspnœa was a symptom that was very frequently noticed in trench nephritis. Œdema of the lungs may have accounted for this symptom in some cases. In severe cases the heart dilates, and the impulse may be displaced outwards.

Uræmia in Acute Nephritis. In those cases where the suppression of urine is considerable *uræmia* may supervene. (1) This may be similar in its biochemical changes to the uræmia associated with secondary contracted kidney, which has been called the chronic or asthenic type of uræmia (*see* p. 530). (2) But there is another special type of uræmia called the *acute* or *sthenic* type, or sometimes *eclamptic* or *convulsive acute uræmia*, which is very characteristic of acute nephritis and which is not associated with a high urea or phosphate retention in the blood. In this type headache and vomiting become more severe, the pulse is slow, there may be Cheyne-Stokes respiration, and there are convulsions. Experience of trench nephritis during the war showed that these symptoms were due to cerebral œdema, since they could always be stopped by lumbar puncture, and the cerebro-spinal fluid was under considerable pressure. The convulsions are due to compression of the brain against the inside of the skull. There is a secondary rise of blood pressure. This type of uræmia has been regarded as due to chloride retention (**18**). The attacks have a very close resemblance to the ordinary attacks of epilepsy. There is often a short tonic stage, and then general clonic convulsions of all the muscles of the limbs, face, eyes, and trunk. Consciousness is lost, the face becomes livid, there is frothing at the mouth, the saliva may be tinged with blood, and the pupils are dilated. After some minutes the convulsions subside, and the patient may at once regain consciousness, and then improvement in the general condition may begin, for convulsions are by no means always an unfavourable sign. In other cases the patient lapses into a state of *coma*, from which he may again pass into convulsions; and these are repeated again and again with intervals of complete coma in which he may die. During the convulsion the respiration is hurried, and the pulse is small and quick; the temperature is variable, and it may reach 104°, or higher. This sequence of events may be repeated several times. Whilst the epileptiform attack is the classical expression of this type of uræmia, it is often absent and headache and vomiting may be present alone, and there may be temporary localised paralyses or hemiplegia and homonymous hemianopia or complete blindness (*uræmic amaurosis*). The latter may last from one to three days, and frequently passes off entirely. As the pupil reactions are unaffected, it is probably due to compression of the higher visual centres. Deafness may be also noticed, and there may be delirium or mania. These various manifestations often precede or follow the convulsions.

Ocular Changes. In the majority of cases of acute nephritis no changes in the retinæ are observed, with the exception of small more or less circular hæmorrhages, which, however, are apt to occur in people failing in health. Out of 119 soldiers suffering from trench nephritis, Foster Moore observed definite eye changes in only five, coming on about two months after the beginning of the

illness. The blood pressure was higher (average 180 mm.) in these cases than in the remainder (average 143 mm.). The changes consisted of exudations at the back of the retina, leading often to its detachment. They were seen as pale, soft edged, oat-shaped swellings, arranged radially in some cases so as to form a star. Later on these swellings coalesced as the exudations became more extensive. Hæmorrhages were also present, and the edges of the optic disc were blurred by exudations (papillitis). In severe cases the swelling of the disc is so marked as to conceal completely the retinal vessels, and resemble the papillœdema of cerebral tumour. More often there is slight prominence, but diffused opacity spreads far on to the surrounding retina. These various changes are seen more often in chronic parenchymatous nephritis. They may be regarded as being due to toxic action. Atrophy of the retina and papilla may follow on the preceding inflammation. *See* Plate 14.

Course. In the majority of cases there are no uræmic convulsions at all. After a few days or a week or two improvement sets in, often quite suddenly. The volume of urine is greatly increased as the dropsy disappears; the blood pressure falls to normal. The albumin and blood disappear more gradually, small amounts being passed for weeks afterwards.

But the course of acute nephritis may be less favourable in several ways. In a small proportion of cases death follows rapidly from uræmia.

In other cases the symptoms may continue. It has already been mentioned that there is derangement of all the renal functions during the acute attack, but certain of these recover first. In some cases there may be early diuresis and disappearance of œdema, but the patient still remains ill. The percentage of urea in the blood remains high, or if this is not greatly raised, the power of the kidneys to concentrate urea is deficient. The diastase in the urine is low. The volume of urine is normal or increased. It contains albumin, but not in very large amounts. Such is the picture of the *azotæmic* type of nephritis, and it eventually leads to secondary contracted kidney.

On the other hand, the œdema may continue. The percentage of urea in the blood soon becomes normal. The volume of urine is decreased, but the percentage of albumin is large. Such cases conform to the *hydræmic* type of nephritis, and the term *nephrosis* has been used for them on the supposition that they showed no tendency to progress towards secondary contracted kidney with cardiac hypertrophy, etc., and that the urea concentration was normal. But there is no justification for this distinction, and the writer has found in some typical cases that the "rate of urea output" and the "blood urea clearance" were below normal, even though the "urea concentration" was apparently high. The case eventually becomes one of subacute glomerulo-tubal nephritis.

In yet other cases the œdema and urinary symptoms clear up entirely; there remains only a raised blood pressure without renal impairment.

Finally, there are two other groups: in one of them there is persistent slight albuminuria from a leaky kidney without casts or signs of renal impairment; in the other the patients suffer for years after from intermittent hæmorrhagic nephritis, also without signs of renal impairment, and brought on by a coryza or other acute infection (**17**).

Diagnosis. This rarely presents any difficulty. The sudden appearance of a general dropsy, with albuminuria or hæmaturia, in one previously quite healthy, or recovering from scarlatina or other fever, can scarcely be mistaken for anything else. If there is a small quantity of albumin only in the course of an acute disease, this may be due to a change in the epithelium, not usually regarded as constituting nephritis, though it is not essentially different from what actually takes place in the typical conditions. In pyelonephritis there is usually pain in the loin and the urine contains pus cells, while albuminuria is slight.

Prognosis. It is, on the whole, favourable, as between 60 and 70 per cent recover completely (**17**). The unfavourable indications are excessive dropsy,

very scanty or suppressed urine, high urea in the blood, very high tension of the pulse, asthenic uræmia, or the later condition of feeble pulse with obviously failing heart, hydrothorax, and serous inflammations. But there are scarcely any of these serious dangers from which recovery may not take place, and sometimes, after living for months on the verge of death, the patient may ultimately get quite well. The prognosis of hæmorrhagic nephritis is good; because there is presumably a free flow of blood through the kidneys.

Prevention. It has been found that the administration of alkalies (up to 200 grains a day) during convalescence in scarlet fever, will prevent, in most cases, the onset of nephritis, and the same preventive measure might well be used in acute tonsillitis, when nephritis is to be feared (**36**). There is some evidence that if a septic focus can be found, its removal prevents future attacks (**37**).

Treatment. Rest in bed and warmth are essential. Various diets have been recommended. The usual diet is confined to milk, farinaceous foods, fruit and vegetables, while the volume of fluid is limited to the pint or 1½ pints of milk allowed. Some physicians, in the early stages, restrict the diet drastically as regards protein, chloride and fluid in the hope of bringing about an early diuresis and cure. For the first day or two glucose in ½ pint of water will be allowed for a child, with barley sugar extra to suck; then fruit, vegetables and some cereals, and salt-free rusks, butter, cream and jam. Sufficient alkali in the form of sodium bicarbonate and potassium citrate—in equal parts—should be ordered to keep the urine just alkaline. Enough fluid should be given to allay thirst, though this is probably not distressing when there is marked œdema. Another method is to give fresh fruit and vegetables such as tomatoes and raw carrots, without added water at first, and as soon as the œdema decreases, the yolks of three eggs, given with sugar and orange juice, and meat, including liver, and then salt-free rusks and butter (**38**). Other physicians have tried the opposite plan of a high protein diet (meat, fish, chicken, eggs, plasmon) so as to obtain the diuretic effect of the urea formed in metabolism, or extra urea has been given to drink with honey and fruit juice. In this diet alkali as above should also be given.

During convalescence iron should be given to restore the condition of the blood, but it is not well to use it in the early stages (*see* p. 431). The treatment of dropsy is considered later. Where the tonsils are septic, it is reasonable to remove them, and this has been carried out successfully during the acute nephritis, though this is not advised; other septic foci should also be dealt with.

Acute Uræmia. The onset is heralded by a rise of blood pressure and frequent readings are desirable. Bleeding from the arm will often prevent convulsions, and 10 to 20 ounces may be removed without danger, though it is, as a rule, undesirable that patients with pronounced renal disease should lose much blood. A valuable method of arresting the convulsions is by lumbar puncture. This was definitely established in trench nephritis; but there is some danger of sudden death from a pressure cone formed against the edge of the foramen magnum, as in cerebral tumour. A recent method is to inject a 25 per cent. solution of magnesium sulphate intravenously, the dose being 0·2 c.c. per kilogramme of body weight. 50 per cent. glucose injected intravenously may counteract the cerebral œdema by increasing the osmotic pressure of the blood. Sedative drugs, *i.e.* chloral hydrate, 5 to 15 grains by mouth, four-hourly, or 30 grains per rectum; or a few whiffs of chloroform may be used to supplement the former methods. In convulsions the patient's tongue should be protected as in epilepsy, by placing a piece of stick between the teeth.

Acute Focal Nephritis. This is a form of acute nephritis now recognised, where there are patchy changes in the kidney, with resulting hæmaturia and/or albuminuria and casts, but there is a sufficient extent of healthy tissue to allow of all the excretory functions being carried out, so that there is no œdema or other symptoms. The "febrile albuminuria" of acute tonsillitis may be an example of this disease. The immediate prognosis is very good; but it is

impossible to be certain that in some cases the disease may not be the beginning of a secondary contracted kidney. The treatment is the same as acute diffuse nephritis. The name "focal nephritis" might suggest that the disease results from focal sepsis in the tonsils, etc.; but the term is not used in this sense. Of course, focal sepsis may cause either acute diffuse nephritis or acute focal nephritis.

SUBACUTE GLOMERULO-TUBAL (TOXIC) NEPHRITIS

(*Chronic Parenchymatous or Tubal Nephritis, Large Mottled or White Kidney*)

Ætiology. This diffuse type of nephritis may appear as a sequel to the acute stage, but its onset may be so insidious that the inflammatory changes in the kidney reach this stage of development before the diagnosis is made at all.

Morbid Anatomy. The *large mottled or white kidney* receives its name according as hæmorrhages or fatty changes predominate. The two kidneys together may weigh as much as 800 grammes; often they weigh 500 grammes. The surface is smooth, and the capsule strips easily; it is of yellowish or greyish-white colour, and is covered with venules radiating from a central point (stellate veins). On section, the cortex is broader than normal, of the same colour as the surface with an appearance of coarse striation, while the pyramids are more or less dark red. Here and there are red spots, due to hæmorrhage. *Microscopically*, the glomeruli show evidence of progressive inflammation. There is proliferative glomerulitis with obvious lobulation of the tuft, which may be swollen; there are adhesions between the tufts and the capsule. There is proliferation of the endothelial cells lining the capsule, so that a *demilune* is formed, and the lumen of the glomerulus may be partially or entirely obliterated. The tuft may eventually become hyaline in whole or in part. This hyaline necrosis is quite different from the focal embolic nephritis of infective endocarditis. Marked changes are seen in the convoluted tubules, similar to those described in acute nephritis. The distension of the tubes with opaque material forming casts, and the compression they exert on the vessels, account for the white or grey colour of the cortex. An increase of interstitial tissue which is partly œdema and partly due to an active proliferation of fibroblasts is widely diffused through the cortex and the intertubal tissue is irregularly infiltrated with leucocytes.

Symptoms. If this stage of glomerulo-tubal nephritis follows directly on an acute attack, there is a continuance of the symptoms already described: general dropsy, effusion into the serous cavities, scanty albuminous urine. In other cases there may be an apparent recovery from the acute attack, and after an interval the symptoms recur.

In cases where the onset is insidious, pallor, loss of appetite, nausea, headache, and frequent micturition are the first signs, and then œdema may be observed in the lower extremities at night, and around the eyelids in the morning. The dropsy gradually increases.

In advanced cases the dropsy becomes general, and the skin of the whole body is œdematous. The face is full and rounded; the eyelids are distended, and almost close the eyes; the limbs become enlarged, shapeless, and remind one of bolsters; the trunk is enlarged; the loose skin of the penis and scrotum is so stretched that the prepuce looks like a bladder, and the scrotum may attain the size of a fœtal head. Wherever slight pressure is applied, as by the finger of the doctor, or by the bands, strings, or folds of clothing, it produces by the displacement of the fluid a deep impression, which is only slowly effaced by the return of the fluid. This is called *pitting on pressure*. Even then, the influence of gravitation on the distribution of the dropsy may be seen, for if the patient lies for any length of time on one side, the arm of that side will become more swollen than the arm which is uppermost; and the same will happen to the side of the face. When this general dropsy, or *anasarca*, is present, there is, as a rule, some effusion into the peritoneal cavity (*ascites*), into one side, or more

frequently both sides, of the chest (*hydrothorax*, dropsy of the pleura), and it may be into the pericardial sac. Of these the first is perhaps most often recognised, while the pericardial and pleural effusions may be comparatively slight. There may be œdema of the lungs which gives rise to no physical signs but only to dyspnœa, and also œdema of the pharynx and larynx. As in acute glomerulo-tubal nephritis these patients occasionally suffer from acute uræmia from cerebral œdema.

If incisions be made into the skin, or if one or more Southey's drainage tubes be inserted, a quantity of fluid will drain away, which may amount to 8 or 10 pints in a few hours, and the dropsical limbs will rapidly get smaller. The fluid is colourless, of low specific gravity (1,007 to 1,012), and contains a small quantity of albumin, inorganic salts, and urea. A feature which is constantly present in renal dropsy is a high degree of pallor—the lips are almost colourless, the cheeks are pallid, and the whole body has a waxy whiteness. This is often not due to anæmia, but to the distension of the skin and subcutaneous tissues.

The urine in parenchymatous nephritis is scanty, highly albuminous (up to 20 or 30 parts per 1,000), and contains casts of all kinds ; fatty or lipoid casts are numerous in the cases of large white kidney with much fatty or lipoid degeneration of the renal epithelium. They are accompanied by leucocytes, loose epithelial cells, and granular *débris*. In some cases the urine contains much blood.

In the blood the cholesterol is increased, while the urea (also non-protein nitrogen) varies from normal up to fully uræmic figures, *e.g.*, over 0·10 per cent. In long-standing cases cardio-vascular changes may be present, as in secondary contracted kidney. The retinal changes described under Acute Nephritis are present in some cases. Extensive œdema of the retina may lead to its detachment.

In chronic parenchymatous nephritis, as also in acute nephritis, there is a tendency to inflammation of the serous membranes. Pleurisy is the most common ; pericarditis is often the precursor of a fatal termination ; acute peritonitis is perhaps more rare, unless it follows tapping the abdomen. Bronchitis is a common, and endocarditis an occasional, complication ; pneumonia not infrequently occurs towards the end. Ulcerative colitis is rather a characteristic complication. Several lesions of the skin may complicate Bright's disease—namely, (1) pruritus and urticaria, the former especially in early stages ; (2) eczema ; (3) an acute general dermatitis, with free desquamation, not unlike exfoliative dermatitis ; (4) patches of erythema affecting the dropsical limbs ; (5) erysipelas ; (6) purpura or hæmorrhage, followed by necrosis and ulceration, conditions which have also been observed in the alimentary mucous membranes ; and (7) very rarely the skin has the appearance of having been dusted with flour or pounded sugar. This is probably due to evaporation of the sweat, leaving crystals of salt on the skin.

Course. In the majority of instances, the disease is fatal. Death is in most cases due to complications, such as pleurisy, pericarditis, pneumonia, œdema of the lungs, œdema of the glottis, increasing dropsy, heart failure, or inflammation or sloughing of the skin ; and this commonly occurs in from six to eighteen months, though some cases go on for two or three years. Uræmia is not commonly by itself the cause of death. In a few instances the disease may disappear completely. In long-standing cases the various changes characteristic of secondary contracted kidney may occur.

Diagnosis. When acute nephritis changes into chronic parenchymatous nephritis there is a gradual transition, so that a distinction between the two clinically is rather artificial. From four to six months is usually regarded as the duration of the acute disease, so that chronic parenchymatous nephritis would be diagnosed if the disease had lasted longer than this. There will be no difficulty in differentiating it from secondary contracted kidney. It might be confused with lardaceous disease or primary heart disease with albuminuria. From

lardaceous disease it is distinguished by the absence of such causes as prolonged suppuration, phthisis, or syphilis, and by early scantiness of urine and abundant deposit. The similarity between this and heart disease may be close, especially when there is much œdema in the latter case. The presence of abundant casts in the urine is an indication of nephritis. The history, the general character of the dropsy, and the large quantity of albumin will help to distinguish primary renal disease from secondary albuminuria.

Treatment. This is not essentially different from that of acute nephritis. Rest in bed and warmth are essential. Where there is nitrogen retention, it is reasonable to employ a rather low protein diet as described in the next section.

Œdema has been successfully treated by giving alkalies in sufficient amount to raise the alkaline reserve of the blood to a normal figure; but some cases are intractable and the administration must be carried out with caution. The alkalies used are a mixture in equal parts of the four salts: potassium, sodium, bicarbonate and citrate, and the amount given per day may be increased up to 1,000 grains or more; frequent blood examinations are desirable and sometimes the œdema increases at first. Caffeine and theobromine are best avoided.

Diminution of the dropsy is sometimes obtained by the use of a diet as free as possible from sodium chloride, as suggested in the provisional theory of Bright's disease. Indeed, healthy persons have sometimes had œdema from eating excessive quantities of salt, because water will be retained with the salt to keep the body fluid isotonic. Treatment along the lines of Epstein's theory may also be tried, and remarkable results in lessening the œdema and promoting diuresis have been obtained. The diet given is very rich in protein, with an almost entire absence of fat. A little carbohydrate is allowed. It consists of lean meat, lean ham, whites of eggs, oysters, jelly, lentils, split peas, green peas, rice, oatmeal, skimmed milk, coffee and tea, salt in moderation, and fluid as reasonably desired. This treatment may do good, not because of any increase in the plasma proteins, but because of the increased amount of urea produced and an even more effective way of producing diuresis is to give urea in 15-gram doses by the mouth. The probable explanation is that the increased urea content of the tubal fluid hinders reabsorption of water at the lower end. Where there is nitrogen retention it is better to employ urea rather than a rich protein diet, since it is probable that the latter predisposes to uræmia. Success has been claimed for thyroid treatment, especially as it has been found that the basal metabolism is often low.

Other long-practised methods of treating œdema are by purgation with 20–40 grains pulv. jalapae co., senna or mag. sulph., and by diaphoresis. Diaphoresis should be promoted by hot-water bottles or by the hot-air bath. The *hot-air bath* is administered by raising the bedclothes from the patient by means of a low cradle and fitting them close about his neck and round the sides and end of the bed. The heat may be supplied by a number of electric light bulbs placed inside the bedclothes or by burning a spirit lamp under a funnel connected with a tube which leads under the clothes. The exposure should be from fifteen to twenty minutes at 120° F.; but it is desirable to take the temperature of the patient as well, as it may be inconveniently raised, if free sweating does not occur. In this case the diaphoretic drug, nitrate of pilocarpine, in a dose of $\frac{1}{6}$, $\frac{1}{4}$, or $\frac{1}{3}$ grain, may be injected subcutaneously.

In extreme dropsy, especially where the skin is tense and threatens to become inflamed or to slough, the dropsical fluid may be removed under antiseptic conditions, either by small incisions with a lancet or punctures with a needle, or by the use of Southey's tubes. Two or more of these may be placed in each leg, and by this means several pints of serum may be withdrawn in a few hours; the tubes should be removed after six hours to prevent sepsis, but drainage may continue through the punctures. Only occasionally, in extreme cases, is it desirable to tap the abdomen or to aspirate the pleural cavity.

Anæmia in prolonged cases should be met by the use of iron preparations (*see* p. 431). In the more chronic forms, with albuminuria but little dropsy, benefit may be derived from residence in warmer climates—Bournemouth or Tenby in the British Isles, the south of France, Italy, or Egypt.

Cases of chronic Bright's disease have been treated by Edebohls in America, by exposure of the kidney, decapsulation, and fixation of the organs; but the benefit of this surgical treatment is very doubtful. Cases of parenchymatous nephritis are most suited to this procedure. Septic foci should also be removed, particular care being taken to exclude sinus infection.

CHRONIC GLOMERULO-TUBAL (TOXIC) NEPHRITIS

(*Secondary Contracted Kidney*)

This type is called "secondary," since it arises as the result of inflammation of the kidney. It is often spoken of as contracted white kidney or small white kidney to distinguish it from the red granular kidney described next; but this method of differentiation is not good because the most chronic type of secondary contracted kidney in middle age is red in colour. Histological studies have shown that there are two different types of chronic glomerulo-tubal nephritis: (1) In the *diffuse* type (chronic nephritis acris), the presence of acute or subacute toxic nephritis associated with much œdema has usually been noted from two to ten years previously, so that the kidney has presumably passed through the stages described under acute and subacute glomerulo-tubal nephritis in a variable number of years. (2) In the *reticular* type (nephritis repens), the patient may have had an acute attack of nephritis, which has apparently completely cleared up, and many years later symptoms pointing to the last stages of granular kidney are observed; but more often there is no history of any acute disease at all; the kidney changes are believed to have arisen insidiously from chronic inflammation lasting for years. The term *nephritis repens*, or creeping nephritis, has been suggested for this type from the histological picture, which suggests an inflammatory reaction with its resulting scarring that has been creeping insidiously through the kidney, leaving portions unaffected. Nephritis repens is broadly divisible into two groups: (*a*) there is the nephritis repens of childhood and early adult life. In these cases, as also in chronic nephritis acris, a variable amount of arterio-sclerotic change (ischæmic nephritis) is present, as described later, but it is not usually marked, and cases of war nephritis have resulted in this type of kidney without any cardio-vascular changes at all. In rare instances this type of nephritis repens has been described in children, associated with delayed rickets and infantilism; (*b*) there is the nephritis repens of middle age, 35–66 (average 47·7 in 15 cases), where the inflammatory process is extremely chronic and the arterio-sclerotic process is very marked. The blood pressure is much raised, and the œdema which is often present has the distribution characteristic of heart failure (**24**). Death may take place from heart failure, cerebral hæmorrhage or uræmia, or a combination of these. The following clinical account does not apply to these cases.

Morbid Anatomy. In the *diffuse* type the kidney is normal or a little on the small side. The capsule strips with moderate ease and the surface is smooth or finely granular and contains flecks of opaque yellow lipoid, which are seen particularly well on section. The demarcation between the cortex and medulla is blurred. Microscopically, the glomeruli show proliferative glomerulitis and hyaline necrosis and proliferative capsulitis in varying degrees. The interstitial tissue in general shows areas of dense fibrosis, enclosing atrophied tubules and small islands of less dense fibrosis, enclosing dilated tubules. There is infiltration with lymphocytes, plasma cells and polymorphonuclear leucocytes in smaller number. The naked eye appearance of the kidney of *nephritis repens* (*reticular* type) is variable; it may resemble that already described, or it may be very

considerably reduced in size with obvious granulations, and certain forms are extremely scarred and irregularly lobulated. On section, the cortex is pale and the medulla often pink, and the demarcation between the two is blurred. Lipoid deposits are usually obvious ; in the very chronic forms met with in middle age the colour is dark red, so that to the naked eye the kidney resembles the arterio-sclerotic kidney described next. Microscopically, the fibrotic areas which contain the damaged glomeruli and atrophied tubules are spread through the kidney in a coarse reticular fashion, surrounding large islands containing dilated tubules, which show a considerable amount of regenerative hypertrophy. Lipoid deposits are often seen, and there is sometimes hypertrophy of the surviving glomeruli. There is general infiltration of the fibrotic areas with lymphocytes, plasma cells and a few polymorphonuclear leucocytes. A variable degree of arterio-sclerotic change, the nature of which is described in the next section, is usually but not always present in both diffuse and reticular types. It tends to be more marked in the long-standing cases.

It is clear that nephritis repens is identical with the " contracted granular kidney " of Bright's disease. The writer has long believed that the smallness of these kidneys is due to their being attacked in childhood before they have reached adult size. This view is borne out by Miss Russell's observations (**24**). If the weights of the kidneys in her series are plotted against the body weight or height, then for a given weight or height the kidneys of the young adult are usually smaller than those of the middle aged, even though the most chronic cases are included in the latter group.

Pathology. There are two ways in which the body compensates for the loss of excretory function in renal disease. In the first place, the arterial pressure is raised by means of a hypertrophied heart and constricted arteries, so that filtration through the impaired glomeruli takes place under pressure. In the second place, the concentration of urea in the blood is increased, and this facilitates its excretion by the kidney, so that a balance takes place, the output of nitrogenous substances corresponding accurately with the amount in the food. The concentration of urea is normally 20 or 30 milligrammes per cent. Values of 100 milligrammes and over are frequently found in this disease when the patients are up and doing their ordinary work. Any great increase in the protein of the food throws more work on the kidney, and this is only performed by some additional retention of urea, so that the percentage of urea in the blood is still further increased. The balance between intake and output becomes re-established, the kidney responding to a higher threshold value of urea in the blood. The importance of limiting the protein of the food will be at once evident.

If the lesion progresses the urea in the blood becomes higher and higher. The same thing will be caused by an acute attack of nephritis supervening on the chronic condition. Characteristic symptoms of intoxication, called *asthenic* or *chronic uræmia*, appear when the concentration of urea is too high. These may begin when the urea is about 200 milligrammes per cent. In the fully developed uræmic condition values for the urea of 300, 400, or 500 milligrammes per cent. have been observed. Besides urea, non-protein nitrogen, creatinine, uric acid, phosphoric and sulphuric acids accumulate in the blood, so that the alkali reserve is lowered (**27**). The alveolar CO_2 is also diminished, but not in proportion to the accumulation of other acid in the blood, so that the acidity (hydrogen ion concentration) of the blood is increased (*acidæmia*). Other unknown acids and metabolites may also be present in the blood. There is evidence that the acidæmic state is not by itself responsible for uræmic coma, because acid values as high have been observed in other patients non-comatose. It is certainly not due to the urea, which is a relatively harmless substance when taken in large doses by the mouth. It might be due to poisoning by excess of the SO_4 or PO_4 ions ; but it is reasonable to regard the muscular twitchings as essentially similar to *tetany* (*q.v.*), especially as the calcium in the blood is low (**28**). Air

hunger or extreme hyperpnœa is the consequence of the acidæmia, the CO_2 in the alveolar air and blood being lowered by this means. In a case of pure uræmia, due to the removal of a solitary kidney, these further biochemical changes were found before death: fall of blood calcium, chloride, hæmoglobin, and plasma albumin, and increase of plasma globulin and ammonia. The blood cholesterol remained normal (**29**).

Chronic uræmia is a characteristic mode of termination in secondary contracted kidney, but it is not peculiar to it. It may occur in arterio-sclerotic kidney occasionally, and in pyelonephritis, particularly where there is suppuration in both kidneys, in polycystic disease, bilateral renal calculus, and occasionally in acute nephritis.

Symptoms. In the diffuse type considerable œdema is usually present in the terminal stages; but in the nephritis repens of young people there is usually no œdema, though slight puffiness under the eyes is not uncommon. In both types the volume of urine is increased, especially at night, and the patient has to get out of bed one or more times to pass water. This is to be regarded as a compensating mechanism, since the kidney excretes at night what it cannot get rid of in the daytime. It is more marked when the protein content of the diet is high. In the final stage the urine is pale and of very low specific gravity, 1,005 to 1,012. Albuminuria is present, but the percentage of albumin is never as great as with large white kidney. Casts and blood cells are seen on examination of the deposit. The blood pressure is raised, but it is not usually so high as in cases of arterio-sclerotic kidney. The heart shows evidence of hypertrophy (*q.v.*). There is marked secondary anæmia.

"Albuminuric retinitis" is very characteristic of secondary contracted kidney. Owing to the vascular changes always present in this condition, the retinal changes often resemble rather closely those which have already been described under arterio-sclerosis (*see* p. 302). On the other hand, the larger, pale, soft-edged areas, or cotton-wool patches (*see* p. 522), are sometimes seen (*see* Plate 14, p. 303). Bright patches of exudation, showing fatty changes microscopically, are sometimes arranged as a star-shaped figure in the macular region.

The patient may continue for years with varying health. In some cases there is nothing at all to suggest the presence of disease until uræmia suddenly comes on. This is of the chronic or asthenic type.

Asthenic Uræmia. The patient complains of feeling weak and sleepy, of nausea, which may be accompanied by vomiting, and of headache. There may be cramps and tingling sensations. Periods of restlessness alternate with stupor. Twitching of the muscles of the face are seen; they may also affect the arms, legs and trunk; but there are no convulsive attacks as in sthenic uræmia. The pupils are contracted, the temperature of the body falls, the breathing is slow, panting, and laborious, the mouth and tongue are dry, and there is great thirst, and there may be troublesome vomiting. The muscular twitchings continue, and the patient becomes restless, indifferent, and drowsy, and coma eventually occurs. As coma develops the breathlessness gives rise to deep hissing respirations; the air hunger may be just as marked as in diabetic coma. The breathlessness increases in proportion as the acid accumulates in the blood. Sudden attacks of breathlessness, sometimes called "renal asthma," have been described, particularly at night. Cheyne-Stokes breathing has also been described. Since a raised urea content in the blood is regarded as the criterion for true asthenic uræmia, these two latter types of respirations are not uræmic, but are due to acute pulmonary œdema. They are commonly seen in cases of arterio-sclerotic kidney (cardio-renal disease), and the cases described by Lewis and others (*see* p. 255), were probably of this nature, since the blood urea was always less than 100 milligrammes per cent., far below the true uræmic value. Further observations have shown that there is no increase of fixed acids in the blood in these cases (**25, 26**). It is probable that in the past the term *uræmia* was

held to cover a number of different states, and it is only with the advent of methods of biochemical investigation that these states are in process of being differentiated from one another. When the symptoms of uræmia are less pronounced the condition is sometimes called *latent uræmia*, a name which has also been given to the results of suppression of urine from obstruction of the urinary passages (*see* p. 549).

Death may also be due to secondary infections, *e.g.* pleurisy, pneumonia, pericarditis, gastro-enteritis leading to severe vomiting and diarrhœa and ulcerative colitis. Hæmorrhages which are of toxic origin due to renal failure (as opposed to those due to high blood pressure and degenerate arteries), may take place from mucous membranes or into the brain, and not uncommonly play their part in causing death, and any of these terminal events may accompany uræmia. But secondary infection is not such a common mode of termination as it is in subacute toxic nephritis.

Diagnosis. This depends on finding a dilute urine containing albumin associated with impairment of renal function, with but little tendency to œdema. The differentiation of intestinal obstruction and uræmia may be difficult as there is a rise of blood urea in both, but in intestinal obstruction there is alkalosis with a high or normal alkaline reserve, while in uræmia the alkaline reserve is low.

Prognosis. This is bad in the developed disease. The tests most valuable in estimating the gravity of the case are the examination of the retinæ and the estimation of kidney function. If there is well-marked retinitis, the patient will probably not live longer than two years. If the blood urea is permanently above 100 milligrammes per cent., uræmia may supervene at any time. Patients may live many years if the blood urea is below this figure, especially if the urea concentration test is fairly satisfactory.

Treatment. After the removal of any condition which can be safely regarded as the cause of the condition—*i.e.* alcohol, lead, constant exposure to cold, septic foci, etc.—the objects should be (1) to diminish the call upon the excretory power of the kidney; (2) to reduce the strain upon the heart and vessels; (3) to remove anæmia; and (4) to treat special complications as they arise.

The most important part of treatment will be to remove as far as possible strain from the kidney, and prevent the retention in the blood of acid products of protein in metabolism, so characteristic of uræmia. The metabolism of food yields varying amounts of acid and basic breakdown products, and foods may be grouped according as the yield of acid or of base is in excess. Vegetables and fruit, including lemons, provide an excess of base over acid as the result of metabolism, whereas eggs, fish, meat, biscuits, oatmeal, rice and wheat produce an excess of acid over base. Milk probably produces a slight excess of base over acid. Hence the advantage of choosing a lacto-vegetarian diet with sugar. But since very little protein is required to make good the wear and tear of the body, and the greater part of the protein taken on an ordinary diet is used merely as a source of energy, while the final breakdown products have to be excreted by the kidney, it is also advisable to restrict the amount of protein in the diet. Eggs, fish, meat, poultry and game, etc., should be entirely excluded. Bread, biscuits and cereals, except oatmeal, may be allowed in moderate amount, because their protein content is low, while the fact that they produce excess of acid over base may be remedied by prescribing sufficient doses of alkali to get the urine neutral (*see* Treatment, Subacute Toxic Nephritis). The amount of milk should also be restricted because its protein content is relatively high (*see* List D on p. 475). However, a warning is necessary, because when considerable amounts of albumin are being lost in the urine it is necessary to make allowance for this in the dietary. The average amount of albumin passed during the twenty-four hours should be determined, and an additional 5 to 10 grams of protein allowed per diem, so as to cover amply the loss from wear and tear of the body. Fats in the form of cream in limited

quantity, butter and olive oil, may be added to make up a sufficient diet; weak tea or coffee may be allowed. A periodical fast day may be instituted, if the nutrition is good. Alcohol should be entirely stopped, or amount at most to a glass of claret or dry sherry daily. Complete rest may be enforced when symptoms are serious, particularly if there are breathlessness when the patient is walking about and attacks of angina pectoris. At all times over-exertion and strain should be avoided. Exercise should be taken within the capacity of the heart. The patient should be warmly clothed, and residence in a genial climate is of great benefit.

Such hygienic measures may tend of themselves to lower the blood pressure. It must be remembered that the high blood pressure is probably itself in many cases a compensatory mechanism, so that the attempt to influence it directly with drugs, even if partially successful, may be bad practice. However, drugs may be used for this purpose if there is troublesome headache. Nitro-glycerine ($\frac{1}{100}$ minim once or twice daily and gradually increased), or sodium nitrate, or erythrol tetranitrate may be used. Antipyrin, caffein, and phenacetin are also useful.

Preparations of iron should be given for the anæmia (*see* p. 431).

Among the complications which require treatment are uræmia, vomiting, cardiac dilatation and failure. In uræmia the chief indication is to get rid of the excessive protein catabolites from the blood. For this purpose sweating should be promoted. A hot-air bath is sometimes useful, and pilocarpine injections have been employed. The bowels should be made to act freely, those purgatives being used that produce large watery evacuations, such as jalap. Irrigations of the colon may be used. Bleeding has often been of benefit, and this has occasionally been followed by blood transfusion from a suitable donor. Great care should be taken to see that the flow of urine remains free. Plenty of fluid should be taken by mouth. Intravenous injections of saline may be given if the blood pressure suddenly begins to fall. It is reasonable to add some sodium bicarbonate to the fluid to combat the acidæmia, and this drug may also be given by mouth.

For vomiting, effervescing mixtures, dilute hydrocyanic acid, a few drops of tincture of iodine in water every hour, or a cold compress or blister to the epigastrium may be tried. For the cardiac symptoms, which result from dilatation and feeble contraction of the ventricle, digitalis should be given, the bowels should be kept open, and generally the case should be treated like one of heart disease.

ARTERIOSCLEROTIC KIDNEY

(*Gouty, Red Granular or Primary Contracted Kidney; Ischæmic Atrophy of the Kidney*[1]; *Cardio-renal Disease*)

Ætiology. Arteriosclerotic kidney is the end result of that arteriolar proliferation which is called diffuse hyperplastic sclerosis, which primarily causes hyperpiesia; and the ætiology is the same as that of hyperpiesia (*see* p. 301). A mild form of this disease is not uncommonly found at post-mortem in elderly people, and this has been called *senile arteriosclerotic kidney;* but this does not require separate description, except to mention that there is no cardio-vascular hypertrophy, so that the blood pressure is not raised. Arteriosclerotic kidney may be complicated by the supervention of an acute or subacute toxic nephritis.

Morbid Anatomy. The average weight of these kidneys is about normal; but they are frequently somewhat reduced in size, though they are rarely as small as the secondary contracted kidneys of nephritis repens; they may be large. Some specimens show no macroscopic abnormality except thickening of the arteries. In the majority the capsule is densely adherent, and, if stripped off, carries with it small portions of renal tissue; the whole surface of the kidney is then seen to be covered with minute elevations (granulations) of $\frac{1}{16}$ to $\frac{1}{8}$ inch in size, consisting of the more healthy tissue, with intervening depressions due

[1] This term is preferable to "Ischæmic Nephritis," which has been recently introduced (**24**), because the changes are not regarded as inflammatory.

to scarring, and here and there may be cysts varying from $\frac{1}{8}$ to $\frac{1}{3}$ inch in diameter, and containing a clear fluid or colloid material. In some kidneys the scarring of the cortex is very uneven, deep clefts or pits appear at intervals on the outer surface, and the capsule is adherent to these, while the surface in between the clefts is smooth. The colour is mostly brownish-red, hence the name red granular kidney. The whole organ is tough ; on section the cortex may or may not be narrow ; the demarcation between cortex and medulla is usually good.

Microscopically, the arterioles show diffuse hyperplastic sclerosis (*q.v.*) with thickening of their coats ; the thickening may be so great that many of them become obstructed and this leads to collapse and ischæmic atrophy of the glomeruli and tubules supplied by them, which then form hyaline scars. The earliest glomerular change is a thickening of the basement membrane of Bowman's capsule, which spreads round and causes narrowing of the neck of the tuft so as gradually to cut off its blood supply. The whole glomerulus appears to shrink, and this is especially the case with the tuft, which loses its shape and is flattened and finally becomes invaded by small lymphocytes, which break through the fibrous investment and demilune which surrounds it. At the same time there is intense hyaline fibrosis of the interstitial tissue in the immediate neighbourhood. The progressive disease of the smallest renal arteries leads to numerical increase of the areas of scarring or contraction.

Symptoms.[1] The onset of arteriosclerotic kidney is generally quite slow, and marked by few distinctive features. Often, indeed, the kidneys are found to be granular in patients who die of other diseases, or a patient is struck down by cerebral hæmorrhage without any symptom having attracted attention to the condition of these organs. Amongst early symptoms, which, occurring in a middle-aged person, should make one think of granular kidney, if not accounted for in other ways, are recurring or persistent headache, shortness of breath, Cheyne-Stokes breathing, especially at night, general weakness, and œdema of cardiac type. Occasionally no symptom may be sufficiently prominent until the sight is affected by arteriosclerotic retinitis, and the patient's eyes are examined with the ophthalmoscope. The blood pressure is usually much above the normal and higher than in the secondarily contracted kidney ; values of 300 mm. are sometimes found for the systolic pressure. The diastolic pressure is also raised, but not in proportion. The urine is normal except for a trace of albumin and a few red cells, leucocytes and hyaline casts. The rate of urea output is usually normal. but may be a little deficient.

Hæmorrhages may occur owing to the high blood pressure and to the changes in the smaller arteries. In addition to retinal hæmorrhages, epistaxis is common and purpura and bleeding from the stomach and bowel may occur. The most important is cerebral hæmorrhage, which may cause death. It may take place in the neighbourhood of the basal ganglia, in the pons or medulla, or hæmorrhage may take place into the meninges.

The commonest cause of death is failure of the hypertrophied heart. This is frequently accelerated by myocardial degeneration. Various grave cardiac irregularities may occur—auricular fibrillation, pulsus alternans, heart block. The mitral valve becomes incompetent, and eventually the complete picture of a failing valvular disease may be developed, with a mitral systolic murmur, engorgement of the lungs and liver, ascites, dropsy of the lower half of the body. The urine is altered in the same manner as it is in a failing valvular disease—that is to say, it becomes scanty, high-coloured, and the albumin increases and the casts become granular. The pulse may for some time retain its hardness, but eventually there is a fall of blood pressure.

As the case progresses there is commonly some slight evidence of renal failure, as indicated by a blood urea of 40 to 50 milligrammes per cent., and the rate of

[1] The symptomatology of Arteriosclerosis and Hyperpiesia should also be consulted.

urea output falls a little. But the renal changes are not usually important unless the case is complicated by a sudden acute nephritis, when the patient may die rapidly of uræmia (*malignant sclerosis*), but more often of acute heart failure (**24**).

Diagnosis. The conditions that justify a diagnosis of primary contracted kidney are a small quantity of albumin in the urine, associated with symptoms of ill-health, and evidence of cardio-vascular disturbance, such as high blood pressure, thickened arteries, cardiac hypertrophy, retinal hæmorrhages, or retinitis, and œdema of the feet.

In a more advanced stage of the patient's illness, it is often very difficult from the clinical features alone to determine whether a case is one of *primary valvular* or *myocardial heart disease* with albuminuria from congested kidneys, or one of granular kidney with secondary hypertrophy and dilatation of the heart. A localised systolic murmur at the apex may occur in both cases; diastolic or presystolic mitral murmurs, and much more, aortic murmurs, are in favour of primary heart disease.

In their typical conditions there can be no difficulty in distinguishing between arteriosclerotic and secondary contracted kidney: in the latter the albumin is usually abundant, and the patient is younger, the blood pressure not so high, the urine more dilute; in fact, the picture throughout is definitely renal, while in the former the symptoms are mainly circulatory.

Prognosis. This is unfavourable, but much improvement may take place, and life may be prolonged in some cases to an advanced age. The greater the extent to which the heart is implicated, the less is the expectation of life.

The **Treatment** is that of arteriosclerosis and hyperpiesia (*q.v.*). Striking results are sometimes obtained with a low protein vegetarian diet as described in the last section. The treatment of chronic cardiac disease should also be referred to.

KNOWN BACTERIAL INFECTIONS OF THE KIDNEY

BACTERIURIA AND BACILLURIA

The following organisms are found in the urine: bacilli of the enteric group and tuberculosis, Brucella melitensis, Leptospira icterohæmorrhagiæ and the ova of Schistosomum hæmatobium—all associated with the corresponding specific disease. Staphylococci commonly accompany genito-urinary tuberculosis or calculi, or are secondary to infarcts in the kidney. *S. albus* can be cultivated from the urinary meatus and hence a few colonies can be disregarded and the same is the case with diphtheroids. *B. pyocyaneus* is secondary to a more virulent organism. Gonococci may come from a urethritis or ruptured prostatic abscess and heavy infection of the urine may be due to fistula between the bladder and colon.

Since the kidneys excrete waste products from the blood stream it is not surprising that bacteriuria is a fairly common condition, and discussion has taken place as to whether bacteria can be excreted without there being any lesion at all of the renal epithelium. Certainly in the bacilluria of typhoid such lesions are not obvious, though it would be very difficult to exclude them if they are only microscopic. Again streptococci circulating in the blood stream as a septicæmia or from some primary focus such as inflamed tonsils may be met with in the urine, though they probably slip through the renal epithelium after lodging as minute embolic foci in the kidney. However, in most cases there is no doubt that the bacteriuria means that pyelonephritis is present, as described later, and this is especially the case with the *Bacilli coli communis*, which is the most important urinary organism and may be present in the urine in enormous numbers and yet give rise to but few symptoms. "Atypical B. Coli," usually as *B. proteus*, are associated with chronic infection in the urinary tract.

From what has been said it will be seen that in most cases the ætiology is the same as that of pyelonephritis.

Condition of the Urine. The urine is often clear when passed, but on standing it deposits a layer like mucus at the bottom, above this there is a haze or turbidity, and at the top a clear layer ; or the urine is entirely turbid, and the turbidity does not clear on standing. The urine is usually *acid*, and it does not become clear either with heat and acetic acid or with alkalies. The presence of pus cells and albumin, even in small amount, proves that there is a pyelonephritis. When the urine has an offensive odour and there is pus, mucus and bladder epithelium it suggests that cystitis is present.

PYELONEPHRITIS

(*Pyelitis*)

The term *pyelitis* for this disease has been in use for over twenty years. However, there is evidence from post-mortem statistics that among these non-tuberculous infections of the kidney pyelitis *alone* is uncommon, accounting for only 7 per cent. of cases, unless there is obstruction to the urinary flow, when the occurrence is 52 per cent. (**30**). In fact, the disease commonly called pyelitis is in most cases a *pyelonephritis*, beginning in the substance of the kidney and spreading to the pelvis, and this is proved clinically by the fact that there is usually more albumin in the urine than can be accounted for by the amount of pus (or blood) present, proving that the kidney itself must be involved.

Ætiology. Pyelonephritis arises from several causes, of which the following have been recognised : (1) The action of turpentine and cantharides when given internally. (2) Gastro-enteritis, colitis, gall-bladder disease, appendicitis, febrile disorders, such as enteric and typhus fever, the exanthemata and pyæmia as well as scurvy, diphtheria, and cholera. (3) It may occur in Bright's disease and diabetes ; in the latter probably as a result of the irritation by the saccharine urine. (4) Many cases are due to a definite local cause, such as the irritation of foreign bodies in the pelvis and infundibula of the kidney, especially calculi and gravel, but also hydatids, blood clots, and carcinoma. (5) Obstruction to the passage of urine may also lead to it by decomposition of the retained urine. Obstruction may be due to urethral stricture, enlarged prostate, renal or vesical calculus, and retention of urine from disease or injury of the spine or spinal cord. (6) Inflammation may spread upwards in the lymphatics outside the ureter to the pelvis in cases of cystitis and other forms of inflammation in the lower urinary passages. The fact that pyelonephritis is three times commoner in women suggests that the infection commonly spreads up from below to the kidney, from a vulvo-vaginitis, for example, which must be a common source in very young girls. (7) There is no obvious primary focus, so that it seems pretty certain that the infection reaches the kidney by the blood stream. Usually one kidney alone is affected. Such patients get well, but they often relapse.

The colon bacillus was found as the causal organism in 76 per cent. of cases, presumably owing to the propinquity of the colon ; in the remainder cocci were found, including *S. aureus* (**31**). Streptococci and staphylococci and other organisms commonly accompany a *B. coli* infection. Pregnancy predisposes to infection, since with the usual position of the fœtus the uterus may press on the right ureter, causing partial obstruction and dilatation of the pelvis above.

Morbid Anatomy. In the common form of the very acute type of pyelonephritis the organ is swollen, soft, hyperæmic, and generally infiltrated with inflammatory cells, but without abscess formation ; this form may develop into gangrene. The commoner forms of kidney infection are, however, local, affect a segment of kidney substance, and may be generally described as of the infarct type. The characteristic feature is the presence of numerous yellow streaks of pus, stretching in a radial direction from the surface inwards through the cortex,

and even into the pyramids. They are sometimes wedge-shaped, or conical, with the base at the surface, in other cases simply linear. The infarct may break down into an irregular abscess cavity which discharges into the kidney pelvis. In other kidneys, where presumably the embolic infection has been less compact, the area shows up in the surface as a group of small abscesses which also appear in section in that segment of the kidney corresponding to the abscesses on the surface. There may be several patches of such purulent infiltration, the intervening portions of the kidney substance being healthy. One kidney only may be affected.

The localised infarct type of pyelonephritis is capable of healing like purulent lesions in other parts; the scar comprises a segment of the kidney substance depressed on the surface, sometimes with a local dilatation of the pelvis. Occasionally there are loculated cysts occupying a segment of kidney substance, in shape very suggestive of an origin from a septic infarcted area. Some of the cysts met with post-mortem, that are roughly classified as "congenital," have probably been caused in this way. A perinephric abscess is frequently due to a cortical abscess spreading to the perirenal tissues.

In acute *pyelitis* proper the mucous membrane is swollen, its vessels are injected; there are often small spots of hæmorrhage; sometimes the inflammation takes on a diphtheritic form, patches of membrane adhering to the surface here and there. In calculous pyelitis there may be ulceration of the surface from the presence of the stone; and such ulceration may, as already indicated, lead to perforation and perinephritis. Or if, either from the dislodgment of calculi or obstruction of the ureter by septic discharges, the inflammatory matter is confined, then a pyonephrosis results.

That type of kidney inflammation which is caused by repeated attacks of pyelonephritis and scarring, is called atrophic pyelonephritis. It may occur on one or both sides; the kidney is small, contracted, and fibrosed, and in extreme cases there may be no kidney substance left. It is sometimes extremely difficult to distinguish from the secondary contracted kidney of Bright's disease. The main distinctions are that in atrophic pyelonephritis the fibrosis and atrophy are patchy to the naked eye, and there is irregular coarse scarring of the surface. There is dilatation of the pelvis, infundibula, and calyces, with flattening of the pyramids, or one or two calyces may be alone affected. In the renal pelvis there may be, besides pus and urine, blood, calculi, or other foreign bodies which have set up the mischief; and the urinary salts may be deposited, namely, urates in acid urine, and phosphates if the urine is alkaline or ammoniacal, as it often is. In some old cases the kidney is so atrophied as to consist of little else than its capsule with septa forming cavities which contain putty-like masses, the result of the inspissation of pus and the deposit of amorphous phosphates.

Symptoms. In the mildest form of acute pyelonephritis where there are, perhaps, only one or two patches of inflammation, the symptoms may not be severe enough for the patient to call in a doctor. In the severer form there is frequently some dull, aching pain in the loin, increased on pressure, with rigidity of the abdominal muscles, or a large tender lump may be palpable in the loin. There is fever, and at times rigors and a leucocytosis. Micturition may be frequent and painful and there may be retention. The cells of the pelvic epithelium may, perhaps, be distinguished; they are conical, pyriform, or fusiform in shape. The patient may vomit, especially if the pain is severe and colicky. Where the pyelonephritis is secondary to infection elsewhere in the urinary tract, the symptoms due to the latter will also be present. In the severest form of all there may be a high continuous or remittent temperature, quick, feeble pulse and all the characteristics of the typhoid state—loss of appetite, dry brown fissured tongue, nausea and vomiting, sometimes diarrhœa, sweating, and rapid emaciation. When both kidneys are extensively affected the renal function is interfered with; there may be increased urea in the blood, acidæmia

and a typical renal œdema ; and eventually symptoms typical of asthenic uræmia may show themselves—coma, twitching of muscles and air hunger.

In the pyelonephritis of children under two years, there is a group of fatal cases secondary to infections elsewhere, *e.g.* otitis media, gastro-enteritis and pulmonary disease. In older children there may be only incontinence of urine and frequency of micturition, though local symptoms of renal disease may occur at intervals. A case of incontinence of urine in a child should always be investigated for bacilluria and pyelonephritis.

The urine in the milder cases will contain pus cells, bacteria (*see* Bacilluria), perhaps a few blood cells, and a little albumin, and is usually acid. In the severer forms the urine contains pus in notable quantities (*pyuria*). When such urine is passed it is turbid, and as it settles the pus forms a very pale yellow creamy deposit at the bottom of the glass, and mixes with the urine only just at the line of junction. The nature of this deposit can be determined by the microscope or by chemical tests, *e.g.* the supernatant liquid is poured off, and some liquor potassæ is added to the deposit ; it quickly loses its colour, becomes translucent, and changes into a viscid, ropy liquid, which falls from vessel to vessel in a more or less coherent mass. If the urine should decompose and become alkaline within the body, the pus will undergo the same ropy change, and the urine will be mixed with this viscid, glairy fluid, instead of with creamy pus. This happens sometimes in pyelonephritis and pyonephrosis, if the urine retained in the dilated pelvis at length undergoes decomposition ; and it happens frequently from the same cause in cystitis.

Purulent urine may be retained by an obstruction of the ureter, with the formation of a hydronephrosis (*q.v.*) or a pyonephrosis.

In chronic pyelonephritis and atrophic pyelonephritis the local pain and tenderness may be almost absent, so that there is difficulty in diagnosis. Apart from bacilluria the urine need not be markedly abnormal. The patient appears to have neurasthenia or chronic ill-health, and asthenic uræmia may end the scene. In these circumstances the blood pressure is not by any means always high or the heart hypertrophied.

Diagnosis. Pyelonephritis must be distinguished by the local signs, and by the presence of pus cells in the urine ; the typical urine has been described on p. 535. Uro-selectan provides a valuable means of diagnosis, because it indicates the functional capacity of the kidney and the size of the pelvis. Retrograde pyelography and cultivation of the urine after ureteric catheterisation are also employed, but not if there is cystitis.

Pyonephrosis may be confounded with the numerous swellings which occur in the right flank, and which will be alluded to under Perinephric Abscess. The latter cannot always be distinguished from pyonephrosis ; but with hydronephrosis there will not be any temperature.

The **Prognosis** depends very much upon the primary cause. Pyelonephritis without obstruction to urinary outflow, usually gets well, although it may linger on for a long time. Pyonephrosis is a serious lesion ; it may be fatal by perforation into the chest or abdomen, by exhaustion from continued discharge, or by the induction of lardaceous disease. Rarely the pus inspissates, and a cure results from the loss of one kidney. Tests for renal functions will indicate whether there is danger of uræmia.

Prevention. That pyelonephritis may supervene should always be borne in mind in the treatment of the urinary organs. In spinal cases it is necessary to try and prevent the onset of cystitis. Owing to war experience, the use of the catheter is now much restricted in these cases, since infection is introduced by such means. In cases where the spinal cord is completely divided, use may be made of certain reflexes that develop. At periodical intervals the skin is stimulated. This leads to flexor responses in the limbs and contraction of the bladder, so that the latter is completely emptied. In other cases when

cystitis is present the bladder should be irrigated with some antiseptic solution, such as salicylate of sodium (5 grains to 1 ounce), quinine (1 or 2 grains to 1 ounce), or borax (5 grains to 1 ounce); and urotropin (10 grains) or helmitol should be given internally. Continuous drainage is advisable by a catheter.

Treatment. If there is obstruction to the urinary flow little good will be done by medical treatment; the case is surgical. A continuous drainage by a catheter may be a palliative. In acute cases due to *B. coli communis*, the first treatment should be to make the urine alkaline throughout the twenty-four hours, as described under Acute Nephritis, and plenty of fluid should be taken. If this is ineffective, after two or three weeks hexamine is given in doses of from 6 to 10 grains and the urine is now made acid by prescribing 30 grains of acid sod. phosphate, separately, three or four times a day. An alternative is to give calcium chloride 15 grains in a salol capsule five times a day; but indigestion may be caused. Betaine hydrochloride 7 grains each dose is another way of giving acid. It is essential to test the acidity of the urine (*see* p. 508). When the urine is alkaline in the first place, the acid treatment should be given first. These two treatments may be alternated several times. In refractory cases, especially in children, success is sometimes obtained by establishing an artificial ketosis; carbohydrate food is removed as far as possible from the diet and fat and protein added, so that the urine gives a strongly marked Rothera's reaction. This may be continued for a week or two; but care must be taken that the child's alimentary canal is not upset by so unnatural a diet. In very chronic cases oil of sandal-wood, copaiba, and benzoic acid, or salol may be given, or hexyl resorcinol 0·3 gramme in gelatine capsules. A nutritious diet with plenty of vitamins and fresh air in the country or at the seaside are desirable. Tr. hyoscyami ℥x may be given for pain, and dry-cupping may be tried, especially if there is much blood. The mandelic acid treatment, recently introduced, is as follows: ℞ mandelic acid gr. 45, sod. bicarb. gr. 20, aq. menth. pip. ad 1 oz. q.d.s. The urine is made acid with ammonium chloride, *e.g.* gr. 30 Ext. glyc. ½ oz. aq. chloroformi ad 1 oz. t.d.s. With methyl red (5 drops to 2 c.c. distilled water) added to urine the colour should be orange.

METASTATIC NEPHRITIS

It is doubtful whether it is really justifiable to describe a separate disease under the term Metastatic Nephritis, considering that it has been found that pyelonephritis is, in many cases, a blood-borne infection. Actually in staphylococcal pyæmia it is common enough to find metastatic abscesses in the cortex of the kidney. If these abscesses break through into the collecting tubules and pelvis, a true pyelonephritis results; but they commonly remain shut off from the pelvis or extend so as to form a perinephric abscess. Hence a metastatic nephritis is necessarily the preliminary stage of a descending pyelonephritis, and the symptoms have already been considered. In those cases where at autopsy metastatic abscesses are found as part of a pyæmia, the symptoms are those of the pyæmia, and the renal abscesses are merely incidental.

In malignant endocarditis, metastatic abscesses may occasionally arise from the breaking down of embolic infarcts of various sizes. These are conical, but generally have a different shape from the abscesses of pyelonephritis, the base being relatively broader. However, the infarcts being often due to streptococcus viridans do not usually breakdown into pus. Embolic infarction may be indicated by pain and by blood and albumin in the urine.

PERINEPHRITIS AND PERINEPHRIC ABSCESS

Perinephritis is the term used for inflammation of the tissues around the kidney.

Ætiology. It arises: (1) From injury—such as blows, kicks, or strains. (2) From the extension of inflammation from the kidney, the pelvis of the kidney or the ureter. This may be the result of pyelonephritis, pyonephrosis,

tubercle of the kidney, or calculus. (3) From inflammation, especially suppuration, in more distant parts spreading to the perinephric tissues; for instance, pelvic cellulitis, appendicitis, abscess of the liver or spleen, caries of the spine and psoas abscess, or inflammation of the gall-bladder.

Symptoms. These are to a certain extent those which accompany other inflammatory processes. The onset may be insidious, when there is nothing but some dull aching *pain;* in other cases it will be marked by rigor, with elevation of temperature, which continues uniformly high, or is intermittent in character. The pain is deep-seated, in the loin or side of the abdomen, and radiates to the hypogastrium, groin, or genitals; that is, over the distribution of the lumbar plexus. The pain in the loin is increased by pressure, and on bimanual examination a certain amount of fulness or resistance may be felt in that region. The patient may be unable to flex or extend the lumbar spine.

As the case progresses, a more or less extensive *tumour* occupies the space between the last rib and the crest of the ilium, uniformly dull, bulging the flank, causing œdema of the loin, and perhaps fluctuating. The leg of the same side is often flexed at the hip joint, and attempted extension causes pain. Attention has also been called to the peculiar way in which a patient stands who has perinephritis, and this even when the inflammation has not reached the stage of abscess: the body is bent over to the affected side, the hip is a little flexed, and the hand rests on the same thigh. A certain resemblance to hip-joint disease is thus often assumed.

The urine is not necessarily affected; if the inflammation has resulted from inflammation of the kidney, pelvis, or ureter, pus from the perinephric abscess may pass into the urine (*pyuria*). In other cases albuminuria may occur from pressure of the abscess on the renal vein.

When pus forms, it is generally situated at first between the kidney and the lumbar muscles, and may make its way in various directions. Externally it usually points between the edges of the latissimus dorsi and the external oblique muscles; or it may pass downwards and point under Poupart's ligament. In other cases it opens into the colon, ileum or stomach; into the ureter, bladder, or vagina; or into the peritoneum, causing peritonitis. Or it perforates the diaphragm and sets up pneumonia, pleurisy, and empyema; or, without perforation, it causes pleuritic effusions, or compresses the base of the lung.

Diagnosis. The conditions that are most likely to be mistaken for perinephritis are lumbago, spinal caries, cancer and tumours of the kidney, hydronephrosis and pyonephrosis, appendicitis, diverticulitis, fæcal accumulations, splenic and hepatic tumours. The careful localisation of the lesion will distinguish it from spinal caries, hepatic and splenic tumours, and appendicitis. Fæcal accumulations, cancer of the kidney, and hydronephrosis are not accompanied by fever; nor is lumbago, and this is often a bilateral trouble. Exploration with needle and syringe may reveal pus.

Treatment. This is mainly surgical. Local applications and opiates will relieve pain. If pus has formed it should be let out as soon as possible.

TUBERCULOSIS OF THE KIDNEY

The kidneys may be infected by tubercle as a part of a *general miliary tuberculosis*. The tubercle appears in the form of minute grey or yellow deposits, 1 or 2 mm. in diameter, scattered irregularly, and, as a rule, rather scantily in the cortex and medulla of the kidney. A few may be seen on the surface, and others are revealed by section; they are round in shape or slightly elongated in the direction of the tubules. They present the characteristic minute anatomy of tubercle. The rest of the kidney is healthy, and, as a rule, there are no clinical symptoms attending their deposition.

The term *tuberculous nephritis* is applied to certain cases of nephritis associated

with active pulmonary tuberculosis; or it may occur in one kidney, when the other kidney is tuberculous; the urine contains albumin and casts. It is supposed to be a toxic nephritis and tuberculous lesions are absent; it may clear up with removal of the primary focus.

Tuberculous kidney proper or *chronic renal tuberculosis* is secondary to a tuberculous lesion elsewhere in the body. In most cases it arises as an infection from the blood stream; it is rather commonly associated with tuberculosis of the genital system (especially the epididymis) and of the bones and joints. It affects men more often than women; nearly three quarters of the cases occur between twenty and forty. It is quite commonly bilateral.

Chronic Renal Tuberculosis

Morbid Anatomy. Under this head are included almost all forms of renal tuberculosis that come under the care of the surgeon. It includes the conditions known as apical tuberculosis, ulcero-cavernous tuberculosis, tuberculous hydronephrosis, caseous tuberculosis, nodular tuberculosis, and tuberculous abscess.

The first change, in the great majority of cases, takes place at the apex of a pyramid. There is a small loss of substance surrounded by a zone of inflammation. The ulceration spreads outwards towards the base of the pyramid, and a cavity communicating with the calyx is formed; the lining of the cavity is a layer of necrotic or caseating tissue. Beyond this is a zone of inflammation which may show grey tubercles, and occasionally there is a complete zone of grey gelatinous tubercles. Outward from the zone of inflammation isolated tubercles are dotted in normal renal tissue or arranged as one or more streaks radiating to the surface of the kidney. On the surface of the kidney groups of tubercles are seen in areas corresponding to the subjacent tuberculous pyramids. One of several, or all the pyramids may be affected in different degrees. Another pathological process may now become prominent; in the wall of the calyx at its neck, or the division of the pelvis at its outlet, or in the wall of the pelvis, fibrous thickening develops and contracts until the passage is finally occluded. If now the urinary secretion in the section that is gradually being occluded is maintained, a localised cyst or partial or total hydronephrosis develops. If, on the other hand, the secretion of urine is abolished, a caseous mass surrounded by fibrous tissue is formed and the whole kidney may be converted into a mosaic of these caseous masses. The ureter is greatly thickened and rigid in a large proportion of cases. There is ulceration, necrosis, and caseation of the mucosa, and tuberculous infiltration with the formation of thick layers of fibrous tissue in the middle and outer coats. Stricture formation may affect one or several parts of the tube, and dilatation of the tube occurs above (**19**). In advanced cases the disease spreads to the bladder.

Tuberculous kidney occasionally heals by the formation of a ring of fibrous tissue round the focus so as to shut off completely the whole kidney, or, less commonly, a part of it; such a condition is called *closed renal tuberculosis*.

Symptoms. In the majority of cases irritability of the bladder with increased frequency of micturition is the first and for a long time the only symptom of which the patient complains. It is accompanied by pain before and after micturition. The urine in the early stage is increased in quantity; it is pale, faintly acid or neutral, and contains albumin and a small amount of suspended pus and fine white flakes. In uncomplicated cases a few tubercle bacilli are found, but no other bacteria.

Slight terminal hæmaturia is frequently observed, and an attack of hæmaturia is occasionally an early symptom. Rarely, severe attacks of hæmaturia are a prominent feature. Continuous slight loss of weight is, as a rule, observed, but there is no rapid or severe emaciation in uncomplicated renal tuberculosis. Renal pain is usually insignificant, and may be entirely absent. With severe hæmor-

rhage there may be ureteric colic from clots. Fever is absent in most cases, but a slight persistent rise of temperature to 99° or occasionally to 100° F. may be observed. A high temperature, if present, is a symptom of either a mixed infection or of general tuberculosis. The kidney is felt enlarged in a small number of cases of uncomplicated renal tuberculosis. Even when it is considerably enlarged it may be adherent high up under the diaphragm and not be felt.

A thickened tuberculous ureter may be detected on deep palpation at the level of the brim of the pelvis in a thin subject, or on rectal examination in the male subject, or on vaginal examination as a thick cord in the lateral fornix. It is a characteristic of renal tuberculosis that the disease may have advanced so far as completely to have destroyed one kidney without causing symptoms that attract the attention of the patient. The symptoms may vary, and in some cases may disappear for considerable periods. In the majority of cases, however, the symtoms are slowly progressive.

In closed renal tuberculosis there is often a history of irritability of the bladder which has subsided some time ago ; the urine contains albumin, a trace of pus, or some red cells. The kidney and ureter may be palpable. X-rays show calcification and cystoscopy shows a closed and drawn-out ureter. Under unfavourable circumstances a closed tuberculosis may become active again.

Diagnosis. The development of symptoms of cystitis in a young adult will suggest tuberculous kidney if there is also albuminuria, which is a constant symptom. Pyuria, with a sterile urine, is also strongly suggestive. In 20 per cent. of cases tubercle bacilli are not found by staining or by injection into a guinea-pig. Tuberculous bacilluria occasionally occurs in phthisis without the kidney being itself tuberculous. With the bacilluria there is probably a non-specific tuberculous nephritis (*see* above) ; but the presence of tubercle bacilli with pus means renal tuberculosis. In many cases, but not in all, cystoscopic examination gives characteristic appearances; in cases of doubt the ureters should be catheterised ; but this cannot be done if the bladder is extensively involved. X-ray of the kidneys gives positive results in 20 per cent. of cases. The shadows are usually more irregular than those of calculi and their density low and uneven ; however, a caseous mass yields a uniform heavy shadow, and if the whole kidney is involved, a mosaic of round or oval shadows is obtained.

Prognosis. As already indicated, healing occasionally takes place without operation ; statistically, there is a mortality of over 50 per cent. within five years of diagnosis. The immediate mortality of operation is 2 to 3 per cent., and up to 80 per cent. are restored to health.

Treatment. The usual treatment is nephrectomy ; the presence of genital tuberculosis is not a contra-indication ; but operation should not be carried out if there is active tuberculosis elsewhere in the body, or if both kidneys are affected. In default of this, ultra-violet light, tuberculin and other general measures described under Phthisis may be tried.

HYDRONEPHROSIS

By this term is meant dilatation of the pelvis and/or calyces of the kidney by retained urine. It occurs at all ages, and is more frequent in females than males. It may be congenital or acquired. ***Congenital Hydronephrosis*** may be in actual existence at the time of birth, when it may be so large as to constitute a serious obstacle to delivery ; or it may develop after birth, although it is due to congenital causes ; or it may be entirely the result of disease occurring in later life. Among the congenital causes are various abnormalities of the ureter, such as twists upon its axis, folds, reduplications, and valvular arrangements of the mucous membrane, contractions, or conversion into a fibrous cord.

Another cause is an imperforate urethra. Congenital hydronephrosis is often associated with other congenital defects and malformations, such as club-foot, hare-lip, or malformations of the external genitals; and those affected with it are frequently still-born, or live only a short time.

Acquired Hydronephrosis. Apart from congenital hydronephrosis, there are four types of acquired hydronephrosis: (1) *renal*, usually associated with calculus, causing a large kidney, in which the calyces are dilated and there is destruction of the renal parenchyma; (2) *pelvi-renal* due to obstruction below the junction between the pelvis and ureter; the obstruction may be in the lumen, *e.g.* an impacted calculus; in the wall of the ureter, *e.g.* a growth or inflammation; or from pressure outside or in the urethra, including enlarged prostate; (3) *pelvic*, where the pelvis is mainly affected and there is not much dilatation of the kidney. This has been called congenital without much evidence, and undue mobility of the kidney, kinking over the inferior branch of the renal artery going to the hilum, valves and folds at the pelvi-ureteral junction have also been brought forward as explanations, again without much evidence. A more reasonable explanation is that there is in these cases an achalasia of the sphincter at the pelvi-ureteral junction. (4) There is some dilatation of pelvis and ureters when there is a permanent increased flow of urine as in diabetes insipidus.

It has been repeatedly stated that tying the ureter in an animal fails to produce hydronephrosis, but this is not so, and obstruction, of itself, is quite sufficient to account for hydronephrosis in many cases without postulating that such obstruction shall be incomplete or intermittent.

When the calyces dilate, the kidney undergoes the following changes of chronic interstitial (consecutive) nephritis: the colour is pale pink or pale yellow; on section it is found that the pyramids are flattened, while the cortex is relatively broad. Under the microscope there is found infiltration of the organ with leucocytes, chiefly around the Malpighian corpuscles, and in the intertubal tissue; there is also some glomerular change, with a slight alteration of the tubal epithelium. In certain cases the process may go on to contraction of the new tissue, and the production of cicatrices. If the obstruction is lower down—for instance, at the vesical orifice of the ureter—the ureter itself is involved in the distension. Moderate degrees of hydronephrosis with consecutive induration of the kidney are common as the result of carcinoma of the uterus, vagina, and bladder. In extreme cases the pelvis becomes distended, and the kidney more and more flattened out; and finally a large cyst is formed capable of containing 40 or 50 ounces, or even several pints of liquid, and consisting of a thin membranous sac, which may present here and there portions of the kidney substance, but in some cases is quite destitute of any trace of it. Inside the sac there are sometimes septa dividing it into separate cavities. If the ureter is involved, it may be enormously dilated, to the size, perhaps, of the small intestine or colon, or it may be entirely merged in the distended pelvis and kidney. Hydronephrosis may affect one or both kidneys, according to the situation of the lesion or lesions causing it. Some dilatation of the right pelvis is commonly produced in pregnancy by pressure of the uterus on the ureter.

The liquid of a hydronephrosis varies with the amount of kidney substance still remaining; generally it is equivalent to a very dilute urine and there may be a trace of albumin and a little pus; but pus in any quantity is not present unless there has been previous pyelitis, and the condition is then a pyonephrosis.

Symptoms. A moderate degree of distension on one side, when the other kidney is healthy, may cause no symptoms whatever. If it is considerable, then a swelling is formed which becomes the prominent feature of the case, and has the usual characteristics of a renal tumour. It occupies one or other flank, extending from the costal margin to the crest of the ilium, and reaching, according to its size, towards the middle line, or even beyond it. A cyst holding 40 or 50

ounces may cause scarcely any prominence of the abdomen, but its presence will be detected by resistance to deep pressure, and by the difficulty of bringing together the two hands, placed one in front, the other under the last rib. With larger cysts, an unsymmetrical enlargement of the abdomen is produced, and the loin and flank are bulged. Sometimes the cyst is limited to the upper part of the abdomen, and may resemble enlargement of the liver by hydatid. The tumour is smooth or lobulated, in some cases tense, in others quite flaccid ; and fluctuation can be sometimes obtained. The colon lies in front of it, and may cause a resonant note.

An important feature of the tumour of hydronephrosis is its liability to diminish in size suddenly, or even to disappear, from the escape of its contents into the bladder. Immediately afterwards the patient has an abundant discharge of urine ; and the cyst again slowly fills. Slighter variations in size or tenseness may occur without any corresponding change in the urine being noticed. Local symptoms may be caused by the tenseness of the cyst, or its pressure on surrounding parts, such as pain, vomiting, dyspnœa, or interference with the heart's action. But these may be entirely absent ; and pain is severe only when the obstruction is sudden and complete. The urine in hydronephrosis may not be much altered, since the healthy kidney compensates for the deficiency of its fellow. In cases of double hydronephrosis uræmia may occur ; the earlier indications of obstruction, when there is no tumour, are pains in the back or abdomen, partial suppression of urine from time to time, and increased frequency of micturition.

Pyonephrosis may be looked on as a hydronephrosis filled with pus ; the physical signs are the same, but there is commonly fever like an abscess in any other part of the body and the treatment is surgical.

Diagnosis. The tumour of hydronephrosis has to be distinguished from perinephric abscess, from pyonephrosis, hydatid of the liver or spleen, and, in extreme cases, from ascites and ovarian tumour. The history (*e.g.* of calculus) may be the same in hydronephrosis, *pyonephrosis*, and *perinephric abscess ;* the first is generally of longer duration, without severe, or even any, constitutional symptoms, whereas the other two conditions are likely to show evidence of suppuration with fever. Perinephric abscess also gives the local signs of acute inflammation. In the absence of fever, pyonephrosis may not be diagnosed from hydronephrosis, and it may develop from it. *Hydatid* of the liver or spleen presses forwards or upwards, bulging the lower ribs, while hydronephrosis occupies the loin first. *Ovarian* tumour should be recognised by the history of the enlargement, the position of the uterus, and the absence of the colon from the front of the cyst. The spontaneous disappearance of the tumour, coincident with an increased flow of urine, is suggestive of hydronephrosis ; but the only certain method of diagnosis is by uroselectan or retrograde pyelography (*see* Plates 39 and 40).

Prognosis. A simple hydronephrosis may cause little or no trouble for many years ; the kidney may gradually undergo atrophy without the distension being such as to cause any serious trouble. The risk in such a case is that the other kidney may be at some time involved (*e.g.* by calculous obstruction). If the cyst reaches a great size, or becomes very tense, it may rupture into the peritoneum, or it may press on adjacent parts—the stomach and diaphragm—and cause death by interference with respiration or circulation.

Treatment. The treatment is palliative, but in the end surgical measures will probably be required. Aspiration may be carried out as a temporary measure if the cyst is large, the needle being inserted at the side into an area dull to percussion ; a suitable place on the left side is just at the anterior end of the eleventh intercostal space ; on the right side, half-way between the last rib and the crest of the ilium, and 2 inches behind the anterior superior spine of the ilium.

NEW GROWTHS IN THE KIDNEY

The following tumours are met with in the kidney: Adenoma, fibroma, forming small round nodules in the pyramids, leukæmic deposit, masses of lymphadenoma in Hodgkin's disease, cavernous angeioma, papilloma, epithelial carcinoma, and embryonic tumours. The fibroma in reality starts as a myoma, and fibrous tissue is deposited as the tumour grows older. Embryonic tumours and carcinoma are, as a rule, the only ones large enough to become of clinical importance. Small accessory suprarenals are also seen in the upper pole of the kidney. They are of no clinical importance.

EMBRYONIC TUMOURS

These are generally primary, and frequently occur in quite young children or infants. The organ is enlarged to an immense size, often filling half the abdomen. It presents the usual characters of a renal tumour, filling out the loin, but increasing downwards and inwards towards the umbilicus, having the colon in front of it, and rounded or oval, with no sharp edges or notches. Histologically the tumour recapitulates the development of the kidney, being composed of tubule cells and stroma containing unstriped muscle fibres. It may contain round cells and spindle cells; and its consistence varies, sometimes being hard, at others so soft as to invite exploration for fluid. The tumour grows rapidly, causes neither pain nor hæmorrhage, but kills finally by exhaustion and emaciation. It is often bilateral.

EPITHELIAL CARCINOMA

This is primary or secondary. In *secondary* carcinoma the nodules are small, and their presence is not generally productive of special symptoms. As a rule, both kidneys are involved. *Primary* carcinoma occurs mostly in persons of middle or advanced age, and is more frequent in men than in women. There are two main types. (1) In the *pelvis* there is (*a*) the villous papilloma, which tends to be multiple in the ureter and bladder, and (*b*) carcinoma of the pelvis, consisting of squamous or transitional cells. This latter keratinises very quickly, becoming a typical epithelioma. It is found in association with calculi; and it may be assumed, as in the analogous case of hepatic cancer and biliary calculi, that the calculi have acted as a constant source of irritation. It mostly affects one side only. It causes considerable enlargement of the kidney from hydronephrosis or from blood in the pelvis (hæmatonephrosis); but it rarely becomes, proportionately to the body, as large as does sarcoma in children. (2) In the second place, there is the tumour which arises from the substance of the kidney itself. The cells very readily undergo fatty degeneration and hydropic distension, and when this is the case, they are called *Grawitz* tumours, or, from the close resemblance of their elements to those of the fasciculate layer of the suprarenal cortex, have been called *hypernephroma*, and they have been thought to arise from suprarenal remains in the substance of the kidney; but they present features which are not present in the suprarenal structures, and are more probably epithelial growths from the cells of the convoluted renal tubules. They are often encapsuled, and present on section irregular division into lobules by fibrous tissue, with scattered areas, some of bright yellow colour, others of red or brown colour, in addition to cysts the walls of which may be calcified. The tumour cells vary in size, often reaching the dimensions of giant cells; and they have a tubular or alveolar arrangement, or are grouped radially round vessels. Clinically these tumours are especially important, as they readily invade the pelvis of the kidney and give rise to hæmaturia. In other cases the carcinoma does not resemble the suprarenal, but has cells of relatively small size with a large nucleus and a protoplasm darkened by numerous granules.

Symptoms. These are tumour, hæmaturia, and pain. The signs of

the *tumour* are similar to those of hydronephrosis (*q.v.*); it is usually smooth but may be nodular; its mobility may be limited to adhesion; manipulation will elicit tenderness. Rarely the tumour pulsates, and a *bruit* may be heard in it. *Hæmaturia* is present in over 90 per cent. of all cases and as an initial symptom in nearly 70 per cent. (**22**); it is intermittent, variable in amount, and may form thin round clots. Albumin does not occur without blood, unless there is independent nephritis or pyelonephritis and in this case pus cells will be present as well. Carcinoma cells are sometimes recognised, but they may be lost among blood corpuscles; or epithelium from the bladder or pelvis may be mistaken for them: and on the whole they cannot be relied upon for a diagnosis. The urine may be perfectly normal. *Pain* and tenderness are variable and often absent in the early stages. The pain may be an aching in the loin or it shoots down the groin to the thigh, as a colic with passage of the clots (*see* Renal Calculus). Extension of the growth to the lymphatic glands may lead to pressure upon the roots of the spermatic veins and the production of a *varicocele*; or *œdema of the legs* may occur.

Diagnosis. Carcinoma of the kidney may be recognised by the co-existence of hæmaturia, pain and tumour of the renal region. Painless hæmaturia is most commonly caused by a tumour of the kidney or bladder. A palpable tumour has to be distinguished, first, from enlargements of other organs; secondly, from other diseases of the kidney. The points of distinction between a renal tumour and other organs have been dealt with (*see* p. 505). If cancer of the *colon* simulate renal cancer, intestinal symptoms are mostly present. *Accumulated fæces* on the left side would show more variability in size and consistence, and the diagnosis can be cleared up by the use of an enema.

The diseases of the kidney which may resemble carcinoma are pyonephrosis, hydronephrosis, hydatid, cystic degeneration, and tuberculous disease. From the first three it should be distinguished by its solid feel. A tense uniform globular surface would be in favour of a cyst, but a lobulated hydronephrosis may be mistaken for new growth. By the time that *tuberculous disease* causes enlargement enough to resemble cancer, it is practically a pyonephrosis. *Cystic* disease commonly involves both kidneys, and has not the other local signs of cancer; the pale abundant urine, with a trace of albumin, should distinguish it.

X-rays after uroselectan, cystoscopy and retrograde pyelography should be used in diagnosis. The X-ray appearances are variable; there may be elongation of a calyx with a possible concavity of one aspect facing a rounded tumour or a filling defect of the pelvis in a pelvic tumour.

Treatment. In operable cases the treatment is nephrectomy; ten patients out of thirty-three have survived from under two till twelve years (**22**).

CYSTS IN THE KIDNEY

The following forms of cystic disease of the kidney occur: (1) Small cysts in granular kidneys already described; (2) extensive cystic change known as *cystic disease* or *polycystic kidney*; (3) simple cysts; (4) dermoid cysts, which are exceedingly rare, and have the same characters as elsewhere; and (5) hydatid cysts, which have been dealt with.

CYSTIC DISEASE

(*Polycystic Kidney*)

This is a congenital disease, and may lead to enormous abdominal distension of the fœtus, with serious difficulty in parturition. Less advanced degrees of it are compatible with life, and it may be found at any age. The condition is usually bilateral. In adults the organs weigh from 1 to 5 or 6 lbs. It is more common in males than in females.

Pathology. On section the kidneys are seen to consist almost wholly of

cysts of various sizes, containing a fluid which is clear or turbid, yellow, pink, red, or purple, sometimes viscid, colloid, or purulent. Always albumin, and sometimes blood discs, leucocytes, and cholesterin, are found in the fluid, but urea and uric acid are generally absent. The cysts are surrounded by fibrous tissue, in which only remnants of renal tissue can be found; they are lined with epithelium. The pelvis, ureter, and bladder are healthy, or the pelvis may be dilated. The pathology of these kidneys is still open to doubt. The view of Shattock has been widely accepted that a fault has occurred in the development of the kidneys. The latter are formed from two different sources. The pelvis and collecting tubules arise from an upgrowth of the ureter which comes from the Wolffian duct; the rest of the kidney comes from the "intermediate cell mass," derived from the mesoblast of the cœlom. When these two fail to meet each other, the secretion of the kidneys does not escape, and cysts are formed above the junction.

Symptoms. In congenital cystic disease the kidneys may occupy the greater part of the abdomen, and press upon the diaphragm; and death may happen *in utero*, or during birth; or the child may survive a few months, or in the event of the disease being unilateral, a few years, when at length death may result from uræmia. The change is often associated with other congenital malformations, both of the urinary organs and other parts.

In adults the symptoms are often very obscure, but resemble those of secondary contracted kidney (*q.v.*). Sometimes there is hæmaturia. Hypertrophy of the heart and high arterial tension and raised urea in the blood occur in advanced cases. There may be lumbar pain. The kidneys are often large enough to be easily felt. They occupy the usual positions of the kidneys, are rounded, nodular, firm or elastic in different degrees, and descend on inspiration, and one is usually larger than the other. The termination is like that of secondary contracted kidney and the **prognosis** depends on tests of renal function.

Diagnosis. This depends on finding a bilateral swelling of both kidneys of different size, usually without constitutional symptoms but with impairment of renal function. X-rays after uroselectan show that all the calyces are elongated into spidery processes (**22**).

The **Treatment** is that of secondary contracted kidney.

SIMPLE CYSTS

Cysts of considerable size are sometimes found. They may be 3 or 4 inches in diameter, and exceptionally very much larger. They arise from the cortex, and project on the surface. Their contents are a clear limpid or gelatinous fluid, containing a little albumin and some salts, but no urea or uric acid. The remainder of the kidney may be quite healthy. Such cysts may be unrecognised during life; if very large, they form tumours which may require to be treated surgically on the same principles as hydronephrosis.

MOVABLE KIDNEY

The name *movable kidney* is given to one that is readily displaced from its normal position, and can be moved more or less freely in the abdomen. This unusual mobility may be congenital or acquired.

Congenital mobility is due to the presence of a *mesonephron*—that is, the kidney is partially or completely surrounded by peritoneum (like the colon), and is thus free to move about among the abdominal viscera. This condition is quite rare. It is sometimes distinguished as *floating* kidney.

Acquired mobility is much more common. It affects females more often than males; and the right kidney is movable thirteen or fourteen times as often as the left. Sometimes both are affected at the same time. The age of the patient

is mostly between twenty and fifty. It mainly results from conditions which stretch or relax the tissues and structures surrounding the kidney, especially the fatty capsule and the peritoneum. Perhaps the most frequent cause is repeated pregnancy, by which the peritoneum is dragged upon and stretched, and fails after delivery to recover its normal tension. But movable kidney is not confined to those who have borne children. Emaciation by reducing the fat surrounding the kidney may be a cause sometimes. Many patients have a pendulous abdomen, and the general want of tone in the abdominal and pelvic tissues which constitutes Glénard's disease. An increase of size of the kidney from any cause must favour it. Tight-lacing has been charged with it, but it frequently occurs independently.

Symptoms. At the present day much doubt is thrown on movable kidney itself as being a cause of any symptoms; these are rather considered to be due to an associated pyelitis, hydronephrosis or other associated disease. There is no evidence that movable kidney causes anxiety or hysteria though it may occur in such patients as in perfectly healthy individuals. The symptoms which have been attributed to movable kidney are a sensation of weight, or dragging, or pain in the loin or side of the abdomen affected; and this may be constant, aggravated by walking or exertion, and relieved by lying down. From time to time there may be severe attacks of so-called *strangulation* of the kidney (*Dietl's crises*), consisting of great pain and tenderness in the renal region, with scanty high-coloured, and even bloody urine. There may be nausea or vomiting, and malaise, but generally not much pyrexia. Such an attack, which subsides in the course of a week or more, is probably due to twisting or kinking of the renal vessels by the movement of the kidney.

The evidence of movable kidney lies in its detection by palpation. It is felt at the end of inspiration as a smooth, firm, rounded tumour in the loin, of the size of the kidney. The examination should be made with both hands, one pressed firmly in between the last rib and the crest of the ilium, the other on the front of the abdomen. If it lies between the last rib and the crest of the ilium, it can be pushed more or less in all directions, but most easily upwards towards the thorax, when it may get entirely out of reach, leaving the flank normal. The best means of confirming the diagnosis is to X-ray the patient in the vertical position fifteen minutes after injecting uroselectan, immediately after the horizontal film has been taken.

Treatment. From what has been said it is the associated condition, which is probably responsible for the symptoms, that requires treatment rather than the mobility itself. If it is desired to retain the kidney in its normal position an abdominal belt, just as described under Gastroptosis, is the best appliance rather than any pad applied directly against the kidney itself. A further desideratum is to strengthen the abdominal muscles by suitable gymnastic exercises. The treatment of acute symptoms consists in complete rest, the use of poultices and hot fomentations to the loin and abdomen, and opium or morphia by injection or suppository.

RENAL CALCULUS

(*Nephrolithiasis*)

The following are the varieties of urinary calculi. The first six are the commoner forms; the others are much more rare:

1. *Uric Acid.* Hard, round or oval in shape, smooth or finely tuberculated, sometimes facetted from contact; of yellowish, fawn, or reddish colour. They vary in size, from that of poppy seeds to that of mustard seeds or peas, and are occasionally very much larger. Frequently they exist in great numbers.
2. *Sodium Urate.* Soft, not generally of large size.
3. *Calcium Oxalate, or Mulberry Calculus.* These are very hard, rough or

irregular on the surface, and of blackish-brown colour; when smaller they are smooth, rounded, grey or brown in colour. Generally they are solitary.

4. *Mixed Calcium and Ammonium-magnesium Phosphate, or Fusible Calculus.* The mixed phosphates are precipitated in urine rendered alkaline by ammoniacal decomposition, such as occurs when the secretion is retained in the bladder or in a dilated pelvis. They rarely form the nucleus of a stone, but are deposited upon other calculi of uric acid or oxalate, upon foreign bodies (*e.g.* in the bladder), and upon the inflamed mucous membrane of the bladder or of the renal pelvis. They may thus enormously increase the size of vesical stones, and in the pelvis may form concretions, which are moulded to all the infundibula and calices (*dendritic calculi*). The deposit is white, soft, and friable; and fuses under the blowpipe into a kind of enamel.

5. *Calcium Phosphate.* White and chalky, rather smooth on the surface, with an earthy fracture, varying in size from that of a pea to that of a hen's egg.

6. *Mixed.* Phosphate-oxalate, urate-phosphate, urate-oxalate, urate-oxalate-phosphate; these account for 86 per cent. of all stones, and each of the two latter for over 30 per cent. (**23**) in India, most of them being found in the bladder.

7. *Calcium Carbonate.* Small, very hard, smooth, grey, yellowish or bronze-coloured, and varying from minute grains up to stones the size of a hazel nut; these are common in cattle.

8. *Cystine.* Usually egg-shaped, the surface granular, glistening with crystals of yellow colour, looking translucent on section with indications of a radiating structure, and rather soft in consistence. They become green on exposure. With a lens the hexagonal form of the crystals may be seen.

9. *Xanthine.* In physical characters like uric acid calculi, but of a cinnamon colour, soluble in liquor ammoniæ and liquor potassæ. They are extremely rare, and have not been found in the renal pelvis.

10. *Urostealith.* Soft, greasy concretions, which have been found in a few cases; one was shown to consist of about one-third cholesterin and fat, one-third uric acid, and some oxalates.

11. *Indigo.* Once found in the renal pelvis by Ord as a calculus weighing 40 grains.

Urinary calculi vary much in size; they may be 2 or 3 inches in diameter, or they may consist of very small particles, and are then known as *gravel.*

The centre or nucleus (*i.e.* the first-formed portion) of most calculi is uric acid; but within that, calcium oxalate or sodium urate has been found. Some calculi are deposited upon a nucleus of blood clot, mucus, or renal casts, and the ova of *Schistosomum hæmatobium* may form the starting-point of renal stones. Most calculi are formed in the urinary tubules, and some even in the epithelial cells (Ralfe); the cell substance acts as "colloid" around which the calculus grows by accretion of other deposits upon it, for there is evidence that in some cases renal calculi may begin in a cyst in the cortex and be discharged into the pelvis (**36**). The effect of the reaction of the urine in precipitating phosphates and urates has been dealt with on p. 507, and further growth of renal calculi probably takes place after they have been discharged into the renal pelvis.

Ætiology. Calculus is very much more frequent in the eastern part of England than in the middle or western parts; and in India in Sind, the N.W. Frontier Province and the Punjab. It is more common in males than in females Experimental evidence suggests that a number of factors are responsible—dietetic, especially whole wheat flour, oatmeal; lack of vitamin A, causing epithelial desquamation in the urinary tract; physico-chemical, a deficiency of phosphates relative to calcium in the diet; infection, the streptococci cultivated from nephrolithiasis have an *elective localisation* (*see* p. 347) for the urinary tract (**23**).

Symptoms. (1) When the stone exists in the pelvis of the kidney, it may be entirely latent, or it may give rise to the symptoms described below, which

apply to the presence of a stone either in the pelvis or ureter, or to the passage of pus from an associated pyelitis; and these symptoms may result from the presence of very small stones or gravel. (2) If it falls into the ureter, it may become impacted or move along with great difficulty, causing *renal colic*, hæmaturia, and, in certain circumstances, *obstructive suppression*. (3) The later effects of renal stones, either in the kidney, or after impaction in the ureter, are pyelitis of all degrees, pyelonephritis, perinephritis, perinephric abscess, hydronephrosis and pyonephrosis, the symptoms of which have already been described.

Gravel and calculus are frequent causes of *lumbar pain*, which is often regarded as "lumbago" or muscular rheumatism. The lumbar pain or aching may be rendering worse by jolting or shaking. Aching pains may also be felt in the iliac fossæ above the pubes and in the penis; they may be brought on by micturition, being felt during or after the act. There may be frequency of micturition. If the symptoms are of long duration, albumin, pus, or mucus may be passed, and from time to time blood in varying quantities. Occasionally, small calculi or gravel are discharged with the urine.

Renal colic is due to a sustained contraction of the muscular fibres of the ureter, and it may be due to irritation by the calculus in the pelvis or by its impaction in or passage down the ureter. It is comparable with biliary colic, and is characterised by intense pains, rigors, nausea, and vomiting. The pain is situated in the loin and flank of the same side, and radiates downwards and inwards to the groin and testicle; sometimes to the thighs, and even to the heel and sole of the foot; at others to the abdomen, chest and back. In the severer attacks the patient is doubled up with the pain, or writhes on the floor, and bursts out into profuse perspiration, or he becomes pale and collapsed, with quick, feeble pulse; but the temperature may be raised. With this there are nausea and vomiting, often a rigor, and sometimes even general convulsions. The testicle on the same side is retracted, and is swollen and very tender. The pain may be less for a time, but soon returns, and altogether it may last a few hours or a day or two, until at length the stone is passed into the bladder, or returns to the pelvis, when there is a sudden relief, and only an aching, smarting sensation in the side is left. The pain may, however, cease when the calculus still remains impacted in the ureter. During the attack, micturition is frequent and painful, and the urine is scanty, coming, perhaps, only by drops; and it may contain blood. By examination of the abdomen the kidney may be found to be tender and the muscles somewhat rigid, but not nearly so rigid as in peritonitis. A stone in the lower ureter may sometimes be detected on rectal examination; or the stone may be detected in the ureter, and its course watched from kidney to bladder.

Such an attack may occur spontaneously, or may be brought on by some movement which appears to dislodge the calculus from its position. Renal colic may recur in the same patient. This, of course, must depend on the number and size of the stones; obviously, if a stone gets back into the pelvis it may set up renal colic on again becoming impacted. Exceptionally a large number of stones in the pelvis of the kidney may be detected by a crackling sensation on palpation. The subsidence of symptoms entirely after a long period of activity may be due to the calculus becoming encysted.

Obstructive suppression is distinguished from the suppression which results from acute congestion or acute Bright's disease, and the symptoms in marked cases are strikingly different. It arises when both ureters are simultaneously compressed, as occurs in women when cancer of the pelvic organs invades the base of the bladder; or when one kidney has been disorganised, or excised, or otherwise placed *hors de combat*, and a calculus becomes impacted in the ureter of the healthy organ. This condition is sometimes called *latent uræmia*. In some cases no urine is voided; in others, a certain amount may be passed in small quantities at long intervals, but it is clear, watery, of very low specific gravity—*e.g.* 1,006—and contains an extremely small quantity of urea or other

solids: and there is no albumin, unless there is blood, or unless the urine is modified by the cystitis which accompanies cancer of the bladder. The patient's condition is not at first materially altered. He may eat as usual, but he loses muscular power, and becomes sleepless, and after some five or six days he is seized with the muscular twitchings or jerkings of *chronic uræmia*, associated with breathlessness and eventually coma, as already described (*see* p. 530). Death, as a rule, ensues from nine to eleven days after the commencement of obstruction, and is very rarely postponed beyond this. Recovery may take place if the obstruction is removed by the passage of the calculus or by the breaking down of any new growth.

Diagnosis. The typical symptoms—lumbar pain, hæmaturia, and albuminuria—may be caused not only by a medium-sized calculus, but also by fine gravel and uric acid crystals, which will readily pass the ureter; and in these cases testicular pain and frequency of micturition may also be present. A severe attack of colic, associated with hæmaturia and testicular pain and retraction, is very strong evidence of calculus; but they may be due to carcinoma, tuberculosis and pyelonephritis.

In carcinoma of the kidney hæmorrhage is often more abundant, and more continuous. Gelatinous red lumps appear in the urine after the blood; and sometimes cancer cells may be found by the microscope. The discovery in due time of a tumour will help the diagnosis. Calculus is more likely in a young patient, but either may be present in middle or old age. *Tubercle* of the kidney may closely simulate calculus, by lumbar pain, frequent micturition, pus in the urine, and even blood. In the former there may be a family or personal history, or present indications of tubercle; hæmaturia and renal pain are less prominent and characteristic. Pyelonephritis is simulated by the frequency of micturition which occurs in renal calculus, especially if hæmaturia is absent. Previous attacks of lumbar pain, and the acid reaction of the urine, if pus is present, are in favour of a renal origin.

X-rays are always now used in the diagnosis of renal and ureteric calculus (*see* Plate 41). However, uric acid calculi are not opaque to X-rays. The shadow of a stone must be distinguished from (1) elongated phleboliths, which may be multiple and run in the line of a vein and not the ureter; and (2) calcified glands which tend to occur in groups. Difficulties in diagnosis may be cleared up by means of uroselectan or pyelography, which will show up the line of the ureter; also the stone may be touched by the catheter. If the bladder be examined with the cystoscope, signs of irritation of the mucous membrane about the orifice of one or other ureter may be observed, and the urine flowing from either orifice may come too slowly, or may contain blood or pus cells (*see* also Examination of Kidney and Bladder). Lastly, an exploratory incision over the kidney or ureter is justified in some cases.

It appears to be quite clear not only that a calculus may cause pain in the opposite flank at the same time as pain on its own side, but also that in exceptional cases the pain has been felt only on the side of the healthy kidney. Stone in the kidney may also cause suprapubic pain, and simulate stone in the bladder very closely. These pains must be set up reflexly, and they show how closely the nervous connections of all parts of the urinary tract are related to one another. Though there are many exceptions to this rule, the symptoms of a calculus in the lower ureter tend to be those which arise from irritation of the lower urinary tract.

Treatment. Gravel, when it is uric acid, should be met by ordering a low purine diet (*see* Gout) and by giving drugs to render the urine less acid. The most efficient are the citrate, acetate, and bicarbonate of potassium or sodium, which may be given in 30 to 60-grain doses in 3 or 4 ounces of water two or three times daily, or in one larger dose before the night's rest, during which time the tendency to uric acid precipitation is greatest. The reaction of the urine should be examined when passed on waking, at 10–11 a.m. when the alkaline tide is about

at its maximum, at night before dinner and before going to bed. A *p*H between 6 and 7 should be aimed at (*see* Reaction of Urine). On the other hand the urine may be sufficiently alkaline to cause phosphate gravel or phosphaturia, with a *p*H 6·8 and over; this may be due to a low-protein diet with excess of vegetables and fruit. Apart from increasing the protein, which, of course, also increases the phosphate excretion, the reaction is made more acid by giving ammonium chloride or calcium chloride (*see* Treatment of Pyelonephritis).

If a calculus has actually formed it cannot be dissolved by any medical treatment, but if small it may be passed by increasing the fluid intake. If not, *nephrolithotomy* should be performed, or *nephrectomy* if the kidney is hopelessly damaged, though the power of an apparently hopelessly damaged kidney to recover some function has recently been emphasised, so that nephrotomy is usually to be preferred to nephrectomy, especially as a stone may develop in the other kidney.

Treatment of Renal Colic. Anodynes are here required, both to relieve the intense pain, and because they may also relax the spasm of the ureter, and so facilitate the escape of the stone. If the pain is severe, a morphia injection should be at once given; or morphia or opium may be given internally, or in suppositories, or chloroform or ether may be inhaled. Papaverine hydrochloride, one of the opium alkaloids, in doses of ½ to 1½ grains, has produced good results. Locally, hot poultices, hot fomentations, belladonna applications, or the hot bath should be used. The patient should be at rest, and warm diluent drinks, barley water, etc., should be taken from time to time.

FUNCTIONAL ALBUMINURIA

It has been already shown that albuminuria may occur in a number of morbid conditions, of which nephritis and renal degenerations, acute illnesses, infective diseases, and venous congestion are the most important. But it is sometimes present in persons who appear to be in perfect health, and show no sign of disease on further examination.

Maclean examined the urines of 50,000 soldiers and found albuminuria in 5·62 per cent. of them. In 2·55 per cent. the albuminuria was well marked. Many of these cases were probably examples of functional albuminuria. Numerous observations have also been made on the presence of albumin in the urine in groups of individuals, such as infants from one to six days old, schoolboys, bank clerks, soldiers, or workers in factories; and invariably albumin is found in a certain percentage, which varies from 5 to 30. In life insurance practice it is common experience that a large proportion of applicants between eighteen and thirty years of age, believing themselves to be perfectly well, have a small quantity of albumin in the urine. Many of these cases, no doubt, are examples of functional albuminuria; but others are the result of a previous nephritis, which leaves a "leaky kidney."

Pathology. The albumin is, as a rule, small in quantity, and there is in some cases a high percentage of globulin. Serum globulin consists of euglobulin and pseudo-globulin, and it is the euglobulin fraction that is present in the urine. This substance is often combined with lecithin and other lipoid substances, and occasionally the urine becomes opalescent when they are present in large amount. In the albuminuria of nephritis there is six times as much albumin as globulin, but in these cases the amounts are often, but not always, about equal. Euglobulin may be discovered by adding 33 per cent. acetic, drop by drop, to urine until a white precipitate is formed.

The following types, mostly in young people, require separate description.

Athletic Albuminuria. Albumin in small, decided, or even considerable amount is sometimes found in the urine of those who have recently rowed or run

a race, or have undergone other excessive physical exercise. There is no doubt that the albuminuria is only a temporary disturbance, indicative of deficient blood supply to the kidney, because so much blood is required for the muscles and skin.

Dietetic Albuminuria. This is due to the ingestion of large quantities of protein food. In a six months' experiment a man took 337 grams protein daily; the albuminuria gradually increased up to 2–4 milligrammes hourly and casts appeared, at first hyaline, later granular; there were no subjective disturbances or rise of blood pressure. Evidently there was renal damage; but this was temporary, as all these signs disappeared ten days after recommencing a normal diet (**32**).

Orthostatic Albuminuria. This includes the cases described as postural albuminuria, and probably also the cyclical, remittent, and intermittent forms. It occurs in persons in good health, more often youths or young adults; and it is characterised by the presence of albumin at certain times of the day, while it is absent at others. Thus, in the early morning it cannot be detected; it is present from about 9 a.m. to 5 or 6 p.m., and again disappears from the urine passed at night. The albuminuria is obviously determined chiefly by the assumption of the erect position, and by the accompanying exercise during the day; and it disappears as a result of the recumbent position at night. The amount of food taken has no influence upon it. Sonne has shown that in these cases the important factor is the presence of lordosis, which occurs naturally in the erect position. The left renal vein is compressed between the spine and the aorta. The albuminuria is caused by the circulatory disturbance. The condition is relieved when the patient is lying down. In ten cases of this kind, by catheterising the ureters he showed that it is only the left kidney which gives rise to albuminuria. This condition has been classed as *lordotic albuminuria*. The albuminuria of pregnancy may be partly a left-sided lordotic albuminuria (**33**).

Paroxysmal Albuminuria. This may undoubtedly occur as a phase of paroxysmal hæmoglobinuria, in which the hæmoglobin breaks up into hæmatin and globulin (*see* p. 444). The patients have malaise, a sallow tint, and subsequently albuminuria; the urine contains at the same time excess of urea and of urobilin.

Diagnosis. The diagnosis may be very difficult, since it has been shown that slight albuminuria resulting from nephritis is often postural and the relative amounts of albumin and globulin are very variable (**35**). The history of previous nephritis or infection, the condition of the patient—whether he is languid or out of sorts—or impaired function of the kidneys, will be in favour of Bright's disease as the cause, though even then the prognosis will not necessarily be bad. The presence of euglobulin and the complete absence of albuminuria during the night will be in favour of functional albuminuria.

Prognosis. The future of these cases is on the whole favourable, and in the large majority the albuminuria entirely disappears, though it may persist for two or three, or even seven or ten years.

Treatment. Except in the dietetic form, no treatment is required. In this case the protein in the food should be diminished.

REFERENCES

1	F. KIDD	1922	*Brit. Med. Journ.*, **i.**, p. 748.
2	P. L. VIOLLE	1931	*General Practice and Franco-British Medical Review*, **7**, p. 209.
3	R. O. WARD	1931	*Brit. Med. Journ.*, **i.**, p. 175.
4	H. SCHALL	1929	*Nahrungsmitteltabelle.* Leipzig.
5	L. MACKEY and Sir A. E. GARROD	1922	*Quart. Journ. Med.*, **15**, p. 319.
6	P. M. T. KERRIDGE	1931	*Lancet*, **i.**, p. 21.

7	E. H. Starling and E. B. Verney	1925	*Proc. Roy. Soc.*, B. **97**, p. 321.
8	G. H. Oriel	1929	*Guy's Hosp. Rep.*, **79**, p. 376.
9	E. P. Poulton and J. H. Ryffel	1932	*Guy's Hosp. Rep.*, **82**, p. 303.
10	T. Addis	1922	*Arch. Int. Med.*, **30**, p. 378.
11	E. Möller, J. F. McIntosh and D. D. Van Slyke	1929	*Journ. Clin. Invest.*, **6**, p. 472.
12	C. L. Cope	1931	*Quart. Journ. Med.*, **24**, p. 567.
13	Clausen	1924	*J. Biol. Chem.* (*Proceedings*), **59**, p. xlvi.
14	W. Cramer	1932	*Lancet*, **ii.**, p. 174.
15	R. W. Brookfield	1934	*Brit. Med. Journ.*, **i.**, p. 848.
16	D. Baird and J. S. Dunn	1933	*Journ. Path. & Bact.*, **87**, p. 291.
17	A. A. Osman	1925	*Guy's Hosp. Rep.*, **75**, p. 306.
18	A. Lemierre	1927	*Guy's Hosp. Rep.*, **77**, p. 325.
19	J. Thomson-Walker	1927	*Brit. Med. Journ.*, **ii.**, p. 625.
20	J. Shaw Dunn, E. G. Oastler and S. L. Tompsett	1934	*Journ. Path. & Bact.*, **38**, p. 421.
21	J. P. Hosford	1932	*Lancet*, **i.**, p. 435.
22	R. H. Jocelyn Swan	1933	*Brit. Med. Journ.*, **i.**, p. 606.
23	R. McCarrison	1931	*Brit. Med. Journ.*, **i.**, p. 1009.
24	Dorothy S. Russell, A Classification of Bright's Disease ..	1929	*Med. Res. Council Spec. Reports*, 142.
25	J. M. H. Campbell, G. H. Hunt and E. P. Poulton	1923	*Journ. Path. & Bact.*, **26**, p. 234.
26	T. R. Parsons and E. P. Poulton	1923	*Bioch. Journ.*, **17**, p. 341.
27	O. L. V. de Wesselow	1924	*Lancet*, **i.**, p. 1099.
28	T. I. Bennett	1928	*Lancet*, **i.**, p. 535.
29	G. Thompson	1932	*Brit. Med. Journ.*, **ii.**, p. 1134.
30	A. G. Gibson	1928	*Lancet*, **ii.**, p. 903.
31	H. Cabot	1926	*Lancet*, **ii.**, p. 53.
32	L. H. Newburgh and Others ..	1930	Quoted in *Lancet*, **i.**, p. 973.
33	F. Cook (Hunterian Lecture) ..	1924	*Brit. Med. Journ.*, **i.**, p. 372.
34	W. Sampson Handley	1923	*Proc. Roy. Soc. Med.* (*Sect. Surgery*), **16**, p. 21.
35	J. W. Russell	1925	*Lancet*, **ii.**, p. 683.
36	H. Carter and A. A. Osman ..	1927	*Proc. Roy. Soc. Med.* (*Sect. Med.*), **20**, p. 43.
37	R. Platt	1932	*Quart. Journ. Med.*, **i.**, p. 499.
38	E. Schiff	1932	Quoted in *Lancet*, **ii.**, p. 1168.
39	E. B. Mayer	1926	*Quart. Journ. Med.*, **19**, p. 273.

DISEASES INVOLVING BONES, JOINTS AND FASCIÆ

THE RHEUMATIC DISEASES

THE derivation of the word rheumatism has already been given (*see* p. 257), and the diseases in Group A of the Ministry of Health's classification, viz. rheumatic fever, subacute rheumatism and rheumatic purpura, have been dealt with elsewhere. Group B comprises " non-articular manifestations " such as fibrositic or muscular rheumatism, and includes lumbago, sciatica and brachial neuritis. Group C comprises joint diseases, viz. rheumatoid arthritis, osteoarthritis, including " senile hip disease," acute and chronic gout, and unclassifiable chronic joint changes.

The importance of the rheumatic diseases is seen from the following statistics (4). Out of 1,000 insured men and 1,000 insured women over sixteen, during each year 930 would seek medical advice for all kinds of affections, and 55 of these would complain of rheumatic disease, made up as follows: A. Acute rheumatism—4 men, 5 women. B. Fibrositis—19 men, 11 women. C. Arthritis—8 men, 6 women. It must be remembered that insured women, owing to marriage, are on the average younger than the men. Of the trades it is the metal workers who suffer most and especially the puddlers among the steel workers, probably because they have alternate periods of very strenuous exercise and of sitting to cool in a draught. In general the incidence increases with age.

It will be convenient to deal here briefly with *infective arthritis*, a miscellaneous group of diseases, in order to exclude them from the rheumatic diseases proper.

Infective Arthritis. Apart from rheumatic fever it will have been observed that in several of the infectious diseases arthritis has been mentioned as a complication, such as typhus, scarlatina, small-pox, typhoid, influenza, dengue, pneumonia (pneumococcal arthritis), streptococcal and staphylococcal septicæmia, gonorrhœa, bacillary dysentery, syphilis, both congenital and acquired, and tubercle. Infective arthritis in these diseases may be a simple synovitis, which soon recovers; or it may result in ankylosis, as in tubercle; or in suppuration, as in invasion by pyogenic organisms. The symptoms are pain and tenderness, with or without swelling of the joints, and it may be only in the history and associations of this arthritis that means of recognising its origin can be found. The fact that salicylates give relief to the pain and lower the temperature is not evidence that the disease is specifically rheumatic fever. The milder forms subside with rest, severer forms require splints and fixation, and where suppuration is recognised the joint should be opened and drained, or the pus may be aspirated, and flavine, 1 in 1,000, injected. Passive movements should be carried out as soon as the acute stage of the inflammation has subsided, so as to prevent fixation.

FIBROSITIS

(*Myalgia, Muscular Rheumatism*)

This name is given to a painful affection of the muscles or fasciæ which depends upon local changes of an inflammatory nature. The incidence is greatest in winter and at a minimum in summer.

The pain is probably caused by swelling of the interstitial connective tissue in the muscles, their tendons and their fascial attachments, which results in compression of the nerve endings. The swelling is due to exudate either as the result of poisons (bacterial or chemical) deposited from the blood stream or of tearing of the tissues through strain or injury.

In one group of cases then the cause of fibrositis is to be found in some source of toxæmia, such as a septic focus or disorder of metabolism allied to gout. Fibrositis is often associated with osteoarthritis. In these cases exposure to cold appears to be an important factor in causing the local deposition. In the second group a history of muscular strain is to be obtained. No absolute distinction can be made between these two groups, since local injury may provide a nidus for the action of toxins.

Symptoms. As a rule only one muscle or tendon is affected, and the pain at the beginning is localised to a single spot. It is experienced whenever the part involved is stretched or pulled upon either by contraction of the muscle directly affected or of its antagonists. Pressure at the site of the disease will also produce pain. If, on the other hand, the patient can be induced to relax his muscles completely, passive movements gently performed are painless, this point serving to distinguish the condition from arthritis of the neighbouring joints. The onset is usually acute, with sharp pain experienced on movement.

A common situation is in the lumbar muscles, when it is often called *lumbago*. Movements such as stooping become exceedingly painful, and walking is only accomplished with a stiff back. Sometimes, after an interval of three or four days, pain is felt in the buttock and sciatica develops, this being presumably due to an extension of the inflammation to the sciatic nerve sheath. If this happens the sciatica overshadows and outlasts the original lumbago. The muscles of the shoulder girdle are often affected, especially the attachments to the humerus of deltoid and pectoralis major. In this case movements of abduction and adduction give rise to pain, and the arm is held to the side in walking, being sometimes supported at the elbow by the other hand to relieve tension in the affected muscles. Here again the inflammation may spread to the nerve sheaths of the brachial plexus, with resultant brachial neuritis.

The muscles of the neck are sometimes attacked, the condition being then commonly known as *stiff neck*. This is particularly apt to occur from exposure to cold, such as results from sitting in a draught.

More rarely one of the intercostal muscles is involved, so that breathing and coughing cause pain. The condition is then known as *pleurodynia*, and simulates pleurisy, but there is no rub, and constitutional disturbance is slight or absent.

Occasionally the muscles of the scalp are affected, when the acts of wrinkling the forehead and mastication are painful.

Myositis ossificans is a disease in which the muscles are converted into osseous tissue. It always begins in early childhood, invades first the muscles of the back, and runs a progressive course. Bony deposits arise also from injury, most commonly in the extensor cruris, and in the brachialis anticus (*traumatic myositis ossificans*). It gives a characteristic radiogram and may be allied to osteoarthritis.

Diagnosis. This depends upon the presence of definite muscular tenderness on deep palpation, and pain which is constantly brought on when the involved group of muscles is put upon the stretch. Here also, as in the case of neuritis, it is most important to be on the look-out for signs of underlying disease of the nerve roots or the viscera, the pain from which is referred to a peripheral distribution, and may, especially in the case of visceral disease, give rise to muscular tenderness and rigidity. The lightning pains which occur in the early stages of tabes are very often erroneously put down to muscular rheumatism. A myositis occurs in various infectious diseases (*infective myositis*), producing a diffuse swelling and infiltration of the muscle, or abscesses may form, as seen in pyæmia (*metastatic*

myositis), septicæmia, glanders, typhoid fever, and malignant endocarditis. Trichiniasis, already described, is essentially a parasitic myositis. Finally, there is a rare form of polymyositis, which is a type of acute rheumatism.

Prognosis. The course of the illness, provided that it is properly treated and is uncomplicated by neuritis, is usually brief. When, however, proper rest cannot be obtained, the pain may persist for many weeks. Complete recovery is the rule, but recurrences are common, especially in the cases of traumatic origin.

Treatment. If septic foci are considered to be the cause of the trouble, these should be eliminated. The bowels should be well opened, *e.g.*, by drinking a pint of saline water on waking, as described under Raynaud's disease. Muscular exercise should be regular but not excessive. Precautions should be taken against undue exposure to cold and wet. Aspirin and phenacetin should be given for the relief of pain, and a mixture containing 10 grains of sod. sal. or 5 grains of pot. iod. In some cases, especially when fibrositis is associated with evidence of gout, atophan is useful. A purine-free and low-protein diet may be valuable. In a mild case in which the pain and tenderness are localised and superficial, vigorous deep massage at the point of maximum tenderness will sometimes bring about a rapid improvement, this result being presumably obtained by the breaking down of adhesions. If, after two or three applications, this method of treatment is not successful it should be discontinued. Heat locally applied by radiation from an electric lamp, and diathermy are useful. A further remedy, for which good results are claimed, is the injection into the muscle or the site of the pain of a solution of quinine and urea hydrochloride, such as is used in local anæsthesia. At the outset of a severe attack diaphoresis is of value and may be prescribed in the form of a Turkish or vapour bath. Once the affection has developed, rest of the inflamed tissues is necessary.

RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

Ætiology. *Rheumatoid arthritis* is also known as the "proliferative" or "atrophic" type, and *osteoarthritis* as the "degenerative" or "hypertrophic type" of chronic rheumatic arthritis. The morbid anatomy of these two conditions is distinct, but it is quite common for osteoarthritic changes to be grafted on a primary rheumatoid arthritis.

Rheumatoid arthritis occurs at all ages, and in all conditions of life: but it is much more common in women than in men, and there is a strong hereditary factor. Cold and damp certainly often dispose to its occurrence or excite fresh attacks. It is less common in warm climates. Traumatism in the form of continued pressures, or constant strain, also predisposes to the disease. *Osteoarthritis* is essentially a disease of the latter part of life, and the sex incidence is more equal, though it is also commoner in women. The predisposing causes are similar to those of rheumatoid arthritis, and trauma is especially important in the mon-articular cases.

Morbid Anatomy. *Rheumatoid Arthritis.* The earliest changes are of a proliferative nature, commencing either in the synovial membrane near the articular margins or in the subarticular layer of cancellous tissue, or in both places simultaneously. The articular cartilage is invaded on its surface after preliminary degeneration by an advancing tide of vascular connective tissue (pannus) derived from the edge of the synovial membrane. The articular cartilage is simultaneously invaded on its deep surface by inroads of vascular connective tissue from the underlying bone. The layers of pannus on two opposed articular surfaces may adhere (fibrous ankylosis), and may even ossify (osseous ankylosis). Increased permeability to X-rays of the epiphyseal region is an early feature and is probably due to absorption of calcium salts. Later, the increased permeability to X-rays is increased by actual absorption of osseous

trabeculæ and their replacement by fat, hence the name " atrophic " sometimes applied to this type. The changes in the synovial membrane are also proliferative with enlargement and multiplication of the synovial villi. Histologically there is evidence of chronic or subacute inflammation in the form of rounded foci of small-celled infiltration. Serous effusion may occur into the joints or the capsule may be infiltrated, causing a spindle-shaped appearance. Similar changes may occur in peri-articular bursæ or tendon sheaths. In the later stages, lipping of the articular margins and eburnation of the joint surfaces may occur, *i.e.* secondary osteoarthritis (**15**).

Osteoarthritis. The first change consists in a degeneration of the central area of the articular cartilage. The changes that follow are in a sense all consequent upon this primary degeneration, although they themselves are more inflammatory than degenerative. For instance, the lateral part of the cartilage proliferates and osteophytes are formed to extend the articular area. The subchondral layer of bone becomes sclerosed, hardened and eburnated in an endeavour to form a new joint surface and thus compensate for the loss of the central portions of the cartilage. The changes in the synovial membrane are at first insignificant. There is villous hypertrophy and increased vascularity of the synovial fringes near the articular margins. Later, however, the synovial membrane and capsule become thickened and fibrous and arteriosclerotic changes may then be seen therein. The histological changes in the synovial membrane and capsule are of the nature of an inflammatory hyperplasia and small-cell infiltration is usually absent. These changes are frequently seen post-mortem in the joints of elderly persons, and are also the result of trauma or long-continued intra-articular irritation. " Loose bodies " in the joint cavities consist in the breaking away of synovial fringes, or of bony osteophytes or nodules of cartilage, so-called epiarticular or periarticular ecchondroses, which occur respectively either in the middle or at the edge of the articular cartilage. It has been claimed, from X-ray evidence, that the characteristic primary lesion is a cyst in the bone itself, surrounded by a densely calcified area, while in long-standing cases multiple cysts are seen (*see* Plate 43, A).

Pathology. There are two factors that will influence the type of rheumatic arthritis produced. Rest tends to cause atrophy of bone, and cutting off the blood supply causes hypertrophy, which is compatible with osteoarthritis, as the disease of arterial degeneration and old age ; in this connection it is to be noted that arthritis occurs in pulmonary osteoarthropathy, where the peripheral circulation may be sluggish. But at any rate in rheumatoid arthritis there is often infection from some primary focus elsewhere in the body, and between 60 and 70 per cent. streptococci, mostly hæmolytic, have been isolated from the blood stream and joints, while the blood serum gave positive agglutination and precipitin reactions ; negative results were obtained in control cases (**16, 17**). This work requires confirmation. In many cases the primary foci are in the teeth, consisting of apical abscesses or pyorrhœa alveolaris (*see* p. 321). Less commonly the tonsils are at fault. Other possible causes are adenoids, suppuration in the nasal sinuses or middle ear, uterus, male urethra, urinary tract, open wounds, and the colon, the latter if there is derangement of function. Most cases are probably of streptococcal origin, but the *staphylococcus* and *gonococcus* may also possibly be concerned, and perhaps others, such as *B. coli.* There is also possibly a tuberculous form, described by Poncet. Rheumatoid arthritis is at any rate very closely allied to acute rheumatism, since subcutaneous nodes of the same characteristic histological structure occur in both.

However, focal sepsis is certainly not the whole story, because it exists in many people who are not troubled with chronic rheumatism at all, and its eradication is often not really curative. There is also the problem of the " soil " to be considered, *i.e.* the condition in the individual that renders him liable to this disease. Certainly the disease when contracted is associated with certain

biochemical changes. Microscopic examination of the capillaries of the nail bed shows that the peripheral circulation is defective, so that in the tissues less oxygen is removed from the blood (3); the sugar tolerance curve tends to resemble that found in diabetes (9). Chronic rheumatic arthritis commonly improves during pregnancy, possibly because the respiratory metabolism is itself increased.

The onset of the synovitis in rheumatoid arthritis, as in acute rheumatism, may be an allergic phenomenon, due to some foreign proteins, just like the arthritis of "serum disease," which may follow the injection of antitoxic serum. There is a group of cases called *intermittent hydrarthrosis*, which is certainly of this nature, since it not only recurs periodically, but is often accompanied by or alternates with other well-known allergic symptoms; the disease is rather commonly associated with psoriasis. The synovitis that occurs in hæmophilia may, perhaps, be partly allergic, but also due to the actual effusion of blood in the joint. Finally, the severe muscular wasting of rheumatoid arthritis is accompanied by paræsthesiæ and atrophy of the skin, and is also remarkably symmetrical—points which favour a nervous factor in the disease, and this is of course very obvious in the multiple arthritis of locomotor ataxy and syringomyelia (*Charcot's disease, see* later).

Symptoms. *Rheumatoid Arthritis.* In a minority of cases, especially in young women, the disease is acute and polyarticular; it begins with fusiform swelling of the proximal interphalangeal joints of both hands symmetrically, with pain and tenderness; and subsequently the metacarpo-phalangeal joints, wrists, elbows, shoulders, and joints of the lower extremities are involved, as well as those of the spine, jaw, and the sterno-clavicular joints. There is slight febrile reaction with quick pulse for some weeks; and when this subsides the joints are still limited in their movements, and relapses of fever and swelling of the joints may occur. At the same time the patient becomes anæmic, sweats profusely, and shows pigmentation. There may be subcutaneous nodes and enlargement of lymphatic glands and the spleen. There is depression of spirits and loss of appetite. With each relapse the movements become more restricted, and, finally, ankylosis may result (*see* Plate 42, A). In a few cases there is carditis as in rheumatic fever. In most cases the disease runs a chronic course throughout.

Very characteristic deformities take place in consequence of the joint changes and the muscular atrophy which is associated with them. Thus the fingers, instead of remaining in line with the metacarpal bones, deviate to the ulnar side, and the joint at the base of the index finger is often greatly swollen; the metacarpo-phalangeal joints are commonly flexed, the first phalangeal joints are over-extended, and the second are flexed; there may be dislocation, especially at the interphalangeal joints, causing quite short, flaccid fingers which are not ankylosed (*see* Plate 42, D). The lower ends of the radius and ulna project at the back of the wrist. The muscles commonly observed to be atrophied are the interossei in the hand, the muscles at the lower end of the femur, and the deltoid over the shoulder joint. The skin over the affected parts becomes smooth and atrophic. The nerves also in connection with the joints are affected by chronic neuritis, causing pains in the limbs.

A similar clinical picture occurs in children before the second dentition; the arthritis observed in the knees and wrists is often associated with enlargement of the lymphatic glands and spleen, anæmia, sweating, varying pyrexia, and arrest of the bodily development (Still's disease). In older persons the disease may also occur with a somewhat rapid onset and affect many joints; or the disease may be more chronic from the commencement. The stiffness is often most marked in the morning, so that movements are at first painful; yet if they be persevered in, the pain will gradually wear off. Sometimes effusion can be readily recognised, and the joint is tense and elastic. In mild cases, which are very common, just one or two joints may be picked out alone.

Osteoarthritis. The onset is insidious, with pain, stiffness and creaking or crepitus on movement of one or more of the large joints; the disease is commonly mon-articular and non-symmetrical, though disease which has as yet produced no symptoms is rather commonly found in other joints if they are examined clinically and radiologically. As time goes on the movements become more and more limited. The general health and nutrition of the patient is unimpaired; there is no pyrexia except very occasionally during an exacerbation.

There are certain well-defined varieties of osteoarthritis. Disease of the hip (Plate 43) (*malum coxæ senilis*) is much commoner in men. The pain and stiffness are followed by very limited movement, eversion and apparent shortening of the limb, and flattening of the buttock. The knee-joint is most commonly affected in women, and this may be partly attributed to the trauma consequent on the increased body weight often associated with the menopause. *Herberden's nodes*, the small nodules or knobs which may form at the sides of the terminal phalanges, are bony outgrowths, and are characteristic of the early stage of osteoarthritis.

Spondylitis deformans, type *ankylopoietica*, occurs ten times as commonly in men as women, mostly between twenty and forty, and is essentially a bony ankylosis of the vertebræ. There may be kyphosis (Bechterew) with compensatory hyper-extension of the cervical vertebræ so as to keep the head erect, and lipping of the anterior edge of the vertebræ owing to pressure, or the spine may remain erect (spondylose rhizomelique of Marie and Strümpell). The bones may show osteoporosis with softening and fragility. The condition is allied to rheumatoid arthritis, though the sex incidence is so different. The back is stiff, and there is tenderness on pressure and percussion over the spine, due to the inflammation, and sometimes the ribs are immovable, so that breathing is entirely diaphragmatic. The rate of progress of the disease varies widely. In some cases the onset is acute and the progress rapid, so that the whole spine becomes rigid within a few months. In others the rate is much slower, and may be arrested when only a portion of the spine has been affected. Sometimes the onset is so insidious that the patient does not seek advice until there is extensive damage. The earliest symptoms are commonly those of lumbago and sciatica, and may be of no great severity. It is not uncommon to meet with a history of such symptoms followed by remission and recurrence after a few months, this happening two or three times before the nature of the disease is recognised. The small joints of the limbs are not often affected. *Spondylitis osteoarthritica*, sometimes called spondylosis deformans, is osteoarthritis of the spine; it occurs almost entirely in males mostly between fifty and sixty, and is the result of heavy labour, especially coal-mining; trauma may be a factor. Pain is not marked unless the exostoses press on emerging nerve trunks. The sedimentation rate is normal, in contrast to the type *ankylopoietica* where it is increased (5).

Diagnosis. In chronic *gout* the articular changes may closely resemble those of rheumatoid arthritis; in fact, in some cases indistinguishable from rheumatoid arthritis the blood uric acid is quite high and the old term of "rheumatic gout" might be applied here. In the acute cases other forms of acute or subacute polyarthritis must not be forgotten, such as congenital syphilitic arthritis and gonococcal arthritis; the localisation is often different, and the history will help. Rarely, repeated attacks of acute rheumatism produce permanent changes in the joints. Arthritis affecting one joint only may be confounded with tuberculosis; but the radiograms of osteoarthritis and tuberculosis are quite different (as seen in Plate 43, p. 559). Disease of the *hip* in elderly people must be distinguished from sciatica and lumbago. This is not easy in the early stage of the disease. Reliance should be placed on (1) local pain and tenderness on pressure over the joint, and pain on movement; (2) referred pain simultaneously along the sciatic and anterior crural and obturator nerves, since these nerves all supply branches to the joint;

(3) limitation of movement; (4) X-ray appearance. Charcot's disease is easily distinguished, and in addition there are nervous signs of *tabes* or *syringomyelia*.

Prognosis. No cure is possible when permanent changes in the joints have occurred, but in the very early stages a cure is possible. However, even in the later stages of the disease very great improvement takes place with careful treatment. In the acute form it is remarkable how altered in outward appearance the joint may be, and yet there may be complete recovery; but it takes a long time.

Prevention. Care must be taken to prevent the occurrence of septic foci. In particular the teeth must be attended to with regularity.

Treatment. The first step is to see if there is a possible primary focus. It is impossible to exclude the teeth and gums as sources of infection after a superficial examination; the required information may be obtained by taking dental radiograms (*see* p. 321). Suppuration at the root may exist when the tooth looks perfectly healthy, does not cause pain, and is not tender on percussion. The affected tooth should be extracted, and cultivations made from the apical abscess so as to prepare an autogenous vaccine. Apical abscesses are sometimes sterile. In severe pyorrhœa alveolaris the teeth should be extracted, but in milder cases improvement often takes place with less radical treatment. When the discharge of pus is free the danger is not so great as when it is pent up behind obstruction. Tonsils, adenoids, and the other possible sources of infection already mentioned should be attended to, and vaccines may be used. If no foci are found, suspicion often falls on the alimentary canal, particularly the colon, and vaccines prepared from organisms, usually *streptococci*, found in the fæces, have often been used. The test of a vaccine is its power to produce a focal reaction in the joints, and it should be continued for a year or longer until an injection produces no more pain in the joints (Beddard). Colonic lavage and intestinal antiseptics, such as salol, bismuth salicylate and β-naphthol, have been used, especially if there is diarrhœa. Another line of treatment is the so-called "protein shock therapy," in which intravenous injections of some foreign protein are used, for instance, 50 to 100 millions of a coli or typhoid vaccine or 10 c.c. of a 10 per cent. solution of Witte's peptone in water. The joints become swollen and painful, and subsequently there is improvement. This method may be used if no primary focus can be found. Intra-muscular injections of sulphur compounds are also given. Injections of gold preparations (allochrysin, solganol) in doses of 0·01 to 0·05 gram every few days, administered in a number of courses, have recently been tried with some success. Erythema, urticaria, and even exfoliative dermatitis may result from poisoning, also nephritis, stomatitis and diarrhœa and vomiting

Apart from specific treatment directed towards the cure of the disease, there are certain general measures and local measures of a palliative kind that must be considered. When the nutrition is poor the diet should not be stinted; on the other hand when the nutrition is good a low calorie diet is sometimes of advantage (3) and a low purine may also be valuable, especially when the blood uric acid is high. Successful results have been obtained from liver treatment (8). A moderate use of alcoholic drinks may be allowed. The patient should be well clothed in flannel, a warm dry atmosphere should be looked for, and changes of temperature avoided. Various health resorts and spas fulfilling these requirements have been found beneficial, such as Buxton, Bath, Harrogate, and Strathpeffer, at home, and Aix-les-Bains, Aix-la-Chapelle, Baden-Baden, and Wiesbaden, abroad. Internally arsenic in full doses, aspirin, sodium salicylate, guaiacol, iodide of iron, and vitamins A and D are most valuable, and they must be continued, with such intermissions as may be desirable, for weeks or months. Thyroid extract has also given good results. The joints themselves should be kept at rest in splints during the active stage of the disease; tincture of iodine may be applied.

After pain has subsided massage and passive and active movements will help to restore the mobility of the joints and the muscular nutrition; it is a good plan to apply heat to the joint before massage is carried out, as the mobility is increased by the vaso-dilatation. In fact, cures have been related after removing surgically the ganglia of the cervical or lumbar sympathetic as in the treatment of Raynaud's disease (6). Histamine injections may also help (7). Peat baths, mud baths, electric light baths, hot air baths and hot water baths, including the whirlpool bath, may be used. Electricity may be given in the form of diathermy, the continuous galvanic current, high frequency, and ionisation with salicylic ions. Sometimes it is found impossible to get a freely movable joint, and then ankylosis in the most useful position should be aimed at.

GOUT

This name is given to a form of arthritis associated with an increase of uric acid in the blood and a deposit of crystalline sodium biurate in the joints and other tissues. In the majority of cases the feet, and especially the great toe joints, are first attacked, whence the classical name *podagra;* but the joints of the hand (*chiragra*) and other articulations are subsequently, and much less commonly, affected first.

Ætiology. Gout is well known to be strongly hereditary, so that the descendants of a gouty stock are liable to outbreaks of the disorder at an early age and with comparatively little exciting cause. It is more common in men than in women, and is a disease of middle life or advanced age, though it does occasionally, in the hereditary cases just referred to, appear as early as the age of twenty; and it has been seen in boys who were only eight, nine, or twelve years old. It has been regarded as a disease of the rich, from which the poor escape; but this is not true, as the disease is often seen in its most typical form among hospital patients and others in poor circumstances. The influence of wealth is related to diet, which is the most important ætiological factor; and the ingestion of large quantities of food, especially those kinds which are rich in purin bodies, with abundance of alcoholic liquors, directly contributes to that condition of the blood and tissues which is the essence of gout. Of alcoholic beverages, malt liquors and the stronger wines, like port and sherry, seem to be more prejudicial than distilled spirits. The effects of dietetic excess are aggravated by a sedentary life; and, as a rule, an occupation is prejudicial in proportion as it tempts to one or necessitates the other. Sepsis, especially dental sepsis, predisposes to gout, as do also those occupations which expose the operatives to lead intoxication (*see* p. 587). In those who are predisposed to it, or who have already had manifestations, an attack may be brought on by an aggravation of the dietetic excesses, or by any departure from the strictest regularity hitherto found necessary, by anxiety and mental worry. Gout attacks more readily an injured joint and it is supposed that pressure of the boot on the metatarso-phalangeal joint of the big toe makes that joint so liable to attack.

Morbid Anatomy. The joint changes in chronic gout are usually but by no means invariably of the osteoarthritic type. The pathological changes are similar, therefore, to those already described with the important addition of deposits of sodium biurate in the constituent elements of the joint. In addition to uratic deposits in the articular cartilage, synovial membrane and capsule and in periarticular structures, collections of the crystals of sodium biurate often occur occupying cystic spaces or "punched-out" areas in the subarticular cancellous tissue; they also take place on the surface of the bones, where they are partly surrounded by osteophytes or sharp projecting spurs from the bones. In bursæ, in tendon sheaths, in the cartilage of the ear, or in the skin of parts not immediately over the joints, the essential change is also the accumulation of biurate crystals. Exceptionally, true gouty deposit has been found in other

situations—*e.g.* on the spinal meninges, and on the meninges of the cerebellum. Arteriosclerosis and primary contracted kidney are often present in gout.

Chemical Pathology. The uric acid of the urine is derived from two sources: (1) From the purin bodies in the food (*exogenous*). These substances (xanthin, hypoxanthin, etc.) are contained in tea, coffee, cocoa, in the nuclei of all cells, and so they are present in meat, sweetbreads and other cellular organs. The purins derived from this source are not altogether excreted as uric acid in the urine. A large amount is destroyed in the body. Still it is possible to raise very considerably the amount of urates in the urine by partaking largely of such rich foods. (2) From the wear and tear of the tissue cells of the body (*endogenous*). If a man takes a purin-free diet, *i.e.* lives on bread, vegetables, milk products and eggs, the uric acid in the urine is purely endogenous; and as this remains constant in amount for an indefinite period on a diet of this kind, it shows that the body has the power of synthesising purins. Histidin and arginin may be one source (Hopkins and Ackroyd). It has also been found that the endogenous uric acid falls to about a half on an almost protein-free diet (**1**), and also on a carbohydrate-free diet (**2**); but in the latter case the blood uric acid rises and an attack of gout may be precipitated.

In gout the blood contains an excess of uric acid. This was first shown by A. B. Garrod by his "thread test." This consists in placing 2 drachms of serum obtained from a blister in a shallow watch glass, adding 10 or 12 drops of acetic acid, placing in the serum three or four threads, and setting it aside for thirty or forty hours at the ordinary temperature. At the end of this time, if the threads be examined under the microscope, crystals of uric acid will be found to have formed upon them. The blood of a normal man contains up to 3 milligrammes per cent. Before an attack of gout the value is 4 to 6 milligrammes per cent. But, in spite of this high figure, the amount of uric acid excreted in the urine is below normal. Further, if a gouty person is given purins in the food there is great delay in their excretion in the urine. This points to the failure of the excretory power of the kidney as being responsible for the high uric acid in the blood. An attack of gout is associated with a sudden rise in the excretion of uric acid in the urine, which reaches its maximum on the second or third day of the attack. At the same time uratic deposits are laid down in the joints and other places. The uric acid in the blood falls. Cinchophen (diphenyl-quinolin-tetracarboxylic acid) has been found to ward off attacks of gout; and it does so by increasing the uric acid excretion in the urine, and at the same time the uric acid in the blood and tissues falls (Folin). It also facilitates the excretion of uric acid if purin foods are given to a gouty person.

It must be remembered that the uric acid of the blood may be increased in diseases, such as leukæmia and severe nephritis, in which gouty attacks are absent, so that gout cannot be due merely to this cause; there must be an additional factor.

The acute articular inflammations of gout are attributed to irritation by the crystalline deposit of sodium biurate, which is found in the tissues; and possibly the visceral attacks are due to a deposition, at least temporary, of the same biurate crystals.

Symptoms. *The Gouty Attack.* In the majority of persons gout first shows itself by an attack of acute inflammation in the metatarso-phalangeal joint of one great toe. Various premonitory symptoms are noted in different cases: in some there may be an unusual feeling of health or exhilaration; but more often there are the following: mental depression; disturbed sleep; odd sensations, itching, or cramps in the limbs; tinnitus aurium; salivation, gastralgia, vomiting, or flatulence; alterations in the quantity and colour of the urine, which is mostly scanty and deposits urates. These symptoms may have been troublesome for a day or two, when the patient is awakened, commonly about two o'clock in the morning, with pain in the great toe. The pain becomes

worse and worse, and the patient finds it impossible to get ease. At the same time there may be a little chill, or even a rigor, and some fever. After some hours of excruciating pain this at length abates, and the patient may fall off to sleep; when he awakes again he finds the affected joint red and swollen. It is exquisitely tender; the skin is tense and shining, and if it can be touched, pits slightly on pressure. The veins around it are slightly distended. During the day the patient may be free from severe pain, but towards evening there is a recurrence of all the early symptoms—that is, of severe pain and some febrile reaction—which remit towards morning, to return again the following night. The joint continues swollen, and the swelling extends in the cutaneous tissues some distance up the foot; the colour is a dull, dusky red. When at length the inflammation subsides, which it does in from five to ten or fourteen days, the skin desquamates in large thick flakes, and gradually assumes its normal colour. In exceptional cases one or two toe-nails may be shed; on the other hand, in mild attacks desquamation does not occur.

The general condition of the patient is one of slight febrile reaction, with more or less gastric disturbance. The temperature is not much raised; the thermometer may reach 101°, but is rarely so high as 102°, and then only for a short time. The tongue is thickly furred, and the patient has no appetite, but much thirst, nausea, and sense of distension at the epigastrium, and is constipated. Phlebitis with thrombosis of veins is not an uncommon accompaniment of the acute attack, and uræmia may also occur if the kidneys are diseased, and there is usually a considerable polymorphonuclear leucocytosis.

When an attack of gout is at an end, the patient often feels better than he has done for a long time before; and he is, as a rule, free from any reminder of his condition for a period of several months, or even two, three, or more years. His second attack may be in the same joint as the first, an almost exact reproduction of it; or it may occur in the opposite foot, or in one ankle, or in the wrist or hand. A third attack often comes at a somewhat shorter interval than that between the first and second, and the periods of repose diminish in length as time goes on. Ultimately a great many joints have been at one or other time affected, and with repeated attacks they undergo changes which result in considerable deformity, so that the old gouty subject becomes crippled in somewhat the same way as the sufferer from rheumatoid arthritis.

When the disease has reached this stage it is in reality a *chronic gout*. If the small joints of the toes and fingers are often first affected, ultimately all the joints of the extremities may become the seat of gouty deposit, the shoulder and the hip less frequently. In the hand the joints are enlarged, are more or less fixed in different positions of flexion or extension, and in severe cases there is deviation of the fingers to the ulnar side of the hand. Similarly the foot may be fixed in a condition of talipes, or the knee or elbow in a flexed position. The swelling about the joints is often assisted by the existence of white deposits called *tophi*, which at first lie close under a thin shining skin, with dilated venules. But subsequently the skin may yield, and the creamy or chalk-like deposit may escape in small quantities at a time; or, more rarely, suppuration takes place around the deposit, and leads to its more rapid elimination. These tophi are not confined to the affected joints; they are seen under the skin of the fingers adjacent, in the bursæ (for instance, over the olecranon), in the tendons, and with considerable frequency in the cartilage of the helix of the ear. If the creamy juice from one of these deposits be examined under the microscope, it will be found to consist of innumerable minute acicular crystals, which are composed mostly of sodium biurate, with a small proportion of calcium urate or phosphate, and sodium chloride.

Gout sometimes occurs in the form of subacute or even chronic arthritis in two or more joints without any preceding typical acute attack in the great toe or hand. There is often a general resemblance to the polyarthritis of acute rheumatism.

Again, a high blood uric acid, presumably of gouty origin, is found in certain cases of typical rheumatoid arthritis.

Under the heading *irregular gout* are grouped certain disturbances which are apt to occur in gouty persons, but which have nothing really to do with the disease itself. They are gastric and intestinal catarrh, bronchitis, conjunctivitis, iritis, gouty urethritis (which is, according to Ebstein, a prostatorrhœa), neuritis, cirrhosis of the liver, and chronic eczema.

Diagnosis. The typical gouty attack occurring at night in the great toe can scarcely be confounded with anything else. It is distinguished from *acute rheumatism* by the dark red, shiny, tense swelling of one joint, the absence of general sweating, and the slight constitutional disturbance. Later illnesses implicating many joints show a closer resemblance. There is generally a history of many previous invasions of single joints, and less fever or sweating than in rheumatism; but the condition of the joints themselves cannot be relied upon as it can in early attacks. The swelling and redness of the back of the hand in gout may be such as closely to resemble *abscess*, but fluctuation can scarcely be obtained, and the history will mostly protect against errors. *Pyæmia* may be suggested by multiple gout, but rigors would be more severe, and the general disturbance more intense. In all cases the ears should be carefully examined for tophi, and, if necessary, microscopic examination of part of the tophus should be made to see if sodium biurate crystals are present, or the murexide test may be employed. In cases of doubt the uric acid in the blood may be estimated by Folin's method. A low value excludes gout, but it does not follow that if the value is high gout is necessarily present.

Radiographic examination of the chronically affected joints may be of value. Since sodium urate is not opaque to X-rays, clear areas in the neighbourhood of the joints may be seen. They have sharply defined edges, as if punched out, and are often round, varying in size up to that of a sixpence. Small pot-holes may be seen in the articular surface. The structure of the bone may appear altered, the striæ becoming irregular, and the shape of the bone may be deformed. This is ascribed to the irritation produced by the uric acid. Finger-like projections or exostoses may be seen projecting from the shaft (*see* Plate 44).

Prognosis. Gout once declared is likely to be repeated unless the conditions, dietetic or otherwise, which have led to it are altered. Acquired late in life, and properly treated, it may not materially shorten life; the associated arteriosclerosis and primary contracted kidney may be serious.

Prevention. The quantity of food taken should always be moderate. Many patients are too fat, so that a loss of weight will be an advantage. Restriction of both protein and carbohydrate foods is generally regarded as beneficial. But, most important of all, a diet containing a minimum of purin bodies should be chosen, since an attack of gout may be precipitated by such food. The foods which contain but little purins are milk, eggs, butter, cheese, fat, white bread, rice, sago, fruits, cabbage, lettuce, cauliflower, and potatoes. The foods which contain purins in quantity and so should be avoided are cocoa, chocolate, barley, oatmeal, flesh foods, including the lean of bacon and ham and most organs. Some of these foods also contain large amounts of oxalates (*see* p. 508) and so should be avoided; this also applies to potatoes. When it is not desired to cut the purins down to the minimum the following articles, containing moderate amounts of purins, may be taken; fat bacon, mutton cutlet, roast pork, tongue, stewed tripe, brains, chestnuts, asparagus, caviare, peas, oatmeal, beans, Brussels sprouts, lentils, radishes, spinach, sorrel, raspberries, rhubarb. Personal peculiarities may have to be consulted, so that indigestion is avoided, and with this proviso fat may be taken in moderation. Alcohol in any form is best avoided by those with a tendency to gout; a light white wine is the least harmful, or a small quantity of good brandy or whisky well diluted. As in diabetes, saccharin may be usefully employed for sweetening. Alkaline and saline waters

are of service, and more still, residence at the spas, where the influence of the waters is combined with a regulated diet, fresh air, and pleasant surroundings.

Cinchophen (trade names, atophan, agotan, phenoquin, and quinophan), described above, is the most valuable drug for preventing attacks of gout. It is given in 15-grain doses three times a day after meals for three days of each week. If there is gastric irritation, sodium bicarbonate, 15 grains, may be given simultaneously. The diet should contain plenty of carbohydrates. Cinchophen poisoning is now well known and the symptoms resemble closely those of poisoning by arsenobenzol (*q.v.*); toxic jaundice from acute necrosis of the liver may be imitated, and is the commonest, but all the "early toxic effects" may be imitated, apart from encephalitis, and there may be transient albuminuria (**12, 13**). Salicylates and sodium benzoate act similarly in increasing the excretion of uric acid in the urine. The bowels should also be kept free.

Treatment. In acute gout the affected foot should be kept raised, and supported on a chair or couch, if the patient is not in bed. It should be wrapped in cotton wool, and in severe cases some anodyne application, such as belladonna liniment, tincture of aconite, tincture of opium, or a lotion of atropine and morphia, may be previously applied sprinkled on lint, and some oiled silk or thin gutta-percha laid over all. Leeches, hot poultices, and ice applications are to be avoided. The diet must be at once restricted in younger patients to milk and farinaceous foods, but in older persons and those broken down by previous attacks it may be more liberal, but still mostly fluid and easily digestible. Alcohol should, if possible, be entirely withheld. Medicinally colchicum has a decided effect in most cases. It may be given as wine or tincture in doses of 15 to 25 minims every six or four hours, in combination with bicarbonate or citrate of potassium, or citrate of lithium. Cinchophen is useless in relieving the inflamed joint. The bowels should be kept active with calomel. If pain is very severe, morphia may be given by subcutaneous injection or internally.

HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY

"Clubbing" of the fingers is the earliest stage of this disease. The terminal digit is swollen and globular; the nail is enlarged and more convex than usual. The soft parts may be involved alone, but the phalanx is often broad and thick. In fully developed hypertrophic pulmonary osteo-arthropathy the clubbing of the fingers is associated with enlargement of the bones of the extremities, particularly those of the hands and feet, and the distal ends of the long bones. There may be effusion into the joints, preceded by stiffness.

"Clubbing" occurs in two groups of cases: (1) Among people who live at great altitudes, *i.e.* the Andes (**11**), and in other cases of prolonged oxygen deficiency, such as chronic pulmonary disease, *e.g.* fibroid lung, phthisis, empyema and bronchiectasis, but also in mediastinal new growths, in compression of the subclavian vein by aneurysm, when unilateral clubbing has been found, in methæmoglobinæmia or sulphæmoglobinæmia, and in congenital heart disease and, rarely, acquired heart disease. (2) In this group are included a varied assortment of cases, cirrhosis of the liver, infective endocarditis, carcinoma of œsophagus, pyloric stenosis, etc. Clubbing has disappeared with relief of the primary cause. Pathological and skiagraphic observations show that in developed pulmonary osteo-arthropathy there is a thin deposit of new bone under the periosteum of the long bones, and especially of the lower thirds of the radius, ulna, tibia, fibula, metacarpals, metatarsals, and proximal and middle phalanges of the hands and feet. The deposit is such as to fill up the concavity between the proximal and distal ends of the bone, and to make, for instance, in the case of a metacarpal, the middle thicker than the ends. Sometimes the joints (wrist, ankles and interphalangeal joints) contain fluid, and the synovial membrane is

thickened. In clubbing of the fingers and toes the primary change is œdema of the tissue between the nail and the phalanx, which separates the connective tissue fibrils from one another (**10**). In later stages this is replaced by fat and fibrous tissue. In early cases, after compressing the sides of the fingers for some little time, a boggy feeling is experienced on compressing the base of the nail, as if it was lying on thick fluid. Two factors probably play a part in the production of the œdema—desaturation of the arterial blood with oxygen and peripheral stasis. The clubbing in the second group of cases can hardly be explained in this way.

ACHONDROPLASIA

This is a congenital disease of the bones and cartilages, which results in permanent stunting of growth and other deformities. No demonstrable change has been found in the endocrine glands. Its hereditary character—it sometimes appears after skipping a generation—is more in favour of an inherited tissue defect. At birth the limbs, especially in their upper halves, are noticed to be abnormally short. The child may be of full weight, but growth is slow, the limbs continue to be short, and the stature is consequently small, though the vertebral column is of normal length. There is a projection of the buttocks which gives the appearance of lordosis and a waddling gait. The head is generally large, somewhat like a rachitic head, with a prominent forehead, but a depressed bridge of the nose. The limbs often show transverse furrows, as if the soft parts were too long for the bones. The hands present a characteristic deformity in that the index and middle fingers diverge from the ring and little fingers when the hand is open (*trident hand*). The deformities are due to defects in ossification of the cartilages of the long bones and of the innominate bones, together with a premature synostosis of the bones of the basis cranii. The cranial bones which are formed in membrane are normally developed, as well as the bones which remain cartilaginous till a late period of fœtal life, viz., the sternum, patella, carpal and tarsal bones, and the costal cartilages. The thyroid is normal; and the subjects of the disease have a good intelligence, and are muscularly and sexually well developed. The disease does not usually tend to shorten life.

The changes occurring in the cartilages are of three types: (1) hypoplastic, with diminution of the cells; (2) hyperplastic, with excessive proliferation and enlargement of epiphyses; (3) softening, with defective columnar arrangement of the cells and increased vascularity. There is no abnormality of the calcium metabolism.

No **treatment** is of any avail.

OSTEOGENESIS IMPERFECTA

As the name implies, there is in this rare condition deficient ossification of the bones, with consequent undue fragility, especially shown in the long bones; and there is an abnormal formation of the skull, which is typical of the disease. The shafts of the long bones are curved and tortuous, and there is some shortening, which is more marked in the proximal halves of the limbs. Fractures, relatively painless, take place with great facility both in the ribs and in the limbs; the bones may unite again under a callus which is thrown out in a circular form. In the skull there is a persistent wide frontal suture, continuous with a large anterior fontanelle; and the posterior fontanelle remains also large. The bones are thin and yield to pressure, and instead of forming in each case a single bone, they present a mosaic of small irregular separate pieces of bone. In the lateral region the skull may be still unossified, and this leads to a characteristic bulging in the temporal region just above the ear, the concha of which is pushed outwards by it. The orbits are oval with the long axis vertical, and during life the eyeballs are turned downwards so as to produce some resemblance

to the condition seen in chronic hydrocephalus. Congenital, infantile and late forms are described. There is a very marked hereditary tendency. The condition is often associated with blue sclerotics (**14**). In the congenital form, there is frequently evidence of intra-uterine fractures which have produced deformities; few of these cases survive more than a few days.

There is a defective proliferation of the osteoblasts and calcium retention is below normal. **Treatment** should be directed to the prevention of injuries. Large doses of calcium gluconate and of vitamin D appear to be useful.

OSTEITIS DEFORMANS

(*Paget's Disease*)

The ætiology of this disease is unknown. Perhaps the most likely suggestion is that it is due to some defect of internal secretion; but syphilis has been considered a cause. It affects both sexes about equally, and is observed in the latter half of life.

Morbid Anatomy. The long bones of the limbs are often attacked in the early stages of the disease. They become thicker. There is an increase in the size of the marrow cavity. At the same time the compact bone becomes looser in texture and more spongy and much thicker than normal. The consequence is that the bones are light, even though they are large. The bones of the lower limb bend under the weight of the body. Similar thickening and porosity are noticed in the bones of the skull. There is kyphosis of the spine. The bones of the face, hands, feet and pelvis and the clavicles and ribs may show similar changes in slight degree. Arteriosclerosis and myocardial degeneration are often present.

Symptoms. The onset is insidious. The patient complains of pain and tenderness in the affected parts. His legs may become gradually bowed and his back bent. The increase in the size of the skull is noticed because he finds that he must wear a larger hat. Often the disease begins in one limb, and the corresponding limb on the opposite side is affected subsequently. In the later stages the patient's attitude is characteristic, with bent back, bowed legs, and large head projecting forwards. He can only waddle along with the help of a stick. The disease is slowly progressive, but does not shorten life, except that sometimes sarcoma develops in the affected bones. The bones are not liable to fracture. The blood phosphatase is increased but the calcium and phosphorus are normal.

Diagnosis. The disease must be distinguished from *acromegaly*, in which the soft parts are affected as well as the bones; *osteoarthritis*, in which the joints are affected, but not the shafts of the bones; *osteomalacia*, in which the bones are soft and liable to fracture; and *syphilis*, in which there is no general enlargement of the skull. The history of the disease and the Wassermann reaction will also help. The X-ray appearances are very characteristic (*see* Plate 45).

Treatment. This is symptomatic. If the Wassermann reaction is positive, anti-syphilitic measures should be adopted.

REFERENCES

1	O. Folin	1905	*Am. Journ. Physiol.*, **13**, pp. 45, 66.
2	G. Graham and E. P. Poulton ..	1913	*Quart. Journ. Med.*, **7**, p. 13.
3	R. Pemberton	1928	*Proc. Conf. on Rheum. Dis., Bath*, p. 182.
4	J. A. Glover, Milroy Lectures ..	1930	*Lancet*, **i.**, pp. 500, 607, 733.
5	C. W. Buckley	1931	*Brit. Med. Journ.*, **i.**, p. 1108.
6	L. G. Rowntree	1930	Quoted in *Lancet*, **i.**, p. 964.
7	A. A. Bisset and A. Woodmansey	1933	*Lancet*, **ii.**, p. 1018.
8	V. Coates and J. L. Delicati ..	1928	*Lancet*, **i.**, p. 1069.

9	G. L. KERR PRINGLE and O. S. MILLER	1923	*Lancet*, i., p. 171.
10	CAMPBELL	1924	*Brit. Med. Journ.*, i., p. 145.
11	J. BARCROFT and others	1922	*Brit. Med. Journ.*, i., p. 648.
12	G. EVANS and A. W. SPENCE ..	1929	*Lancet*, i., p. 704.
13	T. G. REAH	1932	*Lancet*, ii., p. 504.
14	BRONSON, quoted by J. A. FOOTE..	1927	*Clinical Pædiatrics*, 7, 1927.
15	Reports on Chronic Rheumatic Diseases	1935	i., p. 19.
16	R. L. CECIL, E. E. NICHOLS and W. J. STAINSBY	1929	*Arch. Int. Med.*, 43, 571.
	,, ,, ,,	1931	*Amer. J. Med. Sci.*, 181, 12.
17	E. E. NICHOLS and W. J. STAINSBY	1931	*J. Clin. Invest.*, 10, 323.

DISEASES DUE TO CERTAIN DEFICIENCIES IN DIET

ACCESSORY FOOD FACTORS

(*Vitamins*)

THE growth of the young animal depends on two sets of factors : (1) those that are inherent in the organism and are influenced by heredity ; (2) those factors in the environment that exert an influence on the organism from without. Food is the most important of these. Till recently it has usually been considered sufficient to calculate the diet solely on the energy requirements of the individual, while a protein ration was allowed more than sufficient to cover the loss by wastage of the tissues and the amount required for the formation of new tissue in the growing organism. Human experience with scurvy through many centuries has shown that something else is wanted, and we find Bachstrom writing in 1734, " This evil " (scurvy) " is solely owing to a total abstinence from fresh vegetable food and greens, which is alone the true primary cause of the disease. . . . Recent vegetables are found alone effectual to preserve the body from this malady and most speedily to cure it, even in a few days, when the case is not rendered desperate by the patient's being dropsical or consumptive." The general principle that it is impossible to keep animals alive on a diet of purified proteins, fats and carbohydrates with the necessary inorganic salts was enunciated by Hopkins (1906). The special substances that must be present in the diet are called *accessory food factors* or *vitamins*.

Fat-soluble A. Butter, cream, cow's milk, cod-liver oil and other fish oils, and egg yolk provide the most abundant sources of the vitamin. It is also present in the green leaves of plants, *e.g.* green vegetables, and the embryos of certain seeds. In fact, it may be identical with the yellow colouring matter of plants known as carrotene. It is completely absent from certain vegetable fats and oils, such as olive oil, cotton-seed oil, cocoa butter, linseed oil, and also lard (specially prepared pig fat), although bacon, mutton, and beef fat contain plenty of it. It is completely destroyed when oils are " hardened " by the action of hydrogen—a process widely employed in the preparation of edible fats ; but it can stand being heated to 100° C. for an hour or two. Its presence in milk fat is in part dependent on a good supply of this substance in the food of the cow, and this is satisfied when there is plenty of green food available. In the absence of this vitamin from the diet infections readily occur, especially in the alimentary and genito-urinary tract often causing stone in the bladder, in the nasal sinuses and middle ear and round the base of the tongue, while in animals disease of the nervous system has been found. There is also absence of adipose tissue, general visceral atrophy, xerophthalmia (1), and night blindness (*hemeralopia*). The vitamin aids the growth of the soft tissues round the teeth.

Water-soluble B. This is really a group of vitamins of which vitamin B_1, which is the antineuritic or anti-beri-beri factor, and vitamin B_2, which prevents pellagra, are of clinical importance. Both vitamins occur largely together. The richest supply is the germ of rice and wheat, but the outer covering of the grain which forms bran and the *aleurone* layer just beneath it also contain the substance. Egg yolk, ox liver, yeast, and pulses contain plenty of it. A commercial prepara-

tion of yeast called *Marmite*, used for soups, is a convenient source of the substance. B_1 is only very slowly destroyed by being kept at 100° C., but much more quickly at 120° C. Hence no serious loss of the substance need be feared in the baking of bread or biscuits; on the other hand, tinned foods are to be regarded as quite free from it. B_2 is much more heat stable. When rice is "polished," the germ and the whole of the external covering of the grain (pericarp) are removed, and so the whole of the antineuritic factor is lost. When young rats are fed on "polished" rice growth stops immediately, and inco-ordination of the back legs occurs, so that the animal can no longer walk about. Pigeons also develop a polyneuritis, and this is regarded as the same disseae as beri-beri. When severe symptoms have been produced experimentally they can be rapidly cured, sometimes in a few hours, by giving adequate amounts of the antineuritic factor. There is also evidence that lack of vitamin B_2 causes atrophy of the lymphoid tissues of the alimentary canal with stasis and dilatation and anæmia.

Vitamin C (*antiscorbutic*). This water soluble vitamin has now been prepared in the pure state, as *ascorbic acid.* Its richest source is paprika; but raw cabbage leaves, raw swede juice, fresh lemon and orange juice contain plenty; other substances, such as carrots, beetroot, potatoes, onions, grapes, apples, milk and fresh meat, contain comparatively small amounts, while flour, eggs and dried pulses contain none at all. However, if dried pulses, like lentils, peas and beans, are soaked in water and allowed to begin germination for two or three days, they acquire antiscorbutic properties. The vitamin is very sensitive to drying and to high temperature. Dried foodstuffs will not prevent scurvy, and cabbage loses 90 per cent. of its power when boiled in water for an hour, and the loss occurs more quickly still if alkali is present. Hence vegetables should not be cooked for longer than twenty minutes, and soda should not be added. Tablets of dried lemon juice, made up with sugar and tragacanth, retain activity for a year if kept cool.

Vitamin D (*antirachitic*). Vitamin D is fat soluble and occurs in cod-liver oil and halibut oil associated with fat-soluble A; cow's milk, which is rich in fat soluble A, is poor in vitamin D, but owing to the high calcium content milk has powerful antirachitic properties. It has been found that certain *sterols* (especially ergosterol, which occurs in ergot, yeast, etc., and phytosterol, which occurs in wheat and vegetables) after they have been irradiated with ultra-violet light, develop antirachitic properties; the pure vitamin C—*calciferol*—is prepared from irradiated ergosterol. The essential sterol probably occurs normally in the skin, and vitamin D is formed when the child, mother or the cow is exposed to sunlight; hence the value of sun-bathing.

Vitamin E is fat soluble; it has been found necessary for reproduction in rats and mice.

BERI-BERI

(*Kakke, Polyneuritis endemica, Hydrops asthmaticus*)

This is an endemic disease characterised typically by neuritis of the peripheral nerves and vagus resulting in varying degrees of paralysis, anæsthesia, cardiac dilatation and dropsy. It is due to the absence of vitamin B_1 in the diet. Several different clinical types are encountered.

Ætiology. It has been observed chiefly amongst the rice-eating populations in Japan, China, Malaya and the Philippines, but it may occur anywhere when a diet consisting chiefly of cereals is eaten provided the germ and external covering have been removed in their preparation. In whole rice, for example, the husk, pericarp and germ are rich in vitamin B as well as in protein, fat and phosphorus, and during the process of milling these are all removed leaving the residual white, polished rice poor in these constituents. Beri-beri has not infrequently

been encountered amongst sailors on sailing-ships where biscuits made from white flour and tinned food are largely eaten. It has also been recorded in Newfoundland and Labrador, where the population subsist largely on white bread throughout the winter and summer months. During the siege of Kut a remarkable outbreak of the disease took place amongst the British troops when they were subsisting chiefly on wheaten flour, but disappeared when they were compelled to eat barley flour, or *attar*, which is a coarsely ground whole-wheat flour used by the Indian troops. The British troops escaped this owing to their large ration of horse flesh which would not be eaten by the Indian troops. White bread, of course, is largely eaten in England, but here there is sufficient of the accessory factor in the rest of the diet to prevent the onset of the disease. It is noteworthy that exercise lessens the tendency to develop beri-beri (4).

Pathology. In addition to the œdema and anasarca seen during life, ecchymoses under the serous membranes, in the muscles and in the sheaths of the nerves may be found. Dilatation and hypertrophy especially involving the right side of the heart occur, also œdema and fatty degeneration of its muscular walls. The lungs are often engorged and œdematous and the liver and kidneys congested. Wallerian degeneration of the peripheral nerves occurs and often axonal degeneration as well, while there is a cellular infiltration of the endoneurium and perineurium. The vagus and sympathetic nerves may also undergo degenerative changes as well as the anterior horn cells and the nuclear connections of the vagus.

It has been suggested that (5) the swelling of the heart muscle is due to imbibition of fluid which diminishes its contractility without altering the mechanism of its beat as shown by the electro-cardiograph; excessive imbibition also occurs in the skeletal muscles, the nerves and certain glands and this process is held by some to be responsible for both the symptoms and subsequent atrophy which ensues.

Symptoms. The disease takes 80 to 90 days to develop on a diet of "polished rice," and the signs and symptoms, for the most part, are those of multiple neuritis (p. 651), to which there may be superadded certain cardiac features including dyspnœa, œdema of the legs and anasarca. The course is generally afebrile except possibly in its early stages, and it may be accompanied by gastro-intestinal symptoms like epigastric discomfort, nausea and vomiting. Several different clinical types are encountered :—

(1) Mild ambulatory cases with paræsthesias, patchy anæsthesia and diminished tendon reflexes; on an appropriate diet the patients readily recover.

(2) Ordinary beri-beri of which there are two types: (*a*) wet; (*b*) dry. The onset which is generally insidious but may be almost sudden is characterised by heaviness, weakness and numbness in the limbs associated with pain in the calves and a general state of languor. In the *dry* form, as the disease develops, there are loss of power and muscular atrophy beginning in the extensors on the front of the leg and subsequently affecting the other muscles and those of the thigh; later the extensors of the hand, the biceps and sometimes the abdominal muscles, the diaphragm and the intercostals become implicated. High steppage gait and wrist drop often result. Early weakness of the legs may be revealed by the "squatting" test. To elicit this a squatting position is assumed with the knees separated and the buttocks a few inches from the floor. The patient with beri-beri finds himself unable to raise his body from this position and generally attempts to use his hands on his thighs just like the case with pseudo-hypertrophic paralysis. The knee jerks, which are hypersensitive at first, are soon lost and later the Achilles jerk and other deep reflexes disappear. Anæsthesia generally appears first over the skin of the tibia and subsequently extends to other parts of the limbs and trunks. Tenderness of the muscles, especially those of the calves, as well as painful cramps occur just as in multiple peripheral neuritis from other causes, and laryngeal paralysis with difficulty in swallowing may

also supervene. Cardiac irritability is not infrequent, and at any time the *wet* form may develop. The *wet* type is always associated with some evidence of peripheral nerve involvement to which are added various grades of subcutaneous œdema at first involving the tibiæ and later extending elsewhere. General dropsy with effusions into the pleural, peritoneal and pericardial cavities may supervene. Dyspnœa and tachycardia with a rapid, low tension pulse ensue; clinically, the right heart is dilated and there are systolic murmurs associated with a loud and reduplicated pulmonary second sound. Embryocardia is not uncommon. The urine contains little if any albumin and is free from casts.

(3) Acute cardiac type: this may develop in the course of "wet" or "dry" beri-beri or start suddenly without prodromal features. Generally there are a sense of depression, epigastric pain and nausea followed by palpitation, præcordial pain, dyspnœa and signs of congestive failure with engorged cervical veins, cyanosis, pulmonary congestion, tender enlarged liver, subcutaneous œdema and general dropsy, Aphonia and paralysis of the diaphragm may ensue and death supervenes within a few hours to a few days.

(4) Infantile beri-beri, which may assume either acute or chronic forms, occurs in Japan and the Philippine Islands in breast-fed infants whose mothers are afflicted with latent or active beri-beri. Gastro-intestinal symptoms with nausea, vomiting, diarrhœa or constipation are common, in addition to cardiac features. The administration of extract of rice polishings plus the substitution of artificial for breast feeding generally results in cure.

Diagnosis. The nature of the diet and the occurrence of multiple cases of peripheral neuritis should arouse suspicion of beri-beri, especially amongst Orientals. *Wet* beri-beri has to be differentiated from nephritis, ankylostomiasis and cardiac failure, and the *dry* form from alcoholic and arsenical neuritis and other nervous diseases.

Prognosis. The more usual case lasts from one month to a year or more and recovery is often very slow in spite of appropriate dietetic treatment. The danger lies in rapid cardiac failure, and fatal exhaustion sometimes follows vomiting. Vedder, in 1913, estimated the average mortality to be 5 per cent., but in some of the recorded epidemics it has been much higher.

Treatment. It is important where tinned foods, polished rice and white bread are largely eaten to reinforce the diet with eggs, yeast, or Marmite, which have a high vitamin B content, or to substitute under-milled rice and whole wheat flour.

Once the disease has developed the patient should be put to bed and rigidly kept there; small feeds are at first given every two hours consisting of a dry diet low in carbohydrate and containing eggs, milk, liver, yeast or Marmite. In heart failure venesection and vaso-dilators are of definite value, and the bowels should be kept open with salines. During the acute stage contractures must be avoided, and later massage and electro-therapy may prove useful in restoring the atrophied muscles. At this stage a bitter tonic and strychnine mixture may be employed before meals.

EPIDEMIC DROPSY

A nutritional disease occurring in epidemic form in rice-eaters, characterised by fever, wide-spread œdema, cardiac disturbances and sometimes erythematous eruption involving the extremities. Neuritis has been absent in most epidemics. As "Hunger" or "War Œdema" it occurred extensively in the Central Empires during the War.

Ætiology. The disease commences in the rainy season in Bengal, affecting both sexes and being specially common in the third decade. Large numbers of rice-eaters—especially those eating it par-boiled—are often simultaneously

attacked. Some ascribe the disease to decomposition of faultily stored rice in rainy seasons associated with high humidity. Others hold that as there are no reliable means of differentiating it from wet or cardiac beri-beri it should be regarded as a special form of this disease.

Symptoms. These are very similar to *wet* beri-beri, generalised œdema and cardiac dilatation, with enlarged liver and pulmonary congestion being characteristic features. Peripheral neuritis has not been observed in recent epidemics, though there may be complaints of formication involving the feet. Pyrexia is present, associated often with anæmia and sometimes with leucocytosis, and an erythematous eruption may involve the extremities. Diarrhœa is not uncommon and achlorhydria is also reported. Eye trouble—especially glaucoma—is not infrequently encountered.

Treatment. This is similar to that of *wet* beri-beri, and venesection may be necessary for right-heart failure.

PELLAGRA

(*Mal de la Rosa, Mal de Sole*)

Pellagra is a disease of faulty nutrition generally arising in maize-eaters whose diets are deficient in vitamin B_2 and "good" protein. Clinically, there is a symmetrical erythema and pigmentation of the skin in areas exposed to the sun's rays, alimentary disturbances including sore tongue and diarrhœa, and nervous and physical symptoms often ending in dementia.

Ætiology. Pellagra (*pelle*, skin, and *agro*, rough; or *pelle* and *agra* as in podagra) was first described in Italy (1700), in Spain (1735), and in France (1818), and more recently it has been reported from Roumania, Hungary, Corfu, Lower Egypt, Turkey, Sudan and other parts of Africa, Turkey, the Southern United States, Brazil, Argentine, the West Indies, Mexico, India, China and Japan. People of any race, sex or age are susceptible, but adult women are most affected. It occurs amongst the poorer classes, especially in maize-eaters, and may also follow excessive drinking of alcohol made from maize. It is known in England (**14**).

Casal in 1735 recognised the disease as due to faulty nutrition, and Funk (**12**) pointed out its resemblance to beri-beri and suggested vitamin deficiency. It has been regarded (**13**) as due to amino-acid deficiency, zein, the protein of maize, being defective in tyrosine and tryptophane. Generally it is now attributed to deficiency in Vitamin B_2 (*q.v.*). The maize toxic theory has recently come into prominence: this ascribes pellagra to a toxic substance derived from the maize diet, which can be corrected by sufficient "good" protein or perhaps by sufficient Vitamin B_2, which is found to accompany "good" protein. Secondary pellagra is a rare complication of certain alimentary diseases like peptic ulcer and gastric carcinoma: here defective absorption of Vitamin B_2, as well as dietetic deficiency, may play a part.

Pathology. The skin shows erythema, pigmentation and, later, true exfoliative dermatitis, while emaciation is marked and the viscera atrophic. The heart is small. Glossitis with ulceration and subsequent atrophy of the tongue is found, and atrophic and ulcerative changes have been described in the small bowel as well as ulceration in the colon. Osteoporosis with bony changes occasionally occurs. The most characteristic lesions are found in the spinal cord and consist of sclerosis or degeneration of the posterior and lateral columns—especially Clarke's column. The latter are most affected in the cervical and upper dorsal region, and the former in the middle and lower dorsal region. There is round-celled infiltration of the perivascular spaces with pigmentation and degeneration of nerve elements. Diffuse leptomeningitis, thickening and adhesions of the meninges, cerebral atrophy and hydrops of the ventricles may be present.

Symptoms. A pre-pellagrous condition characterised by asthenia, low blood pressure, anorexia and mental depression may reappear annually for some years

before frank pellagra develops. *Alimentary disturbances* appear in early spring: there may be stomatitis and acute glossitis (beet tongue) with aphthous ulceration, denudation of epithelium and, ultimately, atrophy with loss of lingual papillæ. Achlorhydria is the rule and severe non-fatty diarrhœa associated with colicky pain and tenesmus may occur for many months. Anæmia, if present, is generally "secondary" with a low colour index, but occasional instances of megalocytic anæmia have been described. The blood pressure is low, there is associated lassitude and occasionally attacks of vertigo. *Dermal lesions* appear in the early summer and disappear in the autumn. The characteristic features of the eruption are its symmetry, its sharply defined pigmented border and its distribution over areas exposed to the sun's rays. The face, neck, upper portion of the chest, back of the hands and forearms, the dorsum of the feet and the insteps and legs are common sites for the rash which commences as an erythema, like severe sunburn, is associated with itching and burning and may undergo vesiculation. After about a fortnight the epidermis is shed in gray or brown flakes. Pigmentation and thickening of the dermis follow repeated attacks; ultimately, atrophy ensues, the skin becoming thinned, dry and wrinkled. *Nervous manifestations* resemble those of subacute combined degeneration and consist of pains in the back, tenderness of the dorsal and lumbar spines, increase in the knee jerks (75 per cent.), weakness and stiffness of the gait and, finally, paraplegia with signs of an upper motor neuron lesion. Later, vesical and rectal control are lost and flaccid paralysis may supervene. Sensory disturbances with paræsthesias, tremors involving the tongue, limbs and head and athetoid movements are not infrequent. Of the *mental* features depression, gloom, stupor, loss of memory, insomnia, restlessness and irritability are first observed, and, later, delusions and hallucinations. With repeated attacks over years, melancholia, mania and dementia result.

The growth of children is retarded, but neurological manifestations are not so common in them.

Diagnosis. Where the clinical picture is fully developed little trouble is encountered as the skin lesions are so characteristic. In their absence, however, tabes and subacute combined degeneration of the cord may need consideration in the differential diagnosis, and in those cases where alimentary symptoms are prominent the condition may be confused with sprue. Erythema multiforme and dermatitis venenata may need differentiation when the skin eruption alone is present.

Prognosis. The disease is characterised by remissions and a chronic afebrile course extending up to twenty years. Fever is of serious prognostic significance. About 40 per cent. develop serious mental trouble and many of these die in asylums in countries like Egypt where the disease is endemic.

Treatment. The disease is prevented by reinforcing deficient diets with foods rich in vitamin B_2. Once manifestations have developed the patient should be put to bed on a nutritious diet, low in carbohydrate, and consisting of milk, lean scraped red meat (½ lb.), tomato juice, brewer's yeast (1 oz. daily), or Marmite and fruit and vegetables. Acid hydrochlor. dil. after meals, ½–1 drachm in 4–6 oz. water, is useful. Under this *régime* recovery may ensue in from six to twelve weeks, but if relapse is to be avoided the protein and vitamin B_2 requirements of the diet must be permanently adequate.

SCURVY

(*Scorbutus*)

Scurvy is characterised by a profound change in the blood, resulting in hæmorrhages under the skin and in other parts of the body, a spongy condition of the gums, anæmia, and prostration. It is due to the absence of vitamin C—ascorbic acid—from the diet.

Ætiology. It may occur in either sex and at any age; it has arisen over and over again in circumstances entailing a restriction of the dietary in respect of vegetables and fresh meat. Thus it has been in past times the scourge of sailors on long voyages, so that it is frequently spoken of as sea scurvy, though such a term does not now distinguish it from any other form; and it has severely affected armies and other large collections of individuals, such as those in prisons, and sometimes even in hospitals. Cases occasionally happen amongst those who could get vegetables, if for any reason, such as poverty, dyspeptic troubles, or mistaken views, they have habitually abstained from eating them.

Morbid Anatomy. In fatal cases of scurvy the lesions are found which have been mostly manifest during life—*e.g.* the hæmorrhages in the skin and the effusions of blood in the aponeurotic sheaths and under the periosteum, and in infants separation of the epiphyses. Occasionally hæmorrhage has occurred on the surface or in the substance of the brain. Frequently the pleural cavities and pericardium contain blood-stained serum. There may be engorgement of the lung with serum or blood, and sometimes it is even gangrenous. Hæmorrhages may also take place into the cardiac muscle, into the pericardium, or into the mucous membrane of the stomach and intestine; these latter may cause abrasion or ulceration. The liver and spleen are often large, much congested, soft, and friable; and an acute nephritis is described as occurring in severe cases.

Symptoms. The disease generally comes on insidiously, taking from four to eight months to develop. The patient loses colour, becomes weak, languid, drowsy, or apathetic, and complains of flying pains in the loins or limbs. After a time—it may be a week or more—petechiæ appear upon the skin of the lower extremities and other parts of the body, and as a rule each hæmorrhage is situated around the base of a hair. The spots are small, red or reddish-brown, and not raised above the surface. Some others appear which more or less resemble bruises produced by violence, and large wheals or *vibices* may also be present. These various hæmorrhages occur all over the body; and there may be large extravasations of blood in the eyelids, or subconjunctival ecchymoses, though very often the face is spared. Associated with this purpuric condition must be mentioned the occurrence of tense, brawny, indurated swellings in different parts of the body, especially in the popliteal space, the bend of the elbow, under the angle of the jaw, and in front of the tibia; these are due to effusions of blood, or blood-stained fibrin, or simply pale yellow fibrinous material, under the fascia, or between the muscular bundles, or between the periosteum and the bone.

Another feature which is commonly regarded as constant is the condition of the gums. These become swollen, fleshy, or spongy, detached from the teeth, and projecting beyond them in loose, bluish-red masses, which are painful, and bleed on the slightest touch. The teeth become loosened, the patient is unable to chew, and the breath is fœtid. The swelling of the gums may be so great that they project from the lips, and ulceration often results. The rest of the mouth is not affected in the same way. The tongue is large and indented. Sometimes the gums are not spongy, but only pale; and in all cases the change seems to be determined by the presence of teeth, so that it is absent where there is a gap in the series, and in toothless infants and old people.

When all these changes have developed, the patient has a sallow, bloated look, is markedly breathless on exertion, though no physical signs may be detected in the lungs, is subject to fits of syncope, and is totally unfit for bodily or mental exertion. The temperature, however, is generally not raised; the pulse is variable; and the urine is usually free from albumin. Hæmorrhage from the mucous surfaces, especially epistaxis, is not uncommon; and the feet are often œdematous. The blood has the characters of a secondary anæmia, with slight poikilocytosis, polychromasia, and punctate basophilia, and there may be a slight leucocytosis. The red corpuscles fall to 4,000,000 or 3,000,000,

or lower when hæmorrhages are abundant, and there is a low colour index. The coagulation time differs little from the normal.

In more serious cases there is hæmorrhage from the stomach and intestines, or from the lungs; pneumonia, gangrene of the lung, pericarditis, or pleurisy. which may be hæmorrhagic; or enlargement of the spleen and albuminuria, The skin over blood extravasations may slough from pressure or irritation, and leave fungoid and very offensive ulcers. Dysentery sometimes complicates scurvy, but is generally regarded as having an independent origin. The impairment of vision known as *hemeralopia*, or night blindness, frequently occurs; the patient can see clearly and well in the day-time, but in the dusk, or the darkness of night, becomes quite blind, and cannot see his way about. It originates in a disturbance of nutrition of the retina; the ophthalmoscope shows no change in the eye, and normal sight is restored as the scurvy is cured.

Death takes place from increasing exhaustion, with anæmia and emaciation, generally after many weeks. But it may occur more quickly from sudden syncope, from pneumonia or gangrene of the lung, from hæmorrhagic inflammation of the serous membranes, or from cerebral hæmorrhage. In cases which recover the improvement under suitable treatment is at once manifest, and often very rapid; but it is stated that the deeper effusions may leave thickening and fibrous bands, as a result of which the limbs are partly contracted and the corresponding muscles are atrophied. Sometimes the joints are ankylosed.

Infantile Scurvy. This form of scurvy, known abroad as *Barlow's disease*, is seen in children under two years old, and is frequently associated with rickets, another dietetic disease. Scurvy is liable to occur in infants who are fed on sterilised milk, or on malted and other patent foods, and who do not have enough of, or any, fresh milk. Such children do not lose flesh, but become pallid; and then the limbs, especially the lower limbs, are affected, so that they do not voluntarily move them, and cry whenever they are touched or moved, or even when the hand is brought near them. The child lies often with the thighs abducted and the knees flexed, and so may be thought to be paralysed.

The bones are tender, there may be some œdema of the feet, and there may be swellings as a result of sub-periosteal hæmorrhages; and the crepitus of a separation of the bones at the epiphyseal lines may be felt. If any teeth are through, there may be sponginess of the gums with hæmorrhages, as in adults, and sometimes a fungating mass is seen; other hæmorrhages, such as epistaxis or hæmaturia, may occur. The anæmia is of the chlorotic type, and the blood presents an increased number of the mononuclears, some myelocytes, and nucleated red corpuscles.

Diagnosis. There can be little difficulty in recognising this disease when the circumstances are such as have been known to lead to it, but the diagnosis requires care in isolated cases. It is distinguished from *purpura* by the general illness accompanying it, by the spongy gums, and by the deep-seated effusions in the limbs and elsewhere. On the other hand, amongst the poorer classes of the population one may overlook mild cases, where the symptoms mainly consist of vague pains, with anæmia and ill-health, and the patients are likely to disregard a slight change in the gums or a few spots on the skin. An inquiry into the diet will soon determine the nature of the illness. In infants it may be confounded with infantile paralysis, syphilitic epiphysitis, or periostitis.

Prevention and Treatment. It is essential to give food containing the antiscorbutic vitamin. Fresh lemon juice has long been known as a very efficacious preventive and remedy, and it retains its properties to a considerable degree when it is preserved and even when dried (Bassett-Smith). Fresh lime juice is not so efficacious, and preserved lime juice is quite useless. Lime juice obtained its popular reputation because originally the term was used to describe the juice of lemons from the Mediterranean. In the middle of the last century West Indian lime juice was substituted in the Navy under the same

name, but experience showed its uselessness. For soldiers in the field it is probable that dried pulses allowed to germinate just before being used may be the best means of supply of the vitamin; they are convenient owing to their portability. Cabbage is the best vegetable to use, but it must be cooked for as short a time as possible in water without soda. Scurvy has broken out in a camp where the cabbages were cooked with the meat for some hours in a stew. Fresh meat is also of some value. As regards the diet of infants, it is to be noted that cows' milk is one of the less valuable antiscorbutic foods, and such vitamin as is present is diminished by sterilising or pasteurising the milk. It is probable that the vitamin is completely absent in dried milks. In any case, when sterilised or dried milk is used some of the vitamin should be added to the food. The simplest plan is to give the infant a teaspoonful of orange juice; but swedes, which are plentiful and cheap, may also be employed, or tomato juice, a tablespoonful a day at three months, or potato scraped from just beneath the skin after baking. Raw swede juice is obtained by grating the cut vegetable and squeezing the pulp in muslin. For curative purposes large amounts of lemon juice can be taken without causing digestive disturbance if the free citric acid is removed by treatment with calcium carbonate. The pure vitamin, ascorbic acid, which is soluble in water, may be injected intravenously in doses of 100 to 200 milligrammes; it has been used for other hæmorrhagic states such as purpura and hæmorrhagic nephritis. It must be neutralised before being injected intra-muscularly or subcutaneously by dissolving 100 milligrammes in 1 c.c. of a sterile 2 per cent. solution of NaOH.

RICKETS

(*Rachitis*)

Rickets is a disease involving the nutrition and general health of infants and young children, and showing itself (1) in a perversion of the process of ossification, so that the bones are softer than normal, and become bent and deformed by the pressure which they must undergo in everyday use, and (2) in a liability to respiratory and gastro-intestinal infections and to functional nervous disorders.

Ætiology. It is essentially a disease of children, and affects the sexes about equally. The earliest bony changes are noticeable between the of ages six and twelve months. By eighteen months the clinical features are well marked. The children of the poor are much more severely affected with rickets than those of the richer classes, though the latter not uncommonly have it to a slight degree. Its maximum incidence is in winter and spring; it tends to become cured by the summer sunlight, since this increases the amount of vitamin D in the body as already explained; two factors that have been frequently cited as predisposing to rickets—overcrowding in cities and lack of fresh air—are really of importance only in so far as they entail lack of sunlight. *Late* or *adolescent* rickets, which is uncommon, may begin at any time between six and eighteen years.

Pathology. While the absence of vitamin D is the main cause of clinical rickets, there are several other factors which have been shown experimentally to play a part. In the first place, active growth is necessary. In the absence of this lack of calcium or phosphorus by itself does not produce typical rickets, although there soon develops a deficiency of calcium in the bones, which show *osteoporosis* with layers of *osteoid* tissue; but there is little change in the zone of proliferating cartilage. However, rickets may be produced experimentally in an animal by giving a diet sufficient in calorie value but which is either deficient in calcium (calcium rickets), or deficient in phosphorus (phosphorus rickets). Calcification in bone depends on there being present in the plasma a sufficient quantity of calcium (Ca) and phosphoric (PO_4) ions, which unite to form the sparingly soluble salt $Ca_3(PO_4)_2$, which is deposited to form bone. In clinical

rickets the serum calcium may be normal, and the serum phosphorus low (phosphorus rickets) (6). In other cases the calcium and phosphorus are both low (10). In any case the condition of the serum is the direct cause of the rickets; the fault does not lie in the bone, since rachitic bone, when incubated in blood serum from a normal child or in solutions containing calcium and phosphate, shows calcification; but this is not the case when blood serum from a rachitic child is used. Vitamin D probably acts by making the intestinal contents acid, which is their normal state, so that the easily-soluble salt $CaHPO_4$ is formed and readily absorbed. Too much vitamin D produces calcification, especially of the arteries and renal calculi. Without vitamin D the contents become alkaline (11) and the sparingly soluble alkaline salt $Ca_3(PO_4)_2$ is absorbed with difficulty (10). Lack of exercise also predisposes to rickets; if the animal is allowed plenty of exercise, much less vitamin D is required to prevent the onset of rickets. In acute rickets there is a lowering of the plasma bicarbonate, which is not due to ketosis (3). Rickets indistinguishable from the rickets of vitamin D deficiency may also supervene in cœliac disease (cœliac rickets). Owing to the large undigested fatty stools there is lack of growth and at the same time too little vitamin D is absorbed so that there is also a deficient absorption of calcium and phosphorus and the bones are osteoporotic. Both the serum phosphorus and calcium are low. On a low fat dietary the clinical condition improves, growth begins, and rickets results, which may be cured in the same way as ordinary rickets. Diarrhœa is another cause of defective fat absorption; but this does not cause rickets, because growth is stopped.

Morbid Anatomy. A longitudinal section of a long bone of a normal infant shows a clean cut end (epiphyseal line) to the shaft (diaphysis), and a disc of whitish cartilage (epiphyseal cartilage) between this and the bony epiphysis in those instances in which ossification of the epiphysis has occurred. In a rachitic bone quite a different picture is obtained. The width of the epiphyseal disc of cartilage is considerably increased. There is no epiphyseal line, but its place is taken by an irregular frayed end to the diaphysis. This frayed end, which is more vascular than normal, is usually scooped out and expanded laterally, the result of pressure, thus producing the clinical sign of enlargement of the epiphysis. To this altered extremity of the diaphysis the term metaphysis is applied.

Normally, between the hyaline cartilage and the bone already developed several layers can be seen microscopically: (*a*) proliferating cartilage cells without orderly arrangement; (*b*) proliferating cartilage cells arranged in columns between columns of hyaline matrix; (*c*) zone of provisional calcification, which makes the columns rigid and so directs the budding capillaries from the marrow against the cartilage cells, which are either destroyed by erosion or become lost in the medullary spaces; the columns are then partly destroyed and partly act as centres round which osteoblasts arrange themselves to form (*d*) a narrow layer of *osteoid*, *i.e.* bone which contains no calcium; (*e*) ossification, produced by deposit of calcium salts in the osteoid.

In rickets this orderly arrangement is completely lost. The zone of cartilage proliferation is increased vertically and laterally, the columnar arrangement being at first manifest, but the cells in the column are more numerous, and soon this design is lost and the cells appear as masses in a hyaline matrix. The zone of provisional calcification is absent, with the result that the marrow vessels grow in all directions. The osteoid layer is greatly thickened and forms the rachitic metaphysis; in it are islands of cartilage cells, wide spaces containing marrow, and in its deeper parts irregular depositions of calcium forming true bone and producing the characteristic dentate frayed appearance of the end of the metaphysis. Osteoid tissue is also present under the periosteum in larger amounts than normally, producing irregular masses or buttresses and eliminating the sharp angles, borders and prominences of the long bones, and giving rise in the membrane bones of the skull to bossing.

When healing takes place, the first thing to occur is the deposit of calcium in the cartilage where the zone of provisional calcification should have been. This at first is a thin irregular line, but as healing advances it thickens, depositions of calcium occur in the osteoid tissue, and the cartilage in the metaphysis gradually disappears.

The typical microscopical findings in rickets are: (1) the presence of large amounts of osteoid tissue; and (2) the substitution of disorder for order.

The muscles are flabby and wasted. The blood may show a secondary anæmia.

Symptoms. Early in the complaint two symptoms occur which are very constant. One is that the child is restless at night, kicks off its clothes, and lies with its legs and arms exposed; the other is that when it goes to sleep it perspires profusely about the head and neck, so that the pillow is saturated. But the rest of the body is often dry, and the temperature is normal. The first evidence of osseous changes is the *enlargement* of the ends of the long bones. This is well marked at the wrists, where the ends of the radius and ulna are thickened, and at the ankles and at the knees. If the disease comes on after the child has begun to stand or walk, these accomplishments are given up, and the child "is taken off its feet," as the mothers are apt to explain. If the disease begins earlier, then the art of walking may not be attained until the eighteenth or twenty-fourth month. In either case the child tries to walk before the bones are completely consolidated, and the weight of the body causes the tibiæ and femora to be bent or "bowed," generally with a convexity outwards and forwards. Sometimes there is a convexity inwards at the lower part of the tibiæ, the feet being thus widely separated, and this is to be attributed to the child getting about the floor in a sprawling position, using the feet like the hind fins of the sea lion. If, while still unable to stand, the child crawls much about the floor, the weight of the body falls upon the arms, and the radius, ulna, and humerus get correspondingly bent.

In the chest, enlargement takes place at the junctions of the ribs with the costal cartilages, where a series of nodules are formed, reaching on either side from the first rib near the sternum downwards and then outwards to the twelfth rib in the flank. This has been called *beading* of the ribs, or the *rickety rosary*. Deformity is produced by the action of the diaphragm, which sucks in the ribs at their diaphyses and produces a wide groove on either side of the sternum which is unduly prominent. The patient may also become pigeon-breasted. The lower ribs, however, are often expanded over the abdominal viscera, forming the upper arch of a protuberant abdomen, which contrasts strikingly with the narrow chest above, and is separated from it by a transverse depression (Harrison's sulcus). The latter is roughly at the level of the dome of the diaphragm, where the chest tends to fall in. These various deformities are accentuated by the commonly associated bronchitis or broncho-pneumonia, which hinders the entry of air into the chest. These complications are particularly dangerous, because owing to the soft state of the ribs the act of coughing especially is rendered imperfect, and the secretions accumulate in the lungs. The pelvis does not usually show any deformity in infancy, but in extreme cases of rickets the pelvic aperture is considerably misshapen, being mostly of an hour-glass type, and it may afterwards in females offer very serious obstruction to parturition.

The head, besides presenting large fontanelles and often lines of depression corresponding to the coronal and sagittal sutures (*hot-cross bun* type of skull), acquires a somewhat square shape, the vertex being flattened, and the frontal and lateral regions being rather prominent. In pronounced cases the cranium looks very large in proportion to the face, and the circumference of the skull is often increased. *Craniotabes* is the name given to soft areas on the skull due to deficient ossification, which occur chiefly along the margins of the sutures. Another symptom is the *delay in the eruption of the teeth*, the first of which may not appear until the elventh or twelfth month instead of the sixth or seventh; and the order

of their appearance may present many irregularities. The permanent teeth also suffer; the enamel is defective and soft, and the calcium content is lowered. It has been suggested that dental caries in young children is due to lack of vitamin D in the diet of the child or of the mother during pregnancy (**9**).

In extreme cases there is a considerable stunting of all the bones, as well as the shortening by curvature; and children of eight or ten may be no taller than those of three years old. The bones are also more fragile than normal, and *green-stick fractures* are apt to occur. There is decided laxity of the ligaments and hypotonicity of the muscles, so that there is extra mobility of the joints (*acrobatic rickets*). The liver and spleen are easily felt because they are pushed down by the contracted chest, and are ill supported by the abdominal muscles, and there is abnormal prominence of the abdomen (*pot-belly*). The appetite may be very good, and many rickety children show a perfect or even excessive development of fat (*fat rickets*), but in severe cases there is anæmia. The nervous system may also be seriously involved; rachitic children are very liable to infantile convulsions, including the special forms known as *laryngismus stridulus* and *tetany*. Associated with laryngismus is often *facial irritability*, or Chvostek's sign, in which a gentle tapping over the superficial branches of the motor nerves of the face causes contraction of the corresponding muscles. In rickety children also, rather more frequently than in others, occurs the disorder known as *head-nodding* or *head-shaking* (*spasmus nutans*), which is often associated with *nystagmus* These occur in babies of from four months to one year, and may be due to imperfectly lighted rooms in the winter-time, thus being comparable to *miners' nystagmus*.

Rickety children may also suffer from symptoms suggestive of scurvy, such as tenderness of the bones. This is not to be wondered at, since the diet may be deficient in vitamins generally.

Diagnosis. This rarely presents difficulties. Sometimes the inability to walk may lead to a suspicion of infantile paralysis (anterior poliomyelitis), but the limbs can at least be moved, and the deformities of the bones should give the right clue. Syphilitic epiphysitis and scurvy cause great pain and tenderness in the bones affected. A very early indication of rickets is given by the plasma phosphatase, which is raised.

X-rays provide a valuable means of diagnosing the extent of the disease and the progress of cure (**2**). In severe rickets (Plate 46) decalcification of the finer trabeculæ produces a coarsening of the structure of the cancellous bone, and later as the process becomes further advanced the bones can hardly be differentiated from the soft tissues. The appearances vary (1) with the bone examined; thus the end of the humerus in Plate 46 does not show the frayed-out appearance present at the lower end of the radius and ulna; (2) according as the child can still remain fairly active in spite of the disease. In this case, if the lower end of the radius is examined, it is seen that the sharp epiphyseal line becomes lost; the lower end of the diaphysis is expanded laterally; decalcification occurs more rapidly at the centre, so that the end of the shaft becomes cup-shaped. When the child is inactive, the frayed-out appearance is less; there is no scooping out or lateral expansion; but the distance between diaphysis and epiphysis is greater. At the beginning of healing (Plate 47) a new line of calcification appears at the zone of provisional calcification, representing the epiphyseal line of normal bone. Its distance from the diaphysis depends on the width of osteoid tissue and varies directly with the duration of the disease. Gradually the intervening space gets filled up by bone in the form of striæ, and for a long time after healing has occurred a marked contrast may be seen between the dense over-calcified metaphysis and the rarefied cancellous tissue of the shaft in its neighbourhood (Plate 48, *cf.* Plate 49, normal).

Prognosis. Recovery is the rule, the bones ultimately becoming quite firm and solid; but the deformities, if considerable, will be perpetuated. The

risk to life is from the complications, especially bronchitis, with collapse of lung, convulsions, and laryngismus stridulus.

Prevention. Proper infant-feeding is the all-important point. Breast-feeding is the natural method, and provided there is an adequate supply of milk, and the mother takes a varied diet containing all the accessory food factors, there is no fear that the child will develop rickets or other deficiency diseases. If cows' milk is used cod-liver oil should be given as well to supply the vitamin D. In such a diet the supply of calcium and phosphorus will be adequate. A child properly fed will spontaneously take enough exercise by movements of its limbs and body. It should live in well-ventilated rooms, and should be taken out in the fresh air regularly and get all the sunlight possible.

Treatment. Irradiated ergosterol may be given in the form of "radiostol," 15 minims a day; this is also useful for treating dental caries. Deficiency of vitamin D is usually associated with deficiency of vitamin A; the preparations "radiostoleum" and "radiomalt" contain both vitamins A and D. Cod-liver oil, plain or emulsified, is another valuable drug. It may be given three times a day after meals. The dose of the plain oil is 15 drops for an infant six months old, 20 drops up to twelve months, ½ drachm up to eighteen months or two years, and 1 drachm for older children. Exposure to sunlight is another method of treatment obviously less satisfactory (except in refractory cases) because the dosage is less certain. If there is no sunlight, exposure to an artificial source of ultra-violet light, such as the mercury vapour quartz lamp, the tungsten arc lamp, etc., should be carried out. Plenty of fresh air should be allowed. The deformities of the limbs which remain after rickets is cured may, if extreme, be treated surgically.

Renal Rickets (*Renal Dwarfism*).—Associated with severe impairment of renal function in young people, there is a high phosphorus content in the blood. The figure for the calcium varies, but is always low relative to the phosphate. Calcium is mobilised from the bones, which tends to make good this deficiency in the blood. During periods of growth the epiphyseal ends of the bones suffer most.

There are three types according to radiological appearances (**6**): (1) *Atrophic*, in which the whole bone, including the cortex, shows deficient calcification: fractures may be present; (2) *florid* with a characteristic rachitic epiphysis; (3) *woolly*, *stippled*, or *honeycomb*, in which the metaphysis is deeper than in ordinary rickets and the proliferating cartilage is more irregular and broken up: the appearance of the skull is often suggestive of Paget's disease.

There is stunted growth; secondary sex characters are late in development; thirst and polyuria are prominent symptoms; the complexion is sallow and the wrinkled face makes the child look older than its years. The urine is pale, of a low specific gravity and usually contains a trace of albumin. The changes in the bones may show themselves in the form of severe rickets or bowing of the legs, but more commonly as genu valgum. The usual age of onset is from five to seven, but cases have been described as occurring at birth or as late as seventeen years. Healing may occur in the bones but the disease is always fatal from uræmia or intercurrent disease. It has been suggested that the disease of the kidneys is secondary to urinary retention associated with dilatation of the urinary tract, but cases are on record associated with congenital cystic kidneys and bilateral renal calculi, and the dilated urinary tract may well be secondary to the increased flow of urine, as in diabetes insipidus.

Ordinary antirachitic treatment tends to make the condition worse by increasing absorption of phosphates and is contra-indicated.

OSTEOMALACIA
(*Mollities Ossium*)

This is a disease of adults, almost exclusively women, and is due to lack of vitamin D; it is thus closely allied to rickets.

Ætiology. Among the girls and women of India, who, after running freely about the villages, are shut up in purdah after marriage, a series of cases has been described which illustrates the transition between late rickets, occurring usually between twelve and seventeen, and osteomalacia, which occasionally begins as early as sixteen but may develop after the menopause. Tetany occurs in both, and late rickets and osteomalacia may be present in the same patient simultaneously (7). Osteomalacia was also observed in Vienna in 1918 (8). The patients had subsisted on a diet of bread and vegetables with small amounts of flour and sugar, and a little lard occasionally, and it is noteworthy that rickets and late rickets among young adults were also unusually common in Vienna at this time. Osteomalacia commonly occurs in pregnancy, when any deficiency of vitamin D would naturally produce its most marked effect, and this in time past has led to removal of the ovaries being advocated as treatment.

Morbid Anatomy. The bones may be so soft that they can be cut with a knife or indented with the finger. Nearly the whole of the bone is converted into a soft greasy mass or pulpy material, except perhaps a thin shell of compact tissue just under the periosteum ; or even there may be nothing left but the thickened periosteum itself. Microscopically the change seems to be, first, a confusion of the natural minute structure of the bone ; the Haversian systems become fused together, and then absorption of the salts takes place from the innermost rings round a canal, so that the substance is gelatinous and transparent. As the same change proceeds in the rings placed farther out, the innermost rings are entirely absorbed, the lacunæ also alter their shape and size, and finally the Haversian systems are destroyed. The bone becomes spongy and porous (*osteoporosis*), and the enlarged medullary spaces are filled with a marrow which is fatty or lymphoid, with giant cells and osteoblasts. In this there are recent hæmorrhages and pigment resulting from former effusions of blood. In some places the medulla may be gelatinous or watery. Chemical analysis of the bones shows that the inorganic constituents are reduced from 68 to 30 per cent.

Symptoms. The first is pain, which is felt chiefly in the lumbo-sacral region and the hips and spreads down the legs, in the spine, and ribs, and not so often in the upper extremities. The bones are tender on pressure, and there is great pain on movement. Consequently there is a characteristic stiff and waddling gait, and the patient uses her arms as much as possible to help her with her movements. She is languid and is disinclined to do anything and there is great muscular weakness. Owing to difficulty in walking she may become bedridden. The joints are not painful. In course of time a change of figure may be noticed ; the patient loses height from rounding of the spine or bending of the limbs : then, some day or other, a bone breaks with very little apparent cause, or on slight exertion. As a rule, the fracture heals but imperfectly, and subsequently other bones break. Moreover, the long bones show a remarkable degree of flexibility, so that they can be bent into very strange positions, and the more superficial bones may be indented with the finger. The thorax becomes deformed from the softness of the ribs, and dyspnœa may occur in consequence. In rare cases the bones of the skull may be softened. Tetany may occur.

The disease runs a chronic course, and generally lasts from five to ten years. Death takes place often from exhaustion due to difficulty in breathing on account of the softness of the ribs, or from broncho-pneumonia favoured by the deformity, sometimes during parturition from the obstruction which the distorted (rostrate) pelvis offers to the passage of the fœtus.

The **Diagnosis** is not difficult when the changes in the bones have become manifest. Earlier symptoms may be mistaken for *rheumatism*. Spontaneous fracture also may take place in *sarcoma, carcinoma, fibrocystic disease,* and *multiple myeloma* of the bones.

Treatment. Vitamin D must be supplied as described under rickets.

REFERENCES

1	H. N. Green and E. Mellanby ..	1928	*Brit. Med. Journ.*, ii., p. 691
2	H. Chick, E. J. Dalyell, M. Hume, H. M. M. Mackay and H. Wimberger	1922	*Lancet*, i., p. 7.
3	N. Burgess and A. A. Osman ..	1924	*Lancet*, i., p. 281.
4	D. B. Blacklock	1924	*Brit. Med. Journ.*, i., p. 1046.
5	K. F. Wenckebach	1928	*Lancet*, ii., p. 265.
6	L. G. Parsons	1927	*Arch. Dis. Child.*, **2**, p. 5.
7	Grace Stapleton	1925	*Lancet*, i., p. 1119.
8	E. J. Dalyell and H. Chick ..	1921	*Lancet*, ii., p. 842.
9	E. Mellanby	1926	*Brit. Med. Journ.*, i., p. 515.
	M. Mellanby and C. L. Pattison	1928	*Brit. Med. Journ.*, ii., p. 1079.
10	A. Ellis and H. Evans	1933	*Quart. Journ. Med.*, **2**, p. 231.
11	T. Redman	1929	*Biochem. Journ.* 23, p. 256.
12	C. Funk	1912	*Journ. State Medicine*, **20**, p. 341.
13	W. H. Wilson	1921	*Journ. Hygiene*, **22**, p. 1.

SOME CHRONIC INTOXICATIONS

ALCOHOLISM

Acute Alcoholism. The symptoms of drunkenness or intoxication due to taking too much alcohol are familiar, and usually subside as the alcohol passes through the system. Occasionally, however, from the taking of large quantities of spirit in those unaccustomed to it, a fatal result may ensue. It is preceded by unconsciousness, with pupils sluggish or fixed, and generally dilated; small pulse, cold clammy skin, stertorous respiration; and sometimes delirium or convulsions. Very low internal temperatures have been recorded, as if the patient had been lying exposed out of doors.

Sometimes there are unusual reactions, such as wild excitement with violence (*mania a potu*) following the ingestion of comparatively small amounts of alcohol, in specially susceptible persons.

Dipsomania is a periodic over-indulgence in alcohol by persons who in the intervals are temperate or even completely abstinent. Sometimes the recurrent attacks of over-indulgence are the symptomatic expression of phases of a manic-depressive psychosis; at other times they are symptomatic of an epileptic episode; but much more frequently they represent the response of an unstable psychopathic patient who succumbs every now and then to difficulties at home or at business or in other aspects of his personal affairs. In the intervals the patient usually realises that he has drunk too heavily, but may refuse to admit it, or only does so in a modified way. Consequently treatment is difficult.

Chronic Alcoholism. The effects are described in the rest of this section.

Morbid Anatomy. In *chronic alcoholism* the membranes of the brain are commonly opaque and thickened, and the convolutions are shrunken and atrophied from loss of nerve cells and fibres. The changes found in peripheral neuritis, hepatic cirrhosis, etc., are described elsewhere. In death from *delirium tremens* and *acute alcoholism* there is cerebral congestion with small cortical hæmorrhages. Chronic alcoholism may produce changes in various organs, *i.e.* peripheral neuritis, Korsakow's syndrome (see p. 653), polioencephalitis, chronic gastritis, cirrhosis of the liver, myocardial disease, arteriosclerosis, and primary contracted kidney. These diseases are described elsewhere.

DELIRIUM TREMENS

This commonly occurs in those who habitually drink freely, especially after a severe bout. The symptoms may also be brought on in persons who from long-continued excess have acquired unusual tolerance, by sudden deprivation of alcohol, by an injury, such as the fracture of a bone, or by the onset of pneumonia, or other acute disease, or by some mental shock.

Symptoms. The first symptoms are disturbed sleep, restlessness, irritability, and loss of appetite; and with the disturbed sleep there are unpleasant dreams and some delirium. In the morning the patient may be clearly oriented, but the delirium returns at night; the next day the delirium continues, and shows its characteristic features. The patient is constantly talking, addressing either those about him or in response to hallucinations. He talks on his business ("occupation delirium"), frequently changes from one subject to another. His

attention may be secured for a moment, but soon relapses. He may try to get out of bed, or pull the bedclothes about. With this there is very marked tremor of the hands, especially on movement, and the lips and tongue tremble when he speaks. As the condition gets worse he has very definite hallucinations and illusions. Objects in the room or figures on the wall-paper are conceived to be animals or insects; he is constantly seeing cats, dogs, rats, mice, or black-beetles running after him or crawling about the bed; he looks under the bed, or behind the curtains, or peers behind any bystander, and is suspicious of injury from those about him. He may, under some such false impression, strike those who are near; but, as a rule, there is no attempt at violence.

Other symptoms accompany the mental and muscular disturbance. The face is flushed, the conjunctivæ are suffused, the tongue is thickly furred and becomes dry, as the disease progresses. The pulse is quick, soft, at first full, afterwards small and feeble; the temperature rises to 102° or 103°, and there is occasional hyperpyrexia (106° or more). The skin is generally moist or even profusely perspiring; there is albuminuria, and there may be indications of early optic neuritis.

About the end of the third day, with considerable constancy in favourable cases, some improvement begins to show itself. Hitherto sleep has been entirely absent, but now the patient falls into a slumber which may last eight or ten hours, and he wakes much refreshed, the delirium and trembling are less, and gradually improvement takes place in all respects. In more serious cases the pulse is quick and feeble, the patient prostrate; he lies on his back muttering and semi-comatose. Death occurs from exhaustion; from cardiac failure, and this is sometimes sudden; or from pneumonia.

Diagnosis. Delirium tremens may be simulated by *general paralysis of the insane.* Certain physical signs of the latter disease, *e.g.* Argyll-Robertson pupils, may sometimes occur in chronic alcoholism (*see* Polioencephalitis); but the complete syndrome of G.P.I. must be very rare, and in any case examination of the cerebro-spinal fluid should decide the diagnosis.

Treatment. The patient should be kept as quiet as possible in a darkened room undisturbed by visitors. If alcohol has been recently taken in quantity it should be removed by stomach tube. Since the action of alcohol is to prevent the oxygen from the blood stream diffusing into the tissues so that the oxygen pressure in the tissues is lowered, oxygen inhalation, whether by mask or tent, is indicated, and the delirium can be stopped by this means. It is important to ensure sleep, as already described (*see* p. 23). Sometimes the allowance of a small amount of alcohol will procure sleep when hypnotics alone are useless; there should be efficient action of the bowels.

Alcoholic hallucinosis is either a sequel to delirium tremens, or appears independently in a chronic alcoholic. The patient remains completely oriented and the intellectual and sensorial functions are for all practical purposes intact; but there is a mainly auditory hallucinosis, usually of a persecutory kind, and often with a homosexual colouring. Hallucinations of the other senses also occur, especially odours and tactile paræsthesiæ, which are interpreted in harmony with the content of the auditory hallucinosis. Often the auditory hallucinations have the rhythm of some real sound in the environment, and often also they are of persons speaking about the patient, instead of directly to him. There is a certain amount of apprehension, in relation to the persecutory nature of the hallucinatory ideas, and suicide is sometimes attempted as a means of escape.

The onset of the condition is acute as a rule, and after weeks or months, complete recovery usually occurs. How far the condition is actually the result of alcoholism is doubtful; in many cases, the patient's personality has much to answer for; probably the alcoholism and hallucinosis are like the symptomatic outcome of the latter.

On account of the antisocial nature of the hallucinatory content and its effect

on the patient's behaviour, and of the possible suicidal attempts in the earlier stages, as well as of the necessity for avoiding the provocative alcohol, close nursing supervision is imperative, usually in a mental hospital.

CHRONIC ALCOHOLISM

Symptoms. Muscular tremor is one of the first indications of the effects of the poison upon the nervous system. The hands are unsteady, and the tongue trembles when it is protruded. The patient is restless and irritable, he sleeps badly, and wakes unrefreshed, with a feeling of prostration that tempts him to take stimulants at once. Sinking feelings are frequently complained of, which require, according to the patient, to be met by fresh doses of the favourite drink. As things get worse the patient is unequal to any sustained mental effort; even the simplest business transaction must be preceded by a glass. Sensory disturbances may be also present, such as buzzing or rushing in the head, vertigo, muscæ volitantes, flashes of light, or diffused headache. There may be severe neuralgic pains in the legs, possibly the early signs of neuritis. In later stages the mind is seriously involved. Judgment, intellectual capacity, volition, and the moral sense are all weakened. Lack of consideration for his family, actual cruelty, sexual misdemeanour, irritability leading to violent outbursts, inefficiency and lack of interest in business affairs, and failure or refusal to recognise his condition, are characteristic of the chronic alcoholic. Ideas of jealousy and actual delusions of unfaithfulness are not uncommon.

With the occurrence of the first symptoms the functions of the stomach are often disturbed. The patient vomits in the morning directly he rises from bed, he is quite unable to eat any breakfast, and his appetite generally is deficient. The tongue is furred and the breath fœtid. The eyes are suffused, and the face may be tinged with yellow. In course of time the minute venules of the cheeks become dilated, the nose is red and thickened, and sometimes rosacea develops. The face becomes more and more bloated, and the blotching with dilated venules is more marked.

In addition to diseases directly resulting from alcohol detailed above, these patients are liable to succumb with great rapidity to any acute illness such as pneumonia or erysipelas.

Treatment. Usually the patient wants temperance, not complete abstinence, to be recommended; yet the latter is the only rule which will give him a chance of keeping free of his alcoholism. Residence in a hospital or nursing-home over many months, where the doctor can be certain that no alcohol is obtained, enables a habit of abstinence to be begun. At the same time the physician should approach the problem psychotherapeutically; in this way the patient can sometimes be taught to face his difficulties without resort to alcohol. Short of this, the limitation of opportunity, social or otherwise, for drinking is important, *e.g.* patients of this type have been known to remain abstinent after a course of psychotherapeutic treatment in a special hospital, together with a change of occupation on their return to work. The treatment of alcoholism is impossible when the patient refuses all co-operation, because, except in the very advanced stages, he is capable of assuming a normal demeanour at an interview, so that certification as insane is impossible.

Alcoholic pseudoparanoia is commonly a schizophrenic psychosis, with a history of alcoholism. Korsakow's syndrone is described elsewhere.

CARBON MONOXIDE POISONING

Coal gas is nowadays the favourite means of suicide. The immediate effects of the inhalation of coal gas are headaches, nausea and vomiting, followed by increasing dimness of vision, and then by an acute organic mental reaction—

delirium or coma; there may be widespread painful erythematous patches. If death does not occur, recovery is commonly complete, but in a few cases a chronic organic reaction—considerable memory-loss, defect of attention, lack of insight and deterioration in behaviour—follows, commonly after a period of some days or weeks of apparent recovery. Focal neurological signs and peripheral neuritis may also follow. In chronic poisoning, as may occur in men who are exposed for long periods to low concentrations of the gas, *e.g.* workers in garages, there is compensatory increase in the hæmoglobin and red cells of the blood.

Pathology. In the acute stages CO-hæmoglobin is produced with its characteristic spectrum. There are hæmorrhages in the brain; there is congestion, with or without hæmorrhage, in the heart, muscle, liver and other organs, and degeneration and atrophy of the cells—changes produced by the oxygen want.

The **Treatment** in the acute stage consists in administering oxygen containing a mixture of 5 per cent. CO_2 or oxygen alone; there is no doubt that addition of carbon dioxide is really important. When available an oxygen tent should be used. Artificial respiration must be used if necessary; if possible, with the apparatus described elsewhere (*see* p. 44).

LEAD POISONING

(*Plumbism*)

This occurs among those who have to do with lead or salts of lead, either in the preparation of those substances or in industries in which they have to be used. The latter are specially printing, plumbing, type-founding, type-setting, glazing of china and pottery, house-painting, and manufacture of electric accumulators. It also arises accidentally as the result of impregnation of drinking water with lead from service pipes or cisterns. This occurs when the water is soft, but not when it is hard. Lead may cause poisoning when taken as an abortifacient. It enters the system by the respiratory mucous membranes, by the alimentary canal, or very uncommonly through the skin. Legge and Goadby showed that the first is by far the most common way, lead salts being inhaled as a fine dust, *e.g.* by painters, while they are undertaking the preliminary process of rubbing off the old white lead paint. Susceptibility to lead-poisoning varies greatly. Women are more susceptible than men. The tendency to be attacked is increased by starvation, ill-health, exposure to cold, and indulgence in alcohol, and by the pre-existence of gout, syphilis, or disease of the kidney.

Pathology. After absorption of lead through the lungs, it circulates in the blood in the form of colloidal lead phosphate; it then becomes stored as phosphate in the bones and to a much smaller extent in other tissues; if it is absorbed through the alimentary tract a rather large proportion is found in the liver, as the lead is transported there through the portal circulation. Lead is chiefly excreted through the alimentary tract, and the bile is an important vehicle, since the liver secretes lead into the bile; lead is also excreted by the kidneys into the urine.

Symptoms. *Acute poisoning* may follow the sudden ingestion of a large dose of lead. The symptoms are abdominal pain, vomiting, diarrhœa, weakness and collapse, and there may be acute anæmia from blood destruction. In *chronic poisoning* there are four early symptoms—pallor of skin, lead line, punctate basophilia and secondary anæmia.

The *blue line* on the gums, or *lead line*, has mainly a diagnostic importance, showing that lead has been taken into the system. It is a dark slate-coloured or black finely dotted line, which forms close to the teeth either actually at the edge of the gum or just inside the free margin; but it may occur in that part of the cheek opposed to the teeth. It consists of a deposit of sulphide of lead in the tissues around the vessels; this results from the union of lead with sulphur pro-

vided by albuminous substance (partly contained in " tartar ") at the edge of the gum. Where teeth are absent there is no blue line, and also if the teeth are kept exceptionally clean ; or it may be seen only in portions of gum rising between the teeth. The blue line may exist without any other symptoms of plumbism ; it persists for from eight days to three months, or even much longer, after all entry of lead into the system has ceased. The lead line must be distinguished from a blue discoloration which accompanies a marked degree of pyorrhœa alveolaris.

Punctate basophilia is one of the earliest signs of lead poisoning ; the granules are formed from the basophilic substance of the younger corpuscles by the action of lead. Lead phosphate is also deposited in the covering membrane of all the red cells, making them shrink and diminishing their permeability, and so also their fragility to hypotonic salt solutions. In spite of this the membrane is so brittle that the cells break down more readily from slight trauma in the circulation producing a secondary anæmia, and in severe anæmia there is anisocytosis, poikilocytosis and polychromasia. There may be a moderate leucocytosis, in which the lymphocytes, large mononuclears and eosinophils are increased in numbers.

At any stage in the disease acute developments or " toxic episodes " may occur, such as colic, paralysis, encephalopathy, and optic lesions, while other changes associated with chronic lead poisoning become gradually established and these are also described below.

Lead Colic. This is a form of intestinal colic. After a period of impaired health, often associated with nausea and vomiting and always with obstinate constipation, the patient is seized with severe spasmodic pain in the lower part of the abdomen or at the umbilicus ; he is cold, pale and often drenched with sweat ; during the attack the abdominal muscles are contracted, and the pain is rather relieved by firm pressure in many cases, but often the abdomen is tender, and it is generally retracted. On examination the intestines may be felt to be contracted, forming irregular masses in different parts of the abdomen. Sometimes there is vomiting, and the bowels are nearly always confined. The pain diminishes for a time and then recurs, and it is generally relieved in the course of one to three or four days. It is due to spasmodic contraction of the intestine from the direct action of the lead on the muscle fibres.

Lead Paralysis. This is often described under the head of multiple neuritis, but it has also been thought to be due to a selective incidence of the poison upon the motor cells of the spinal cord.

However, lead probably acts primarily on the muscles, and the nervous lesions may be secondary. It picks out especially those muscles which are liable to fatigue ; the lactic acid produced in these circumstances dissolves the circulating lead phosphate which becomes deposited in the muscle cell.

The characteristic feature is the distribution of the paralysis, which is in most cases confined to the upper extremities, and though it may affect one arm before the other, is usually symmetrical. The first muscles to suffer are the long extensors of wrists and fingers, so that when the arms are held out with forearms pronated, the hands and fingers hang down. Hence the affection is sometimes known among workmen as " the dangles." The index and little fingers, possessing additional extensors of their own, suffer less than the ring and middle fingers, which may be affected alone. If the hand and the first phalanges are supported in the horizontal position, the remaining phalanges can be extended, showing that the lumbricales and interossei are still active. The supinator longus as a rule escapes. As the result of long-continued weakness backward displacement of the carpus sometimes occurs, and a prominence forms on the back of the wrist.

While this is the most characteristic form of lead palsy other groups of muscles are sometimes affected. Of these the commonest are—(1) the intrinsic muscles of the hands ; (2) the muscles of the shoulder girdles, especially biceps, brachialis anticus, deltoid and spinati ; and (3) the anterior tibial group in the lower limbs.

Although there may be complaint of muscular pains at the onset, there is no peripheral sense of numbness or tingling, nor any cutaneous anæsthesia. The affected muscles waste, and on electrical examination show the reaction of degeneration.

Encephalopathy. This may be in the form of hemiplegia, or of hemianæsthesia. More severe cases, not infrequently fatal, occur in which convulsions, delirium, and coma, with, perhaps, optic neuritis and some fever, are the symptoms. Such cases often run a very acute course, and appear to be more frequent in females (Oliver). Anæmia is the first symptom, and then colic, headache, vomiting, diplopia, or defective vision from optic neuritis. In a few days the patient is convulsed, becomes comatose and dies. In other instances, there is mental disturbance in the form of insomnia, visual hallucination and violent excitement.

Ocular Lesions. These are frequent, and include inequality of pupils, diplopia from paralysis of certain eye muscles, optic neuritis with or without hæmorrhages, neuro-retinitis, primary and secondary optic atrophy, and a bilateral amblyopia without change in the fundus, similar to uræmic amaurosis. The latter lesions are often due to a lead nephritis.

Albuminuria is a result of lead poisoning in two or three ways. It may occur temporarily in lead colic; and it is often present with œdema and diminished output of urine owing to tubal nephritis, as in cases of encephalopathy (Oliver), or of granular kidney in more chronic conditions of plumbism. The relations of lead, gout, and granular kidney are very close. Gout, at least in the south of England, is common in those who suffer from chronic lead-poisoning, which causes, it is said, diminished excretion of uric acid. And it has also been observed that sufferers from gout are very readily affected by lead.

The *liver* changes are fatty infiltration, congestion and deposit of hæmosiderin. Van den Bergh's test is commonly positive and sometimes there is frank jaundice (1).

Lead poisoning affects the functions both of menstruation and of gestation. Menorrhagia is very common, but occasionally there is amenorrhœa or dysmenorrhœa. In pregnant women there is a large proportion of miscarriages and stillbirths; and of children born alive many are under weight, and many die within a year. Amongst those who survive, convulsions, imbecility, and idiocy are above the average proportion.

Diagnosis. This depends for the most part upon the history of lead poisoning, upon the presence of a lead line upon the gums, and upon the discovery of lead in the excretions. The history may have to be investigated with the greatest care, as lead may get into the system by the most unexpected means. If paralytic symptoms are present, a history of colic is often obtainable, and in nearly all cases the lead line is present, though in very cleanly persons it may only be found between the teeth, or possibly not at all. The common type of lead palsy is readily distinguished from musculo-spiral paralysis by the escape of the supinator longus in the former and the simultaneous affection of both arms.

Lead is present in the fæces in larger amounts than in the urine, so that the former should be used when lead is being tested for; but the presence of lead in the fæces does not prove that it is in the system; only its presence in the urine proves this.

Prognosis. Recovery, though slow, is, with proper treatment, usually complete. If at the end of two years from the commencement of treatment any weakness still remains, it is likely to be permanent. Severe cerebral symptoms endanger life, but if death does not occur, recovery may be complete.

Prevention. It is essential to remember that dust and fumes are more important causes of industrial plumbism than ingestion from dirty fingers. The measures employed to minimise dust and fumes are: Exhaust ventilation applied by large hoods over the work benches or locally to the point where fumes

are being produced (*e.g.* in " lead burning ")—insistence on wet processes, including the daily hosing of sheds in accumulator works, etc.; the complete enclosure of necessarily dusty processes in dust-tight chambers. In the painter's trade the mixing of paints from dry powders and the rubbing down of painted surfaces (except with oiled sand-paper used *wet*) are now illegal. Domestic lead poisoning must be prevented by forbidding the use of lead water-pipes in certain areas, and by avoiding the use of lead and pewter vessels for cider and wine.

Treatment. The patient should give up his occupation, or prevent in whatever way may be necessary the introduction of more lead into the system. The most effective way of eliminating lead from the system, *i.e.* from its place of storage in the bones, is to give a low calcium diet, which may include meat, liver, potatoes, rice, tomatoes, bananas, peeled apples, tea, coffee, sugar and salt-free " nephritic bread," and butter fat prepared by melting butter in hot water and skimming off the fat. Milk, eggs, green vegetables, and many fruits are excluded. An acidosis is then produced which dissolves out lead phosphate (and calcium phosphate) from the bones so that it is excreted. 200 c.c. of dilute phosphoric acid or 10 grammes of ammonium chloride daily, in 10-hourly doses, are taken dissolved in plenty of water. A less effective method, but one that may be necessary when there is nephritis, is to give 20 to 40 grammes of sodium bicarbonate daily without dieting. Potassium iodide (5 to 15 grains) is also not very effective. Such treatment must only be given when there are no acute developments, and must be carefully watched, since, by the mobilisation of the lead, it may give rise to them. When acute symptoms are present a high calcium diet is advisable, *i.e.* 3 pints of milk, and calcium lactate 30 grains daily (3), to drive the lead into the bones.

Colic generally yields readily to a full dose of opium or an injection of morphia, combined with a simple purgative, *i.e.* an ounce of castor oil with 15 or 20 minims of tincture of opium or magnesium sulphate. Hot fomentations and pressure to the abdomen and enemas may be tried. Atropine, nitro-glycerine and benzyl benzoate may be used freely. In *paralytic affections* appropriate splinting is of the first importance, the paralysed muscles being placed in the position of relaxation. Massage, movements, and galvanism are also valuable. This treatment should be carried out for months. For *acute cerebral attacks* Oliver recommends the inhalation of nitrite of amyl and lumbar puncture with removal of from 1 to 3 ounces of fluid. Oxygen might be tried as in alcoholism. *Anæmia* must be met by suitable treatment with iron preparations (*see* p. 431). Liver extract might be tried.

CHRONIC MERCURIAL POISONING

The use of acid nitrate of mercury in the felting of hair in felt hat manufacture is the greatest cause of chronic mercurial poisoning in the world to-day. Many workers are affected with the anæmia, salivation, and stomatitis which are the familiar results of overdosing with mercury used as a drug.

The characteristics of mercurial poisoning are excitability of temper (mercurial " erethism ") and the tremulous movements of the limbs and body known as " mercurial tremors," or " trembles." They affect the arms first, and then spread to the legs and the muscles of the rest of the body. The movements are at first brought out only by excitement, later whenever the patient makes any muscular effort, and finally they become constant, and even persist to a certain extent during sleep. The tongue is tremulous, and speech is hurried, abrupt and jerky. Ataxia and even paralysis may be present in bad cases, and the patient may be quite unable to walk without support. In some cases there are tonic spasms of the flexors of the forearms after violent movements, or hard work. Anæsthesia, vertigo, delirium, hallucinations and restless excitement may also occur. In the earlier stages there is some resemblance to disseminated sclerosis, but there is no nystagmus; and if the movements become constant, paralysis agitans is, to a certain extent, simulated. Mercury also causes tubal nephritis.

Recovery may take place if the disease is not too advanced.

Treatment. Removal from the fumes of mercury is essential. Tonics and iodide and bromide of potassium are of most value as drugs; and sedatives, such as opium, chloral and belladonna, may be useful.

CHRONIC ARSENICAL POISONING

This is less common than lead poisoning, but it may arise in the following circumstances: among persons employed in arsenic factories, and in industries involving the use of arsenical pigments; among persons using such coloured articles as, for instance, certain grey and green wall-papers; occasionally from the use of large doses of arsenic in medical treatment; and in accidental impregnation of beverages with arsenic, such as occurred in the Manchester epidemic of peripheral neuritis, when an impure sulphuric acid was used in the process of malting. Poisoning by arseno-benzol has already been described.

Symptoms. In the case of exposure to arsenical dust, which is highly irritating, the effects are manifest on the skin and accessible mucous membranes; when the arsenic is taken internally, the alimentary mucous membrane, the peripheral nerves, and the skin through the circulation are affected. In the first case the prominent feature is irritation of the skin resulting in a form of eczema or dermatitis, which is seen especially in the warmer or moister parts, such as the axillæ, between the scrotum and thighs, at the edges of the nostrils, and the eyes. Redness of the conjunctiva and smarting of the eyes, sore throat and irritation, with frequent hawking, are also present. Later there are symptoms of general poisoning, but these are more prominent when the poison has been injected in small doses frequently. There is gastro-intestinal irritation, with perhaps sickness, diarrhœa, and abdominal pains. With this are often combined emaciation, weakness, muscular cramps, and frontal headaches. Peripheral neuritis is a characteristic feature (*see* p. 651), and a disorder of the skin of which pigmentation and thickening of the epidermis, especially on the palms and soles, or *keratosis*, are the prominent features. Transverse ridges and furrows appear on the finger-nails; and in acute cases curved white lines (*leuconychia*) have appeared, showing interrupted nutrition at the time of the poisoning.

Treatment. This consists in removing the cause, when the symptoms will subside; medicinally iodide of potassium may be given in 5-grain doses. Peripheral neuritis may, however, persist for several months.

CHRONIC MANGANESE POISONING

Commercially manganese is used in making chlorine, paint, varnish, enamel, and linoleum, for the marbling of soap and in the manufacture of steel.

The clinical features of manganese poisoning resemble paralysis agitans and suggest that there is a lesion in the corpus striatum. There are emotional disturbances with periods of uncontrollable laughter or weeping, mental languor, muscular rigidity and tremor. The gait is shuffling, and there is a tendency to fall down. There are no signs of disease of the pyramidal tracts (2).

REFERENCES

1 W. Blair Bell, W. R. Williams, and L. Cunningham .. .. 1925 *Lancet*, ii., p. 793.
2 J. R. Charles .. .. 1922–3 *J. Neurol. & Psycho-pathol.*, 3, p. 262.
3 J. C. Aub and others .. .. 1925 *Medicine*, 4, p. 1.

DISEASES OF THE NERVOUS AND MUSCULAR SYSTEMS

UNDER this heading we have to deal with disorders of the brain, spinal cord and nerves—disorders which manifest themselves through the functions of motion, sensation, the special senses and the intellect and emotions.

Although the nervous system is affected by the same pathological processes as the rest of the body, there are certain peculiarities of structure and function which distinguish the effects of disease of this part from all others.

The first point of importance is the extreme specialisation of function which reaches its height in the higher parts of the central nervous system. Thus it happens that a minute lesion may produce symptoms and signs which we can attribute with certainty to the situation of the disease. Such a group of symptoms and signs is said then to have a *localising value.*

A further consequence of specialisation of structure is the tendency of certain poisons—bacteriological or chemical—constantly to pick out certain groups of nerve cells or fibres. This *selective incidence* must depend upon peculiarities of a chemical or physical nature resident in the nerve cell which render it especially liable to some poisons, resistant to others. Thus it happens that a particular sign comes to be very frequently associated with the same pathological process. But we must always remember that the *sign is the result of the localisation of the lesion and not of its pathology.* The spirochætal poison of syphilis, for instance, has a selective incidence upon minute centres in the mid-brain which control the reaction of the pupils to light. Loss of the pupillary reaction to light—the Argyll Robertson pupil—is therefore one of the commonest signs of nervous syphilis. But we are not entitled to conclude that the Argyll Robertson pupil is *always* due to syphilis. Any other cause operating in the same situation *may* produce the same sign—for instance a tumour, or the virus of encephalitis lethargica.

A second distinctive feature of nervous diseases is due to the relatively enormous length of the nerve cell. When the axon of a nerve cell is injured or diseased the distal part undergoes degeneration down to its peripheral twigs. Thus a lesion of the first thoracic nerve root within the vertebral column will result in degeneration of nerve fibres supplying the small muscles of the hand, and consequent paralysis and atrophy of these muscles. And a lesion of the cells in the upper part of the motor cortex will cause degeneration of the pyramidal fibres coursing down the spinal cord as far as their termination in the lumbar enlargement, with paralysis of the lower limb. The lesion, therefore, may be at a very considerable distance from the part in which the symptoms are manifest.

A third striking feature of the nervous system is the way in which its parts are enclosed, and, as it were, insulated from other tissues—the central nervous system by means of the meninges and the peripheral nerves by their neurolemmal sheaths. Associated with this is the observation that primary tumours of the nervous system never erode the meninges—however malignant they may be within these bounds—or invade other tissues. Nor, on the other hand, do malignant growths elsewhere ever directly invade nervous tissue (although, of course, they may produce damage by mechanical compression).

Another peculiarity of the nerve substance is the absence within the brain and spinal cord of any fibrous supporting tissue, its place being taken by the much more delicate neuroglia. Hence the tendency of suppuration to spread widely instead of becoming limited by a fibrous barrier. There is a similar liability in hæmorrhage, whether accidental or the result of vascular disease. The pressure of the effusion easily suffices to tear through the fine neuroglia fibrils and excavate the substance of brain or cord. In conditions of chronic inflammation, however, the neuroglia cells proliferate and form an excess of fibrils which leads to an increased density. Moreover, the degeneration products of nerve fibres undergoing "secondary degeneration" (*e.g.*, a degeneration of pyramidal fibres in the cord secondary to a lesion of the internal capsule) appear to provoke a similar reaction on the part of the neuroglia cells, so that after the decayed nerve fibres have been absorbed by scavenging cells their former course is marked by an increased density of neuroglia, which is often both visible and palpable. Such appearances led, in the early days of neuro-pathology, to the assumption that the overgrowth of neuroglia was the primary disease process, the destruction of nerve cells being a secondary result, and the pathological process at work was named "*sclerosis.*" We now believe that this conception was inaccurate, and that the primary effect of injury or disease is degeneration of the nerve cells with secondary neuroglial overgrowth.

A further point of importance is the fact that the brain and cord are enclosed in a tough fibrous membrane within a bony cavity. There is little room, therefore, for expansion, and a bruise such as elsewhere in the body would result in local swelling and pain, or a benign tumour not invading the nervous tissues, may readily cause serious damage by compression.

Apart from the spread of organisms by direct continuity there are two main channels through which bacteria or toxins may gain entrance to the central nervous system. The main pathway is through the blood stream. But in at least two diseases—tetanus and diphtheria—the toxin travels centrally from the site of infection along the nerve fibres.

Before proceeding to the systematic description of the diseases of the nervous system, something must be said of its general anatomy and physiology, and of the clinical methods of investigating the symptoms which its diseases produce.

APPLIED ANATOMY AND PHYSIOLOGY

Our knowledge of the structure of the central nervous system in man greatly exceeds that of its function. There are many parts, which, though well defined by the anatomist, are clinically "silent." Partly, perhaps, for this reason the lesions afforded by disease do not lend themselves easily to systematic exposition in terms of physiology. In the following pages an attempt will be made to present simply that which is of practical value.

The Lower Motor Neuron. This comprises a cell situated in the anterior horn of the spinal grey matter, or one of the motor nuclei in the brain stem, and an efferent fibre which, passing through one of the anterior spinal nerve roots, or motor cranial nerves, has its termination in a motor end plate in contact with a striped muscle. The function of the lower motor neuron is the conduction of all nervous impulses to the muscle from the central nervous system, whether these are concerned with voluntary movement, postural tone or reflex action. The nutrition of a muscle also depends upon its connection through the motor fibre with an intact motor cell. If this connection is broken or if the cell is damaged, the muscle wastes.

The signs of a lower motor neuron lesion, therefore, are loss of voluntary power, loss of tone, loss of reflex action, and wasting, in the muscles affected. When the lesion affects the motor cells directly and progress of the disease is

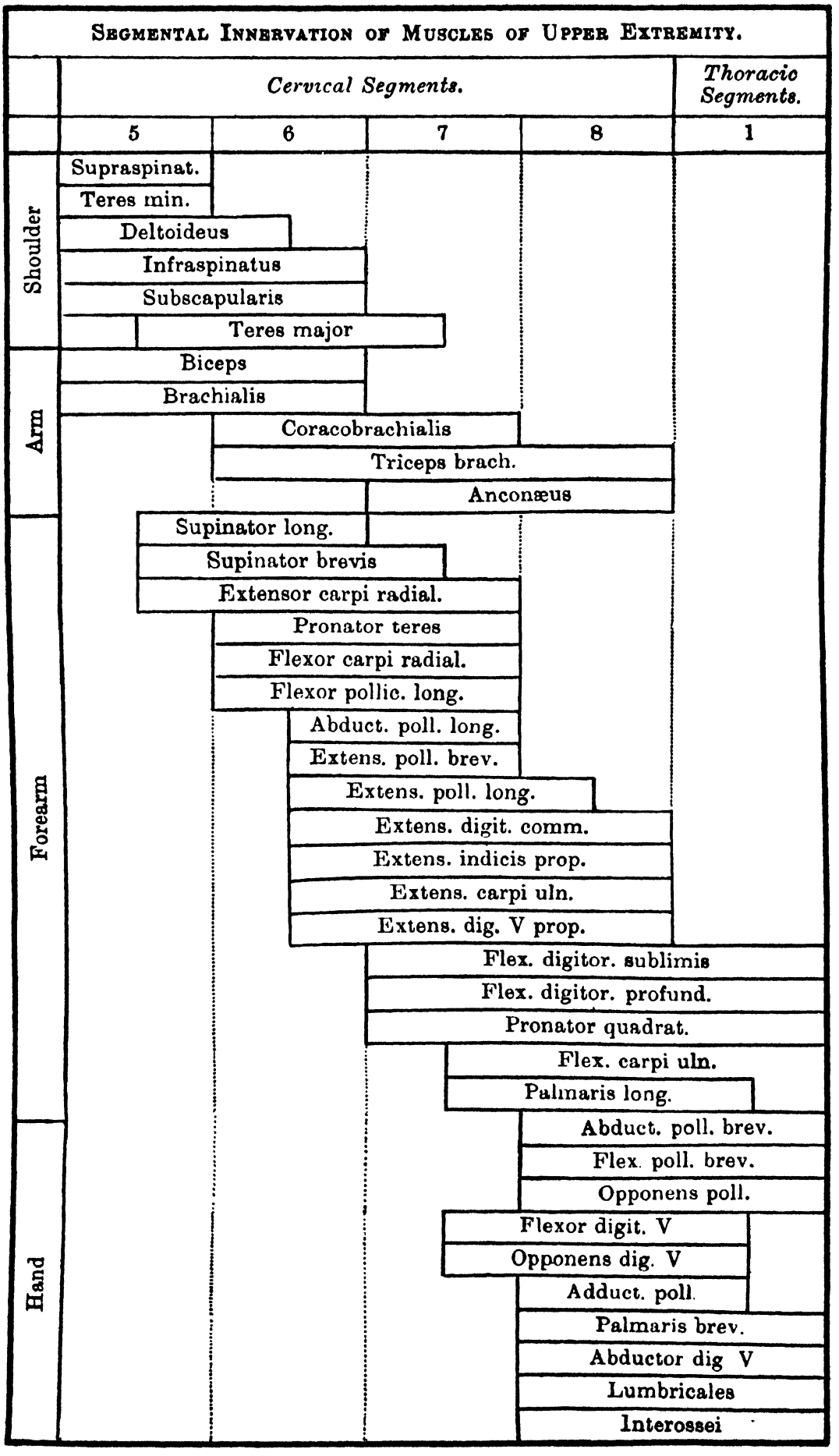


Fig. 62.—Table showing Segmental Innervation of Muscles of Upper Limb. (Bing.)

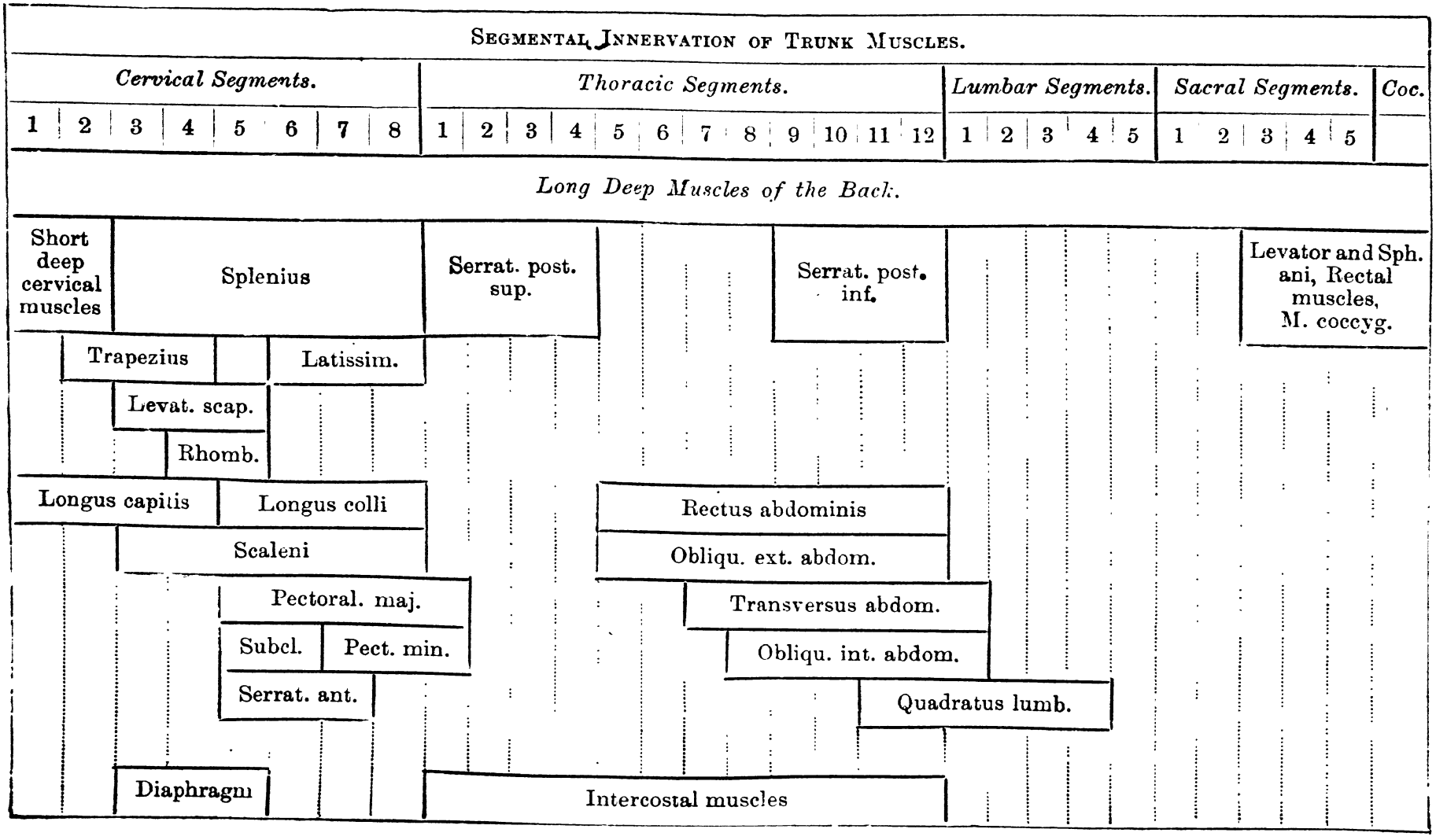


Fig. 63.—Table showing Segmental Innervation of Muscles of Trunk. (Bing.)

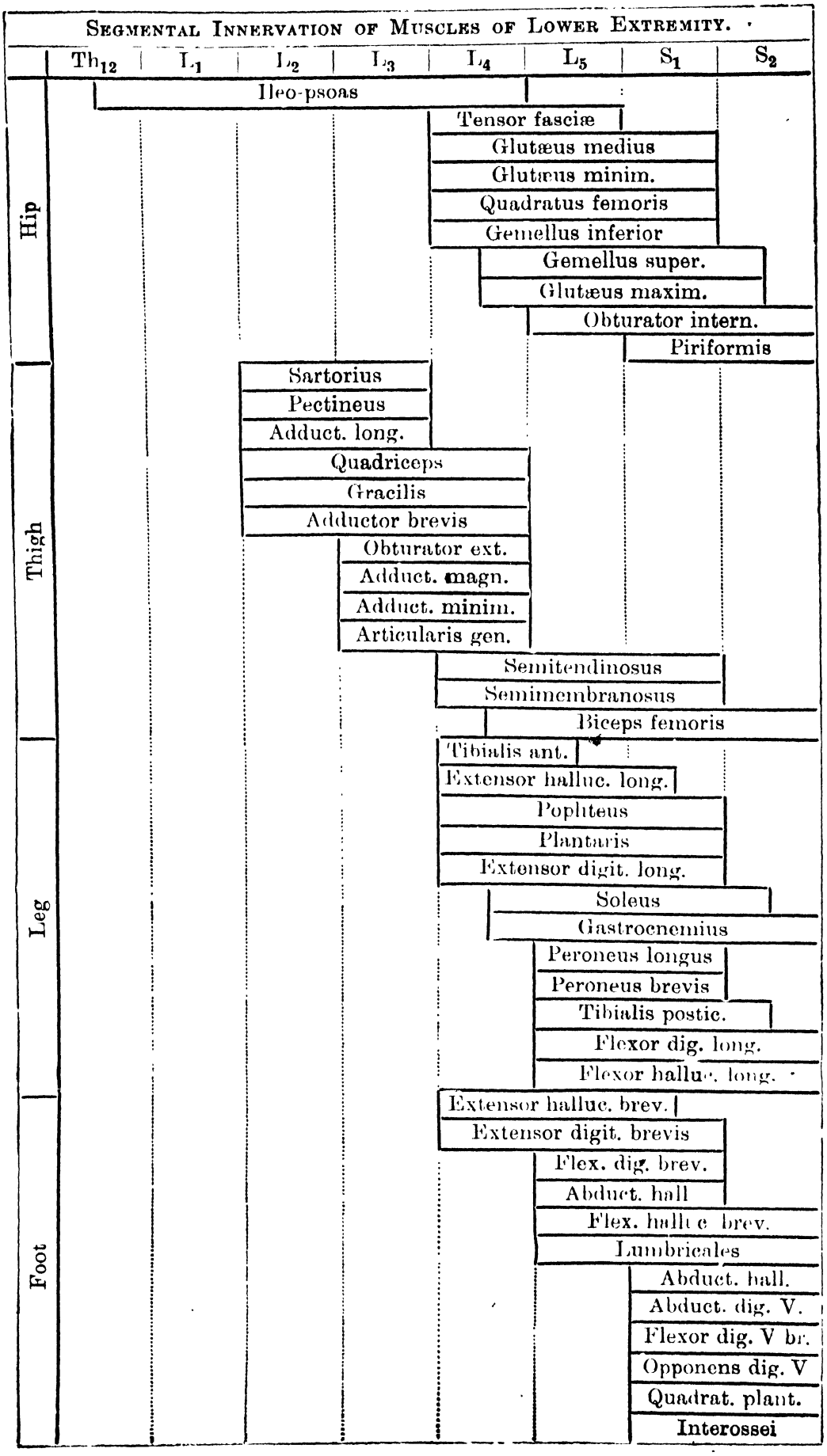


Fig. 64.—Table showing Segmental Innervation of Muscles of Lower Limb (Bing.)

forms of sensibility on the opposite side of the body, though, as the fibres of the fillet and those of the spino-thalamic tract lie apart up to the level of the mid-brain, either may be affected separately. A lesion above the optic thalamus will result in an incomplete sensory loss on the opposite side of the body. Some degree of appreciation of contact, pain, and extremes of heat and cold will be preserved. Actually, in the case of lesions above the thalamus sensation is, as a rule, most severely affected in the hand and foot, with relatively little impairment over the proximal parts of the limbs and the trunk. The nearer the lesion is to the cortex, the more likely it is that the sensory defect will be of a dissociated type with little affection of the cruder forms of sensation and severe disturbance of the spatial and discriminative forms of sensibility.

Lesions of any part of the sensory pathway may give rise to sensations described as numbness, tingling, or pins and needles—these being called paræsthesiæ. In the case, especially, of lesions which cause partial loss of cutaneous sensation, there is often an associated hyperæsthesia—that is, although the stimulus required to produce any sensation is greater than normal, the sensation when it comes is of abnormal character, unusually vivid, as a rule painful, and with a tendency to spread more widely than normal. Pain is a variable quantity in lesions of the sensory nerves. When the peripheral twigs are involved it is not, as a rule, a marked feature, but may be severe with lesions of the nerve trunks or their branches, and is of almost constant occurrence in disease of the posterior nerve roots. Lesions of the longitudinal tracts in the spinal cord do not, as a rule, give rise to pain, though there are some striking exceptions (as in tabes dorsalis). Lesions at or near the thalamus are apt to cause severe pain of widespread distribution with associated hyperalgesia.

Reflex Function. A reflex action may be defined in its simplest form as an exhibition of activity in an effector end organ—muscle or gland cell—in response to stimulation of a receptor end organ, the stimulus being conducted from receptor to effector through the central nervous system. The act is not voluntarily performed though the individual may be conscious of it. The simplest reflex arc therefore must comprise at least two neurons, receptor and effector. Between these, as a rule, intervene many connecting, or association, fibres.

The most primitive reflex systems are those concerned with the regulation of the alimentary and excretory functions. The centres for these reflexes are ganglion cells lying in the walls of bowel and bladder. Therefore, even when the spinal cord is destroyed reflex activity of this kind continues. Under normal conditions, however, the primitive or lower reflex centres are in some measure controlled by the activity of higher centres. In some instances and to some extent the lower centres are under voluntary control. When, as the result of disease, the control imposed by the higher reflex centres, or by the will, is lost, the activity of the lower centres may be increased and give rise to positive symptoms. The reflex functions which are of most importance in clinical neurology, are those concerned with the regulation of postural tone and equilibrium, with micturition and defæcation, and with the protection of the body from excessive or noxious stimulation.

Regulation of Postural Tone. From animal physiology, we know that in the cat transection of the brain stem between the level of the red nuclei and that of the entry of the fibres of the eighth nerve, results in a generalised increase of muscular tone, which follows a definite pattern (predominance of the extensor groups) and is known as decerebrate rigidity. In man, as we have already observed, following a lesion of any part of the pyramidal tracts, there is increased tone in the affected muscles which also follows a regular pattern. The phenomena are closely comparable, and it is assumed that in both cases the cause is release of reflex tonic centres from control.

As a result of the increased muscular tone, reflex contraction in response to sudden stretching is much enhanced. It is, therefore, easier to make a muscle

contract by tapping its tendon, and the contraction is brisker. Persistent stretching of a muscle by leverage at the joint may result in a brisk contraction whose rebound stimulates further contraction and so on, the phenomenon known as clonus.

Diminution or abolition of the tendon reflexes may be caused by any lesion which interrupts the reflex arc concerned. This reflex arc comprises afferent fibres from the muscle and tendon, association fibres which run for some distance in the posterior columns before entering the grey matter to make contact with the anterior horn cells, and the lower motor neuron units. The tendon jerks, therefore, may be impaired or lost in disease of the peripheral nerves, posterior columns, central grey matter of the spinal cord or anterior horn cells.

The tendon reflexes of chief importance, together with their spinal and peripheral pathways, are as follows :—

Reflex.	Spinal Segment.	Peripheral Nerve.
Biceps jerk.	C. 5 and 6	Musculo-cutaneous
Triceps jerk	C. 6 and 7	Musculo-spiral
Supinator jerk	C. 5 and 6	Musculo-spiral
Knee jerk	L. 2, 3 and 4	Anterior crural
Ankle jerk	S. 1 and 2	Sciatic

Equilibrium. The maintenance of the correct posture of the body in relation to the force of gravity, of the head in relation to the body, and of the eyeballs in relation to the head, is a function of postural tone. As, however, disorders of balance constitute an important group of neurological symptoms, the physiology of equilibrium deserves a separate note.

The maintenance of equilibrium depends mainly upon afferent impulses received from three sources, the eyes, the labyrinths and the muscles themselves. These afferent impulses are co-ordinated in reflex centres situated in the brain stem and cerebellum to produce a smooth outflow of tonic impulses to the appropriate muscles.

The impulses derived from the muscles themselves are the most important. A man with both labyrinths destroyed can maintain the erect posture and walk blindfold, whereas, on the contrary, a patient with loss of muscular sensibility from destruction of the posterior columns exhibits a gross disturbance of balance despite the integrity of eyes and labyrinths. The impulses derived from the eyes are of least importance.

The main function of the labyrinth in man is to maintain the balance of head and eyes. The labyrinth on each side directs the head and eyes towards the mid-line. Thus, in the case of a destructive lesion of the left labyrinth, the occiput tends to fall towards the left shoulder ; and when the patient is asked to look towards his extreme right the eyes swing back towards the left owing to the unopposed action of the right labyrinth ; the consequence being, if the patient persists in the attempt at deviation to the right, a regular oscillation of the eyeballs known as nystagmus.

The symptoms resulting from destructive lesions of the labyrinths vary greatly with the acuteness of the lesion. With gradual destruction, the co-ordinating centres are able to deal by means of compensation, so that no symptoms appear, but an acute lesion may produce violent giddiness and even throw the patient to the ground. The exact position of the co-ordinating centres in man is unknown, but lesions in any part of the brain stem from the medulla to the level of the posterior end of the third ventricle, or of the cerebellum, are apt to produce disturbance of balance and nystagmus.

Micturition. The control of the bladder in man has recently been investigated by Denny-Brown and Robertson, whose main conclusions are as follows :—

The nerve supply of the bladder and its sphincters (internal and external) is derived from three sources. Of these the most important is the pair of pelvic nerves arising from the second, third and fourth sacral roots. Stimulation of these nerves causes contraction of the bladder wall (detrusor) with relaxation of the internal sphincter. The pudic nerves, also derived from the second, third and fourth sacral roots, innervate the external sphincter, which contracts when they are stimulated. The third source of supply is by way of the hypogastric nerves derived from the eleventh and twelfth thoracic and first lumbar roots. Stimulation of these nerves causes contraction of the internal sphincter with some degree of inhibition of the detrusor. Section of both hypogastric nerves in an animal, however, causes little or no disturbance of micturition. This source of nerve supply therefore appears to be of relatively little importance. After all these nerves have been severed, and the vesical plexus is thus isolated, the bladder will continue to discharge its contents periodically.

Under normal conditions the accumulation of fluid within the bladder sets up rhythmic contractions of its wall. These contractions are controlled by a restraining effect which at low volumes is subconscious in its operation. This restraining effect can be enhanced or removed by voluntary intent. Thus the will to urinate results in increased force of contraction with reciprocal relaxation of the internal, and subsequently of the external, sphincter, and the act of micturition occurs. On the other hand, even when the bladder is full, the contraction can be inhibited by an effort of will, which together with voluntary contraction of the external sphincter prevents micturition. The paths by which this control is effected lie in close proximity to the pyramidal tracts.

Passive distension of the bladder gives rise to a sensation of increasing discomfort. The rhythmical contractions at low volumes give rise to no sensation, but are more and more apt to intrude upon consciousness as the bladder wall becomes stretched.

Following a sudden lesion of the spinal cord or cauda equina there is paralysis of the detrusor vesicæ with tonic contraction of the internal sphincter. With recovery from the phase of spinal shock automatic micturition appears. In the case of a lesion of the cauda equina the volume of urine which the bladder will contain is small and expulsion is feeble. Following a lesion of the spinal cord which leaves the sacral segments and their connections with the bladder intact, the viscus is capable of greater distension and contracts more forcibly, and the act of micturition may be facilitated or inhibited by the elicitation of other reflexes dependent upon the isolated segments of spinal cord.

Defæcation. Denny-Brown and Robertson have also investigated the nervous control of defæcation and conclude that its mechanism is closely comparable with that of micturition. The main nerve supply to the rectum and anal canal, including the internal sphincter, is derived from the pelvic nerves arising from the second, third and fourth sacral roots. The nerve supply to the external sphincter is from the pudic nerves which also arise from the second, third and fourth sacral roots.

Automatic defæcation, however, can occur when the rectum and anus are cut off from these sources of nervous supply and must depend upon the function of reflex centres situated in the walls of the viscera. Tension upon the walls of the rectum results in muscular contraction with reciprocal relaxation of the internal sphincter. The whole process is involuntary, though it may be facilitated by voluntary contraction of the abdominal wall. Voluntary control of defæcation is limited to the action of the external sphincter, which can be opened or closed at will. When the central nervous connections of the rectum are intact, the reflex contractions show a progressive character and better fusion, so that the response to distension is more massive and more complete than it is when the

rectal plexus is cut off from central control. Following a lesion of the spinal cord or cauda equina there is a phase during which the rectal reflex is inhibited and the tone of the internal sphincter is increased. Following this, automatic defæcation is established, the loss of voluntary control being due to paralysis of the external sphincter.

Protective and Other Reflexes. Of the protective reflexes which are of importance in clinical investigation, the simplest is the *corneal reflex*—closure of the eye in response to a stimulus (tactile or otherwise) applied to the cornea. The reflex arc comprises on the afferent side branches of the trigeminal nerve. Most of the corneal surface is supplied by the ophthalmic division, but there is a small segment at the lower part of its circumference supplied by the maxillary. The efferent fibres are those branches of the facial nerve which supply the orbicularis palpebrarum. The corneal reflex may be diminished or lost in the case of lesions of the afferent or efferent fibres just described, or from lesions of the Gasserian ganglion, the sensory root or nucleus of the trigeminal nerve, or the nucleus or trunk of the seventh nerve.

Pupillary Reflex. The reflex contraction of the pupil to light is also in a sense a protective reflex. The afferent pathway comprises the retina, optic nerves and optic tracts, and the primary visual centres in the superior corpora quadrigemina. Hence, association fibres connect these afferent pathways from both sides with the cells responsible for innervation of the pupils which lie in the anterior part of the third nerve nuclei. Thus, both pupils contract in response to illumination of one eye. The reflex may be diminished or lost as the result of lesions of the retina, optic nerve, optic tracts, superior corpora quadrigemina, third nerve nuclei, or third nerves. In the case of a lesion of one optic nerve, illumination of the eye on that side will cause no contraction of either pupil, but illumination of the other eye will cause simultaneous contraction of both pupils. Under these circumstances, the pupil on the affected side is said to react to consensual but not to direct stimulation. The contraction of the pupils which occurs with ocular convergence and accommodation is an associated movement rather than a reflex.

Plantar Response. This is a reflex of great clinical importance. Under normal conditions in man stimulation of the sole of the foot by firm stroking contact causes flexion of the great toe. In the presence of a lesion of the pyramidal tract, this movement is reversed—the great toe moves upwards (extensor plantar response), and this movement is often accompanied by contraction of the flexor muscles of the lower limb as a whole. In the case of a complete transverse lesion of the spinal cord, after the phase of spinal shock is past, the contraction of the flexors is not confined to the limb whose sole is stimulated. Both lower limbs may be withdrawn simultaneously in a strong flexor spasm (mass reflex). The upgoing movement of the great toe and with it the flexor spasm of one or both lower limbs may be obtained from stimulation not only of the sole of the foot but from other areas, especially if the stimulus used is of nocuous quality (scratching or pinching). The more complete the transection of the spinal cord, the wider the reflexogenous zone, and the greater the tendency towards a massive response, so that in the case of a complete lesion a dragged pin applied to any part of the lower limbs may provoke the mass reflex.

The character of this reflex, of which the extensor plantar response is a part, suggests that it is a protective movement of withdrawal. The reflex centres concerned lie in the lower part of the spinal cord. They are normally inhibited from above, and their activity is manifest only when the inhibitory influence is removed by disease.

The Abdominal Reflexes. Stimulation of the abdominal wall by stroking contact or a light scratch causes, under normal conditions, a brisk contraction of the underlying muscles. This probably has a protective origin, its purpose in the quadruped being to shake off flies. The reflex is lost when the afferent nerves from the skin or the motor nerves to the muscle are destroyed, and also when

foramina of Monro, the third ventricle and the aqueduct of Sylvius into the fourth ventricle, and so through the foramen of Magendie into the subarachnoid space, where it surrounds the whole of the brain and spinal cord. As the nutrient vessels enter the substance of brain and cord they invaginate the pia mater before them, and so there are formed around them perivascular spaces which are continuous with the subarachnoid space and contain cerebro-spinal fluid. There is some evidence to show that the fluid in these perivascular spaces plays the part of a medium of exchange between the blood and the nerve cells analogous to that played by the lymph in other structures of the body, and that the waste products of nervous metabolism are by this route drained into the cerebro-spinal fluid. The fluid obtained from lumbar puncture will therefore contain such waste products in addition to the pure secretion of the choroid plexus. The path of absorption of this fluid into the blood stream is by way of minute invaginations of the arachnoid membrane into the walls of the venous sinuses of the brain (arachnoid villi), and the rate of absorption is normally parallel with that of excretion.

As the result of disease, the outflow of cerebro-spinal fluid from the ventricular system may be obstructed, in which case that part of it which is proximal to the obstruction becomes distended. The expansion so caused may result in a great increase of the intracranial pressure.

LESIONS OF THE PERIPHERAL NERVES AND NERVE ROOTS

A lesion of one of the peripheral nerve trunks causes muscular weakness and wasting: loss of sensation—all forms being affected: and loss of reflex function. The distribution of these changes can be studied with the aid of diagrams. Lesions of the anterior or posterior nerve roots cause motor and sensory symptoms respectively, with loss of reflex function in both instances. The distribution of these also can be studied with the aid of appropriate diagrams and tables.

LESIONS OF THE SPINAL CORD

The results of a transverse lesion show themselves mainly as an interruption of the *conducting* power of the cord; but if the lesion is at all extensive vertically, its effects upon the *nerve-cells* must also be considered—*e.g.*, both upper and lower motor neurons are affected. The results also vary, according as the lesion is *bilateral* or *unilateral*, in consequence of differences between the motor and sensory fibres in the process of decussation.

Results of a Unilateral Transverse Lesion as Affecting Conduction (Brown-Séquard Syndrome)

On the same side as the lesion and below it.	On the opposite side below
Paralysis of muscles.	Loss of senses of pain, heat, and cold, and sometimes of touch.
Hyperalgesia.	Muscular power and nutrition, the muscular sense, reflex action, and temperature are normal.
Loss of appreciation of posture of limbs, of passive movements, of separation of points applied to the skin, of size, shape, weight, and consistence of objects, and of vibrations of tuning-fork.	
Tendon jerks at first lessened, then increased. Plantar reflex extensor, abdominal reflexes absent (if lesion high enough to affect them).	
Vasomotor paralysis and elevation of temperature.	
The sense of touch is retained, as well as sense of pain, heat and cold, the nutrition of muscles and their electrical reactions.	

Results of a Bilateral Transverse Lesion as Affecting Conduction

Anæsthesia below the level of the lesion.

Paralysis of all muscles below the level of the lesion ; there is no wasting ; the electrical reactions are not altered. Abdominal reflexes absent ; tendon jerks increased ; plantar responses extensor.

Loss of sphincter control.

These symptoms vary with certain conditions as follows : *if the lesion is of acute onset* there is at first, during the period of spinal shock, complete flaccidity of the paralysed muscles with abolition of tendon jerks and plantar responses. After a few weeks, *if the lesion is incomplete*, the paralysed limbs become spastic in extension with increased tendon jerks and extensor plantars. *If the lesion is complete* the paralysed muscles remain flaccid, but the lower limbs are subject to involuntary flexor spasms which may result in contracture ; the tendon jerks return : the plantar responses are extensor.

To these symptoms in each case may be added those caused by damage to the nerve cells of the particular segment affected, together with the motor and sensory fibres directly connected with it by the anterior and posterior nerve roots. These will naturally vary with the *level of the lesion.*

A bilateral lesion of the upper cervical region will produce spastic paralysis of all four limbs with sensory loss below the level affected. The local destruction of anterior horn cells will add to this, wasting and weakness of the sternomastoids and trapezii. Only patients with partial lesions at this level survive. A complete lesion causes paralysis of the diaphragm.

A lesion of the cervical enlargement will produce wasting and weakness of the muscles supplied from the segment affected, *e.g.*, in the case of the fifth cervical segment the deltoids, spinati, and biceps, with loss of the biceps tendon jerk (*see* Diagram, p. 594). Below the level of the lesion spastic paralysis and sensory loss.

In addition, all lesions above and including the first thoracic segment will produce paralysis of the cervical sympathetic fibres either in their downward course from the medulla, or at the point of their emergence in the first thoracic root (*see* Fig. 68, p. 606).

Lesions of the Thoracic Region produce little in the way of segmental signs. Nevertheless palpation may sometimes determine the presence of wasting and weakness of the intercostal muscles supplied by the affected segment. When the lesion is below the level of the eighth thoracic segment the upper halves of the recti abdominis are spared. Therefore the upper abdominal reflexes are preserved, and when the patient attempts to raise his head the umbilicus is pulled upwards by the unopposed action of the upper halves of the recti. As before, there will be sensory loss and spastic paralysis below the level of the lesion.

Lesions of the Lumbar Enlargement may be clinically divided according to their level as follows :—

Third and fourth lumbar segments : flexion of hip preserved ; apart from this lower limbs paralysed ; atrophy of quadriceps and adductors ; absent knee jerks ; brisk ankle jerks and extensor plantar responses.

First and second sacral segments : flexion of hip, adduction of thigh, extension of knee and dorsiflexion of foot preserved ; atrophy of calf muscles and intrinsic muscles of foot. Weakness of flexion of knee and extension, abduction and external rotation of hip. Knee jerks present ; ankle jerks and plantar responses absent.

Third and fourth sacral segments : paralysis of large bowel and bladder ; anal reflex lost.

Reference to the segmental sensory charts on p. 599 will indicate the extent of the sensory loss in each case.

Lesions of the Cauda Equina, when complete, may involve all the nerve roots

to use these muscles for the particular purpose of speech. Typically the man with a motor aphasia knows what he wants to say, but cannot say it.

Together with motor aphasia is usually associated *agraphia, i.e.* the patient is at the same time unable to express his thoughts in writing; and in certain rare instances the existence of agraphia has been recorded apart from aphasia in association with lesions of the second frontal convolution (Fig. 75).

In relation to aphasia may be considered *motor apraxia*, a condition in which without loss of power, sensibility or co-ordination the ability is lost to perform certain purposeful movements (such as brushing the teeth, lighting a match). This phenomenon has been observed after lesions of the upper left frontal convolution, of the upper part of the left parietal lobe, and of the corpus callosum, and is closely analogous to motor aphasia and agraphia, which may perhaps be considered as special types of apraxia.

Frontal Lobe. It has already been observed that the posterior part of the frontal cortex contains centres for rotation of head and eyes to the opposite side. A cortical lesion, therefore, may give rise to epileptic attacks, of which forced conjugate deviation may be the distinctive feature. On the left side a lesion situated far back and low down is likely to cause aphasia. A peculiar symptom met with in lesions of the upper and posterior part of the frontal lobe is known as forced grasping or tonic innervation in the opposite hand. The patient being asked to make a fist, or grasp an object firmly, is unable for the moment to open his hand again, this failure being due to persistent contraction of the muscles just innervated. This symptom, though rarely encountered, would seem to have a constant localising value. It is important in looking for it to make sure that the patient's inability to unclasp his hand on request is not due simply to confusion.

The remaining parts of the frontal lobe are relatively silent—that is to say, that lesions affecting them are not attended by any distinctive symptoms.

Parietal Lobe. On the left side, as we have seen, the parietal lobe is largely concerned with speech, while on both sides it contains the termination in the cortex of the sensory pathways. Through its lower part run the fibres of the optic radiation. The symptoms which are apt to result from a parietal lobe lesion, therefore, are sensory disturbance, homonymous defects in the opposite visual field, and on the left side aphasia. The postero-superior part of the parietal lobe, however, is relatively silent.

Temporal Lobe. The upper convolution contains the centre for hearing, but destructive lesions do not give rise to deafness, since the lower auditory centre on each side is connected with both sides of the brain. A lesion on the left side may encroach upon the speech area and is especially apt to cause difficulty in naming objects. The olfactory phenomena of the uncinate epileptic attack have already been described, and the fact has been mentioned that the optic radiation in a part of its course passes through the posterior part of the temporal lobe, so that homonymous field defects may play a part in the symptomatology of temporal lobe lesions. Nevertheless, a considerable lesion of the middle part of the temporal lobe, especially on the right side, may be silent.

Occipital Lobes. Lesions of the occipital lobe give rise to visual symptoms, which have already been described.

Silent Areas. There are many parts of the brain which may be destroyed or damaged by disease without the production of any symptoms of localising value. Indeed, it is surprising, in some cases, to see how much of the brain may be put out of action without any symptom at all.

Cortical lesions, elsewhere than in the specialised part already described, give rise to epileptic attacks of a generalised character, minor or major. Any extensive lesion of the white matter is liable to result in deterioration of the highest functions—such as impairment of the memory, especially for recent events, and changes for the worse in character and disposition. In the causation of such

symptoms, the amount of brain substance destroyed appears to be of more importance than its situation.

Basal Ganglia. Lesions of the basal ganglia are associated chiefly with motor disturbances such as rigidity and involuntary movements. Disease of the *corpus striatum*, especially the lenticular nuclei, results in a group of symptoms which, as they were originally described by Parkinson, in *paralysis agitans*, are frequently called Parkinsonian. There is rigidity of face, trunk and limbs which differs in quality from that seen in disease of the pyramidal tracts. The muscles yield slowly to passive movement (lead pipe rigidity) or in a succession of small jerks (cog wheel rigidity). Apart from the rigidity, there is slowness of movement, and there are involuntary movements taking the form of a regular rhythmic tremor, which is maximal in the extremities. The same group of symptoms may result from lesions of the *substantia nigra*.

A lesion of the sub-thalamic nucleus or nucleus of Luys results in involuntary movements of the opposite side of the body, including face, trunk and limbs, of the kind known as choreiform. These are jerky, purposeless contractions in various groups of muscles with no regular order or sequence.

Other types of involuntary movement, attributed with less certainty to disease of the basal ganglia, are those met with in athetosis and torsion spasm. In the former condition there are slow, writhing movements, which are most marked in the face and limbs. They are usually associated with some degree of rigidity of the pyramidal type and distribution. In torsion spasm, the movements are slow and massive, involving trunk and limbs in a more or less regular sequence, which produces the most violent contortions of the whole body.

The sensory disturbances which result from a lesion of or near the optic thalamus have already been described. Lesions in this neighbourhood are often associated with involuntary movements of the choreiform or athetoid variety.

Hypothalamus. This anatomical term includes the structures lying ventral to the optic thalamus, that is between it and the pituitary body, comprising the floor of the third ventricle, infundibulum and tuber cinereum. It has been shown by animal experiments that lesions in this situation may produce polyuria, obesity and pathological drowsiness, and similar effects are seen in tumours involving this area.

Corpora Quadrigemina. A lesion of these bodies causes vertigo, inco-ordination of the gait of cerebellar type and double ophthalmoplegia. The latter is of the nuclear type, and in the beginning may be limited to ptosis and paralysis of upward movement of the eyes, with which may be associated myosis and inactivity of the pupils. Deafness may also occur from involvement of the inferior corpora quadrigemina.

Crus Cerebri. Paralysis of the limbs on the opposite side and of the third cranial (oculo-motor) nerve on the same side is characteristic of a lesion of the cerebral peduncle at its inner and posterior part; this has been called the syndrome of Weber. Tremor of the opposite limbs with oculo-motor paralysis on the same side, or Benedikt's syndrome, is also due to a lesion of the crus cerebri. Gordon Holmes notes that lesions of the *mid-brain* (which includes the corpora quadrigemina and the crus cerebri, with the substantia nigra and red nucleus) have not infrequently been accompanied by definite, rather slow, tremors of the limbs.

Pons Varolii. This portion of the brain contains the pyramidal tracts, and the nuclei of the fifth, sixth, and seventh nerves. Large central lesions may paralyse all four limbs from the proximity of the two tracts to the middle line. A one-sided lesion in the upper part produces hemiplegia of the ordinary type on the opposite side of the body; but a lesion in the lower part, while involving the same pyramidal fibres for the arm and leg, is below the facial fibres for the opposite side, and destroys the facial nerve roots of its own side. There is then produced a variety of hemiplegia known as *crossed hemiplegia*, the

face being paralysed on the side of the lesion, but the arm and leg on the opposite side. A lesion involving the nucleus of the sixth nerve on one side will give rise not only to paralysis of the external rectus on this side, but also to paralysis of the internal rectus of the opposite eye in attempted conjugate deviation of both eyes towards the side of the lesion.

Medulla. Any extensive disease in this neighbourhood is incompatible with life owing to involvement of the vital centres. A unilateral lesion causes weakness of the tongue and palate on the same side and motor and sensory loss on the opposite side of the body. With this may be associated motor inco-ordination on the side of the lesion from involvement of the cerebellar tracts, and also on the same side miosis and enophthalmos from involvement of the cervical sympathetic centre (*see* p. 606).

Cerebellum. The main afferent pathways to the cerebellum are the dorsal and ventral spino-cerebellar tracts, which convey impulses from the muscles and joints: fibres from the vestibular nuclei, which convey impulses from the labyrinths: and a large number of fibres from each cerebral hemisphere, which descend on either side of the pyramidal fibres in the corresponding half of the mid-brain (fronto-pontine and temporo-pontine tracts), end in the pontine nuclei, and thence are connected with the cortex of the opposite lobe of the cerebellum. The main efferent pathway from each lobe of the cerebellum is through the superior cerebellar peduncle, which crosses the mid-line to end in the opposite red nucleus. From the red nuclei arise the rubrospinal tracts which decussate shortly after their origin, and end in connection with the anterior horn cells of the spinal cord. On the efferent side, therefore, each lateral lobe of the cerebellum is, by means of this double decussation, connected with the lower motor neurons of its own side of the body. It receives impulses from the muscles of its own side, and from the cerebral hemisphere of the opposite side. The impulses derived from the labyrinths appear to be destined mainly for the middle cerebellar lobe.

Lesions of the cerebellum in man cause inco-ordination of voluntary movements, disturbances of posture and gait, and nystagmus. The most important symptom of a lateral lobe lesion is inco-ordination of the limbs on the same side. Although there is no loss of power, or ability to initiate movement, the working together (synergy) of the different muscle groups is defective. The result is disorder in the inception, progress and termination of willed movements, especially those in which large numbers of muscles are involved, or in which rapid alternation is required between opposing muscles. The disorder of function is more apparent in the upper than the lower limb. Asked to touch his nose with the tip of his forefinger, and then to touch the tip of the observer's finger, and to continue this alternation as rapidly as he can, the patient shows zig-zag deviation from the line of movement, particularly as his finger nears the target, and a tendency to under-shoot or over-shoot the mark. The limbs on the same side as the lesion are often hypotonic, the occiput as in labyrinthine lesions tends to fall towards the shoulder on the side of the lesion, and in walking the patient deviates or staggers towards the same side. The eyeballs tend to drift towards the opposite side of the midline so that nystagmus is obtained when the patient is asked to look towards the side of the lesion.

In lesions which are confined to the middle lobe of the cerebellum all the symptoms which have been described may be lacking, the outstanding clinical feature being an unsteady reeling gait, with no particular tendency to deviate or stagger towards one side or the other.

CLINICAL EXAMINATION OF THE NERVOUS SYSTEM

In the examination of the nervous system it is convenient to proceed according to a regular plan, which enables the observer to make a rapid survey of the case.

In the course of such a survey points will be noted which call for more detailed examination of particular functions, methods for which will be described in the text under the appropriate headings. The subjoined scheme is intended to serve as a practical guide to routine examination; the smaller type denotes points which are not considered essential in the absence of special indications for their use.

SCHEME FOR ROUTINE EXAMINATION OF THE NERVOUS SYSTEM.

1. Cerebral function.
   - Intelligence.
   - Temperament.
   - Speech.
2. The special senses.
   - (*a*) Vision.
     - Acuity.
     - Fields of vision.
     - The fundus oculi.
   - (*b*) Hearing.
   - (*c*) Smell.
   - (*d*) Taste.
3. The cranial nerves.
4. Sensory functions.
   - Sensibility to cotton wool.
   - Sensibility to pin prick.
   - Sensibility to temperature.
   - Sense of position.
   - Sensibility to vibration.
   - Stereognosis.
5. The motor system.
   - Involuntary movements.
   - Atrophy or hypertrophy.
   - Tone.
   - Power.
   - Co-ordination.
   - Electrical reactions.
6. The reflexes.
7. Sphincter control (urethral and anal).
8. Trophic changes.
9. Posture and gait.
10. Cerebro-spinal fluid.

1. CEREBRAL FUNCTION

Intelligence. A fair measure of the patient's intelligence may usually be made from the manner in which he gives the history of his illness. If the intellectual functions appear to be defective, further examination should be made. In estimating powers of memory for the remote past, it is important to compare the patient's account of his life with that given by friends or relations. Memory for the recent past may be tested by asking the patient to give an account of the past twenty-four hours, and it is important to make sure that he is correctly oriented as to date, place and persons.

Temperament. Variations from the normal may appear in the form of dominating moods of depression or elation, or as emotional instability. Such variations are most commonly met with in cases of functional nervous disease, in which further questions should be directed to the investigation of special pre-

occupations or troubles, and inquiry made as to the presence of imaginary ideas, feelings of inadequacy, obsessions or feelings of compulsion.

Speech. This may be affected by lesions at a high or a low level, the resultant disturbances of function being known as aphasia and dysarthria respectively. Aphasia means a partial or complete loss of the ability to comprehend ideas conveyed by words, *or* of the power of verbal expression. Dysarthria implies a defect in verbal articulation due to weakness or inco-ordination in the muscles involved.

The presence of aphasia will be detected in the course of obtaining the patient's history, and should be further investigated along the following lines :—

1. Can the patient understand spoken words ? Give him at first simple commands such as " Put out your tongue," proceeding to more complex directions, such as " Touch your right ear with the middle finger of your left hand."
2. Can he understand written words ? Give him similar commands in writing, first in block capitals, then in ordinary handwriting.
3. Can he spontaneously utter intelligible words ?
4. Can he write spontaneously ?

Failure in test 1 alone would indicate a pure word-deafness, in test 2 alone a pure word-blindness. These two conditions are very rarely met with as a result of minute lesions of the incoming auditory or visual paths to the speech centre. More commonly there is failure in both tests as part of general sensory aphasia.

Failure in test 3 alone indicates pure motor aphasia, in test 4 pure agraphia. These two functions also are most commonly lost together.

The patient with motor aphasia from a lesion of the foot of the inferior frontal convolution can understand reading and writing, and his intelligence is therefore unimpaired. He is rarely dumb, but his vocabulary is reduced, sometimes to a few very simple words, such as " Yes " and " No," whether he tries to express himself vocally or in writing. He is, of course, conscious of his own disability and its nature.

The patient with sensory aphasia, in addition to his failure of comprehension, also shows errors in the expression of speech, since his word-blindness and word-deafness render him unable to test the correctness of the words he is writing or uttering, a process which is apparently an essential adjunct to the mechanism for outgoing speech. He may talk fluently enough, but tends to mix up words and syllables, and may produce an unintelligible jargon, similar defects being shown in writing. He will naturally make mistakes in reading aloud, writing to dictation, or repeating words heard.

There appears to be a special tendency simply to forget the names of people and things, and to be unable to name objects seen, in lesions of the posterior part of the temporal lobe.

It is important to find out in a case of aphasia whether the patient is left-handed, and if not whether left-handedness is hereditary in his family.[1] Aphasia is found in lesions of the left side of the brain in right-handed people, and *vice versâ;* a right hemiplegia, if severe, is nearly always accompanied by aphasia, which is greater in proportion to the degree of paralysis of the arm.

(For further details as to the localisation of speech function *see* p. 614.)

Dysarthria. Since the muscles involved in articulation are innervated from both hemispheres, it is only when there is a lesion of the cortico-bulbar path on each side that an *upper neuron* lesion gives rise to paralytic dysarthria. This condition occurs in multiple vascular or syphilitic lesions of the brain, being commonly accompanied by emotional instability and a severe degree of mental impairment. It is called pseudo-bulbar palsy to distinguish it from the dysarthria caused by lesions of the *lower neurons, e.g.* that met with in progressive muscular atrophy affecting the medulla. Speech in all these cases is clumsy, as if

[1] Foster Kennedy has shown that in a right-handed person of strongly left-handed stock the speech centres may be situated in the *right* hemisphere, and *vice versâ.*

the patient had a hot potato in his mouth, and in true bulbar palsy the patient sometimes becomes completely anarthric.

Dysarthria may also result from a disturbance of the cerebellar co-ordinating mechanism, as in disseminated sclerosis and in some cases of cerebellar lesions (p. 718).

The above forms of dysarthria become apparent when the patient is giving his history, but in a suspected case of dementia paralytica in which the articulatory defect may be due partly to loss of power, partly to loss of co-ordination, and may be an early sign, it is useful to enjoin upon the patient the pronunciation of certain test phrases, such as "Methodist Episcopal," "West Register Street," etc. The defects to be looked for are slurring, elision of syllables or transposition of syllables or words.

2. SPECIAL SENSES

Vision. *Acuity.* In default of regulation test type, the acuity of vision may be roughly tested by getting the patient to read aloud from small print with each eye in turn; if acuity is poor, allow him to wear glasses if he has them; if these are correct, and the defect lies only in an error of refraction, his visual acuity should be normal with glasses.

Visual Fields. These may be roughly tested as follows: The patient places a hand over his right eye, and fixes the gaze of the other upon the pupil of the observer's right eye; the observer himself closes his left eye, and fixes his attention upon the patient's left eye; he then takes a small white object upon a handle —the most convenient is an ordinary white-headed hat-pin—and holding it midway between himself and the patient, brings it in gradually from the periphery towards the centre of the visual field, instructing the patient to say "Now!" when he sees it. In this way the observer can compare the field of each of the patient's eyes with his own and can discover defects of any considerable size. Examination of the visual fields is a most important procedure, and may lead to valuable discoveries, especially in the case of lesions affecting the optic tracts (*e.g.* pituitary tumour) or optic radiations (*e.g.* a vascular lesion at the posterior end of the internal capsule) (*see* p. 611).

Fundus Oculi. For the physician the eye is the window of the brain, and the electrical ophthalmoscope renders examination of the optic disc so easy that it should be made in every case in which nervous disease is suspected. The main changes to be looked for in the disc are œdema and atrophy.

Papillœdema is usually the result of increased intracranial pressure, and the mechanism of its production is discussed later (*see* p. 634). In a typical early case the central vein is engorged, the physiological cup filled in with exudate, and the edges of the disc, instead of being clear-cut, are hazy; later the œdema may be such as to give the disc a "chrysanthemum-head" appearance, and there are patches of exudate and hæmorrhages in the retina surrounding the disc.

In *optic atrophy* the disc appears paler than normal, and in an advanced stage of the condition stands out a dead white against the surrounding pink retina. The minute appearances vary somewhat with the cause and are discussed later (*see* p. 635).

It is important to realise that, while optic atrophy is always associated with some defect of visual acuity, the presence of an advanced papillœdema is consistent with the preservation of normal vision, and it is not until the swelling begins to subside and the condition passes into one of secondary atrophy that acuity becomes diminished. Other evidence of value may be found in some cases of brain disease from an examination of the retinal arteries, whose condition is perhaps the best index of that of the cerebral arterioles. In cases of cerebral arteriosclerosis the retinal arteries are often tortuous and thick-walled, nipping the veins where they cross them; there may also be visible beading of the

any one of the muscles which turn the eye inward the images seen by the two eyes will be crossed; *i.e.* if the right eye be closed the left-hand image will disappear, and *vice versâ* : while in paralysis of the muscles which move the eye outward the images will be uncrossed; *i.e.* if the right eye be closed the right-hand image will disappear. In the case of the muscles which move the eye obliquely the false image will also appear tilted at an angle to the true image depending (Fig. 76) upon the muscle involved.

The accompanying chart, devised by Bishop Harman, shows (1) the movements of the ocular muscles; (2) the position of the false image in paralysis. It should be remembered that in certain diseases, *e.g.* disseminated sclerosis and syphilis of the nervous system, ocular palsies may occur which are of very brief duration. It is therefore important in taking the history of a case of nervous disease to inquire for transient diplopia.

In the course of testing the ocular movements the examiner will note the presence or absence of *nystagmus*. This is a condition in which conjugate movements of the eyes are poorly sustained, and in place of a steady deviation we see a succession of jerky oscillations. These may be slow or quick, coarse or fine, lateral or rotatory.

It should be remembered that in persons weakened by old age or constitutional disease prolonged deviation of the eyes in a single direction will readily cause fatigue of the ocular muscles, and so give rise to oscillatory movements somewhat resembling those of nystagmus.

The Fifth, or Trigeminal Nerve. The distribution to the skin of the three branches of the sensory division of this nerve is shown in Fig. 66.

Sensibility to cotton wool, pin prick, and heat and cold over this area may be tested as presently to be described in relation to the other cutaneous areas. The buccal and nasal mucous membranes of the corresponding side are also supplied by each nerve. The earliest objective sign, however in lesions of the sensory root or its ophthalmic division is a diminution or loss of the corneal reflex on the affected side. This sign may be sought as follows: The patient is directed to fix his vision on some object to his extreme left, while the observer, standing a little behind him on his right, brings a wisp of cotton wool into light contact with the right cornea in such a manner that the object is felt before it is seen. The process is repeated for the left cornea, and the threshold for the blinking reflex on the two sides is thus compared.

The motor branch of the fifth nerve supplies all the muscles of mastication. In paralysis of this branch, when the patient's teeth are tightly clenched the observer by placing his thumbs against the anterior borders of the two masseter muscles can detect the weakness on the affected side, and when the mouth is opened wide the point of the jaw is deflected towards the paralysed side.

Subjective sensations of numbness, tingling, or pain in one or more of the areas supplied by the sensory root may precede objective phenomena in lesions of this nerve.

The Seventh, or Facial Nerve. In complete paralysis of this nerve the affected side of the face is mask-like, immobile, and expressionless; the naso-labial fold is smoothed out; the wrinkles disappear from the forehead; the eye is wider open than on the sound side; and the corner of the mouth hangs downwards.

The patient may complain of irritation of the conjunctiva on the affected side (owing to loss of the blinking reflex from paralysis of the orbicularis palpebrarum) as well as a certain clumsiness in speaking. Lesser degrees of weakness may be detected by requesting the patient to close his eyes tightly and show his teeth at the same time, a procedure which usually unmasks any asymmetry that may be present. The patient is also made to open his mouth widely, which brings the naso-labial grooves into prominence, when they may be compared.

The Eighth Nerve. The examination of the auditory functions of this nerve has already been described under the Special Senses. In cases of vertigo,

or of nerve deafness, in which it is desirable to investigate the vestibular functions, a simple method is as follows: The patient is made to stand up and turn rapidly round five times, first clockwise and after a short rest counter-clockwise. Immediately after the last turn in the clockwise direction (*i.e.* from his left to his right) he is made to fix his gaze on a point to his extreme left, and after turning in the opposite direction on a point to his extreme right. In each case transient nystagmus should be observed, and if the function of both vestibules is normal, the rapidity of the movements of the eyes and their duration should be the same when the individual is rotated clockwise or counter-clockwise.

The Ninth, or Glosso-pharyngeal Nerve. This nerve supplies sensory fibres, the posterior third of the tongue and the soft palate, and motor branches to the pharynx. The sensory function many be tested with a wisp of cotton wool fastened to the end of a probe.

The Tenth Nerve, or Vagus. The simplest objective test for the vagus is to ask the patient to say "Ah!" and watch the palate. Normally one sees the median raphé of the soft palate rise straight up, but if one side be paralysed, the healthy side alone pulls upwards, and the raphé deviates to the sound side, forming a characteristic dimple.

(For further symptoms *see* p. 640.)

Eleventh, or Spinal Accessory Nerve. In order to test the function of this pair of nerves, which are purely motor, one asks the patient to shrug his shoulders, which is effected by the trapezii, and then to flex his neck against resistance, which brings both sternomastoids into play in such a manner that the contractions of the two muscles may be easily compared.

Twelfth, or Hypoglossal Nerve. This nerve also is purely motor in function, supplying the tongue and most of the muscles attached to the hyoid bone. To investigate its function one asks the patient to protrude his tongue. In bilateral paralysis there is no movement; in cases of unilateral paralysis the tip of the tongue is pushed over towards the side paralysed by the sound muscles on the other side. If the paralysis is due to a lower motor neuron lesion (*i.e.* of the nuclei or fibres of the hypoglossal nerve), there is atrophy of the muscles on the affected side, and the superjacent mucous membrane is thrown into wrinkles.

4. SENSORY FUNCTIONS

Sensibility to Light Touch. The patient is asked to say "Yes" each time he appreciates the touch of a wisp of cotton wool or a camel's-hair brush. The examiner begins with a few touches over areas of skin not suspected of being anæsthetic, and if contacts are missed in other regions, applies the stimulus again to the normal areas from time to time to ensure that the failure to respond is not due merely to lack of attention.

The sensitiveness of the limbs is first explored by means of a few touches applied to each hand and foot; the investigation should then be carried longitudinally up each limb, and finally a series of stimuli should be applied, following the circumference of the limb at one or two levels. This will ensure that a small area of segmental anæsthesia is not missed. The skin area of the trunk is investigated in a similar manner. If a zone is discovered in which sensation appears to be lost or blunted, this must be carefully tested, and the resultant area of anæsthesia outlined in blue pencil on the skin, from which it may be copied on to a chart.

The investigator should not be content with an objective examination, but should direct the patient to inform him if at any point the stimulus appears relatively less distinct than in normal areas, and should especially inquire whether touch is appreciated equally on both sides of the body.

Sensibility to Pain is investigated along similar lines, the point of an ordinary pin being employed as stimulus. Here again it is most important to discover from the patient any quantitative diminution of sensation.

Kernig's Sign. In meningitis and some other conditions it is found that if the thigh be flexed at a right angle with the body, either by placing the patient in a sitting posture or by raising the thigh vertically while the patient is recumbent, it is impossible to extend the leg on the thigh to the same extent as usual, in consequence of the contraction of the hamstring muscles (*see* Fig. 77). The muscular spasm in this case is mainly due to a voluntary contraction whose object is to ward off the pain caused by stretching inflamed nerves or nerve roots.

Voluntary Power is systematically investigated by asking the patient to perform various movements against resistance, flexion and extension of the fingers, wrists and arms, pronation and supination, and so on.

In case of weakness due to a lesion of pyramidal fibres the muscles most affected are in the upper limb the extensors, with earliest loss of power in movements of the fingers and extension of the wrist, and in the lower limbs the flexors, with earliest involvement of dorsiflexion of the foot.

Inco-ordination of movement in the absence of weakness may be due to loss of sense of position and passive movement. This is best called ataxia in order to distinguish it from the inco-ordination of cerebellar disease, though the latter is sometimes spoken of as cerebellar ataxia. Many methods have been devised for testing co-ordination, of which the simplest and best are as follows :—

Finger-nose-finger Test. The observer holds up his right index finger in front of the patient and within his reach. The patient is instructed with the tip of his right index finger to touch first the end of his own nose, then the tip of the observer's finger, and to repeat these movements alternately as quickly and as neatly as possible. The observer meanwhile changes the position of his finger in relation to the patient between the contacts.

Inco-ordination is revealed by deviation from the line of movement with clumsiness and delay in arriving at the mark, and by a tendency either to stop short of it or overshoot it (dysmetria).

Diadochokinesis Test. The patient holding his arms semiflexed with the elbows to his sides, and fingers clenched, performs alternate movements of pronation and supination simultaneously with both forearms as rapidly as possible.

Inco-ordination is revealed by dysdiadochokinesis; the affected limb lags behind its fellow; its action is clumsy and unbalanced, and is made to appear more so by superfluous movements at the elbow and shoulder.

The Heel-knee Test. The patient in the recumbent position lifts one heel high into the air, places it gently upon the opposite knee and slides it steadily down the anterior border of the tibia as far as the ankle. This series of movements should normally be performed smoothly and evenly. Inco-ordination is revealed by unsteadiness and irregularity.

Electrical Reactions. The nature of the response of a muscle to electrical stimulation is sometimes of value in distinguishing between the different causes of paralysis, and in determining the moment at which recovery begins after a lower motor neuron lesion.

The student is presumed to be familiar with the methods of physiological application of the electric current to the stimulation of muscle and nerve, which are to be found in the text-books of physiology.

The faradic current is an adequate stimulus to nerves and nerve endings, and when applied to normal muscles in health provokes a brisk and well-sustained contraction, which is especially well marked if the electrode is placed over the point at which the motor nerve enters the muscle.

In the case of a complete lower motor neuron lesion there is no response to faradic stimulation either of the nerve or muscle involved; in the case of incomplete lesions there may be a quantitative diminution of the response.

To the galvanic current muscular contraction is only obtained when the circuit is closed and opened; none is observed during the continued flow of the current.

As there are two poles, four series of contractions may be observed, two on opening and closing the circuit where the stimulating electrode is the kathode and two on opening and closing the circuit when the anode is used as the stimulating point.

These are usually represented by letters as follows :—

K.C.C. = Kathodal closing contraction.
A.C.C. = Anodal closing contraction.
A.O.C. = Anodal opening contraction.
K.O.C. = Kathodal opening contraction.

In health, galvanic stimulation is effective whether applied to the muscle or the nerve, resulting in a short sharp contraction. If the strength of the current be constant and moderate, it is found that K.C.C. is greater than A.C.C.

In the case of a lower motor neuron lesion galvanic stimulation of the nerve no longer produces a response. The muscle, however, shows certain changes in its response, which are described as the reaction of degeneration (R.D.).

Qualitatively the response to galvanism is slow and sluggish, instead of short and sharp, and quantitatively it is found that with a constant strength of current A.C.C. is equal to or greater than K.C.C.

The return of faradic excitability in a muscle is usually the earliest sign of recovery from a lower motor neuron lesion.

In certain diseases, Thomsen's disease and myasthenia gravis, there may be characteristic changes in the electrical excitability, which are described under these headings.

6. THE REFLEXES

The reflexes are divided into superficial, deep, and visceral. Their presence depends upon the integrity of the sensory and motor end organs and the afferent and efferent paths involved in the reflex arc. They may also be modified by destructive lesions of higher centres, which have a controlling or inhibitory influence over them.

The reflexes of chief value in clinical examination are the following :—

Superficial Reflexes. The pupillary, corneal and pharyngeal reflexes are described under the Cranial Nerves. The abdominal reflexes are obtained by light stroking of the skin, with resultant contraction of the underlying musculature. There may be distinguished an epigastric mid-abdominal and lower abdominal reflex on each side. These are present and equal on the two sides in the great majority of healthy adults. They may, however, be absent when the abdominal wall is loose and pendulous, as in a multipara, in cases of intra-abdominal disease, such as typhoid, and when the patient is unduly cold.

Their absence, apart from these causes, implies an affection of pyramidal fibres ; the abdominal reflexes are lost on the opposite side of the body when the lesion is above the pyramidal decussation, on the same side if below it. Loss of these reflexes is frequently an early sign of pyramidal involvement, and a constant quantitative difference between the responses obtained on the two sides of the body may be of value in diagnosis in cases where there is no absolute loss. The cremasteric reflex is obtained by stroking the skin along the inner surface of the thigh ; the response is drawing up of the testicle. Together with the abdominal reflexes, it is lost in the affected side in cases of pyramidal lesion.

The Plantar Reflex. In conditions of health stroking the outer margin of the sole of the foot produces flexion of the small toes and of the great toe at the metatarso-phalangeal joint. This response may be complicated in ticklish persons by voluntary movements of withdrawal or rigidity due to apprehension. For the elicitation of the test it is best to have the lower limb lying passively extended. The skin should be warm and dry. The nature of the optimum stimulus depends in each individual case upon a number of variable factors. As a rule, firm pressure with the thumbnail drawn slowly from the heel towards the base of the toes along the outer border of the sole is sufficient, or a blunt-pointed instru-

ment may be used. The reflex response is lost in lesions of the reflex arc of the first sacral segment; in coma; with the sensory disturbances involving the sole foot in tabes; with paralysis of the toe muscles, as in acute poliomyelitis; and when the feet are cold. In the presence of a lesion of the pyramidal fibres, in place of the normal response Babinski's sign is elicited on the corresponding side; this consists of an upward movement of the great toe, with abduction and fanning of the others, and is accompanied by a contraction of the hamstrings. In cases of complete transverse lesion of the cord there ensues at first loss of the plantar responses, but with recovery from spinal shock there develops a mass movement of withdrawal of both limbs in response to stimulation of the sole of either foot.

Deep Reflexes. These are true reflexes, the activity of which is an indication of the state of the muscular tone, while their presence depends upon the integrity of the reflex arcs and end organs concerned.

They are tested by placing the limb in such a position as to relax the muscle whose tendon jerk is to be elicited. The observer then puts the muscle under slight tension and gives the tendon a sharp tap with a percussion hammer. The response is a contraction of the muscle and movement of the part. The deep reflexes of most clinical value are the following:—

The Triceps Jerk. This is obtained by semiflexing the arm at the elbow and striking the tendon just above its insertion into the olecranon.

The Biceps Jerk is obtained by flexing the elbow joint, placing the thumb upon the biceps tendon just above its insertion and slightly stretching the muscle. The thumb is then struck, and the biceps contracts.

The Supinator Jerk. To obtain this, the observer holds the patient's hand loosely with elbow semiflexed and forearm semi-pronated, and strikes the outer border of the radius just above the styloid process. The response is a contraction of the supinator longus (brachio-radialis) flexing the elbow.

The Knee Jerk. With the patient lying on his back, the observer, supporting the knee from beneath in a position of slight flexion, strikes the ligamentum patellæ sharply with the hammer. The result is a brisk contraction of quadriceps femoris. The knee jerks may equally well be obtained with the patient sitting in a chair and having one leg crossed over the other. It is essential that the limb should be fully relaxed. If the reflex is not elicited then, the patient's attention should be distracted, as by getting him to hold the fingers of one hand in those of the other, and to look up to the ceiling while he pulls at his hands (*Jendrassik's reinforcement*).

The Tendo Achillis, or Ankle Jerk. This is obtained by putting the calf muscles slightly on the stretch and tapping the tendo Achillis, the response being a brisk contraction of the muscles.

Ankle Clonus. *Ankle clonus*, or *foot clonus*, is a similar phenomenon, which occurs in certain spinal and other diseases, but is not, like the knee jerk, present in health, except in a modified form. To elicit it, the patient should be seated or recumbent; the leg is lifted with the left hand under the knee, so that the knee is slightly bent, and the foot, held firmly by the toes in the right hand, is sharply bent towards the knee. Immediately the calf muscles contract, but as the pressure on the foot is maintained, they relax, again contract, and so alternately contract and relax for an almost indefinite period, constituting the so-called *clonus*. The contractions occur at the rate of about seven in a second. The modification of this phenomenon which occurs in health is the series of rapid alternating movements which can be kept up continuously and without effort when, in the sitting posture, the foot rests upon the ground by the toes only.

A *knee clonus* can be sometimes obtained either as a result of percussing to get the knee jerk, or by pushing the patella down towards the tibia, while the leg is extended on a couch.

Exaggeration of the deep reflexes and ankle clonus are found together with absent abdominal reflexes and Babinski's sign as the result of pyramidal lesions. Loss of the tendon jerks may result from disease of the muscles, peripheral nerves, anterior or posterior roots, or anterior horn cells.

Quantitative alterations of the tendon jerks are of value when there is a marked difference in vigour between, for instance, the knee jerks and the ankle jerks, or between the responses obtained on the two sides of the body.

The state of the deep reflexes in general, however, may be influenced by many conditions, such as emotional excitement, fatigue, temperature and intoxication.

7. SPHINCTER CONTROL

The Bladder. Apart from obvious retention or incontinence of urine, the patient should be questioned with regard to a history of difficulty in commencing micturition or the more common fault of being unable to delay the act once conscious of the need (precipitate micturition).

The Rectum. The early symptoms of paralysis affecting this part are constipation, or more truly dyschezia (*see* p. 357), and when recourse is had to purgatives difficulty in controlling a loose motion, with occasional soiling of the garments.

8. TROPHIC CHANGES

The nutrition of the tissues is profoundly affected in some diseases of the nervous system, but there is no evidence of separate trophic nerves or neurons. The most marked effects are seen in lesions of nerve trunks and their centres, *i.e.*, those which injure the lower neurons, motor and sensory. Thus lesions of the anterior cornua (acute poliomyelitis) or of the nerves (injury, neuritis) are accompanied by marked wasting of muscle, which is not present in lesions of the brain or cord, involving the upper neurons only. Wasting of muscle is first shown by flabbiness, later by actual diminution in size. Its extent can be estimated by measurement, but it must be remembered that subcutaneous fat may completely mask a good deal of wasting so far as bulk is concerned. Other parts besides the muscles are often involved. The skin in some chronic cases becomes thin, red, and shiny—the "glossy skin" of Paget; erythematous, bullous, and vesicular eruptions (*e.g.* zona), œdema, whitlows and ulceration of the skin may occur; the finger nails are pinched, from wasting ot the subcutaneous tissue; the growth of hair and nails is retarded; and the nails are brittle. The bones may also suffer in their nutrition, becoming brittle or breaking easily; and if paralysis occurs in early life, growth of a whole limb may be retarded, so that it is eventually 1½ to 2 inches shorter than its fellow. In acute cases the temperature of the skin is raised, the vessels dilate, vesicles or bullæ form, and bedsores occur on the slightest irritation or pressure.

9. POSTURE AND GAIT

If the patient is not bedridden, he should be made to walk up and down the room in his ordinary manner, and any peculiarity of his carriage or gait should be noted. The changes characteristic of various lesions are described under other headings. It should be noted here that account must be taken of skeletal deformities and disease of joints, and further that weakness of certain groups of muscles (*e.g.* the hamstrings and glutæi) may lead not only to abnormalities in the gait, but also to the adoption of certain postures calculated to preserve the centre of gravity in the appropriate position.

10. CEREBRO-SPINAL FLUID

Examination of the cerebro-spinal fluid in disease often yields information of the greatest value in diagnosis. This fluid, as obtained by lumbar puncture, is

normally clear and colourless, and contains a trace of sugar sufficient to reduce Fehling's solution.

Pressure. Increased pressure of the fluid may be due to acute inflammatory changes in the meninges, with consequent outpouring of exudates into the subarachnoid space, or to increased intracranial pressure, as in cases of cerebral tumour. Variations in the intracranial pressure are under normal conditions transmitted through the fluid surrounding the spinal cord to the site of lumbar puncture, and if a manometer be attached to the needle these variations may be measured. The normal pressure with the patient in the lying posture varies from 60 to 150 mm. of water. A pressure above 200 mm. indicates a pathological increase of intra-cranial pressure. In a normal person digital compression of the jugular veins causes a sharp rise in the cerebro-spinal fluid pressure. The absence of such a rise indicates an obstruction in the spinal subarachnoid space, and is sometimes a useful point in evidence of compression of the spinal cord by growth or inflammation.

Blood in the spinal fluid taken for examination may come from a vein accidentally wounded at the moment of lumbar puncture. It may, on the other hand, be an indication of hæmorrhage into the subarachnoid space. A useful point of distinction is that blood from an accidental source, if left to stand, will coagulate in the test tube, leaving a colourless supernatant fluid. In the case of a pre-existing subarachnoid effusion coagulation will probably have taken place already at the site of hæmorrhage, and some hæmolysis will also have occurred. If the blood-stained fluid is allowed to stand the red cells settle to the bottom of the tube without the formation of a clot, and the supernatant fluid is coloured yellow or brown from the presence of altered blood pigment.

Bacteriology. In cases of acute infective meningitis the causal organism may often be seen in smears, and may nearly always be grown from cultures. When tuberculous meningitis is suspected the bacillus should be sought for and is often found, or the fluid may be injected into a guinea-pig.

Cell Content. The number of cells per cubic millimetre is of great importance. The normal value is below 3; any rise above this figure must be considered pathological, and is usually evidence of acute or chronic inflammatory changes in the meninges.

In cases of acute meningitis due to the meningococcus, pneumococcus, streptococcus, etc., the increase is in polymorphonuclear leucocytes, which are often sufficiently numerous to give the fluid a turbid appearance.

In tuberculous meningitis the majority of the cells are lymphocytes, usually in large numbers.

In acute poliomyelitis during the first week of the illness there is an excess of lymphocytes varying from 15 to 100 per cubic millimetre, and in encephalitis lethargica there appears to be a similar increase in the majority of cases.

In the various forms of cerebro-spinal syphilis there is an almost constant increase in the number of lymphocytes, ranging from figures just above the normal to 200 or 300 per cubic millimetre, the number depending upon the stage of activity of the disease and the degree of meningeal involvement.

An excess of lymphocytes may occasionally accompany a tumour of the brain or cord.

Protein Content. This may be roughly estimated on a quantitative scale by precipitation by boiling 2 c.c. of the fluid with 0·3 c.c. of 30 per cent. trichloracetic acid and comparing the density of the coagulum with that of standard tubes containing known percentages of albumin precipitated in the same way. The normal content is 0·025 per cent. This is increased in fluids from patients with acute infective meningitis as a rule to about 0·3 per cent., sometimes higher. In cerebro-spinal syphilis there is nearly always an increase, though the figure is not as a rule higher than 0·10 per cent. There is also a moderate increase in the other diseases enumerated in which raised cell counts

are found. A raised protein content is also encountered in certain cases of cerebral tumour and in polyneuritis.

The highest amounts of protein, however, are found in compression of the spinal cord. When, from any cause, the subarachnoid space is completely occluded at a level above that at which lumbar puncture is performed, the fluid obtained from the lower secluded sac has certain definite characteristics. It is clear, of a golden yellow colour, contains an enormous excess of albumin—up to 4 per cent.—and fibrin, so that it undergoes massive spontaneous coagulation. This is known as *Froin's syndrome.* The presence of simple excess of albumin in quantity greater than that met with in other conditions, without the golden colour or fibrin, may precede the appearance of the Froin syndrome, or appear as a stage in its retrogression.

The occlusion of the subarachnoid space may be due to disease of the vertebræ (caries or growth); fibrinous or cicatricial adhesions of the meninges, as after an acute meningitis or in syphilis; or the growth of a tumour from one of the meninges or within the cord. The cerebro-spinal fluid obtained from above the level of the block shows in every case a relatively normal appearance and albumin content. The Froin syndrome may be produced experimentally in animals by artificial compression of the cord with subdural injections of paraffin wax.

The cell count in Froin's syndrome depends on the pathological nature of the compressing cause, being high in the case of syphilis, low in all other cases.

Chlorides. The percentage of chlorides in normal cerebro-spinal fluid is constantly between 0·70 and 0·76 per cent. (NaCl). This may be slightly lowered in acute general infections, but a figure below 0·68 per cent. as a rule indicates meningitis. The lowest percentages are found in tuberculous meningitis, in which a figure of 0·60 per cent. or less is common. The point is, therefore, of considerable value in differential diagnosis.

The estimation is made by titration with standard silver nitrate, using potassium chromate as an indicator. Two cubic centimetres of cerebro-spinal fluid are required for the examination.

Wassermann Reaction. This is positive in the cerebro-spinal fluid at an early stage in every case of dementia paralytica, and in the great majority of active tabetics.

As regards cases which show clinical evidence of meningo-vascular syphilis the reaction is positive in a large majority of those in which the spinal cord is involved, not so constant when the disease is confined to the brain.

The Colloidal Reactions. It has been found that the cerebro-spinal fluid in certain diseases contains substances (probably foreign proteins) which, when added to a colloidal suspension, cause precipitation. Lange, employing a suspension of gold chloride, first applied this knowledge as an aid to differential diagnosis, and the colloidal gold test now in general use bears his name. It has been found that whereas in normal fluids there is no precipitation, in syphilitic diseases of the brain or spinal cord some degree of precipitation is almost constant. The test is performed by adding 0·1 c.c. of spinal fluid to 0·9 c.c. of normal saline, and from this preparing successive dilutions of 1 in 20, 1 in 40, and so on, to weaker dilutions in a series of twelve tubes. To each of these 2·5 c.c. of colloidal gold are added. The results of the test are expressed either in a graph or numerically, complete precipitation being taken as 5 and no precipitation as 0. In general paralysis of the insane (syphilitic encephalitis) the precipitation is maximal in the first tubes of the series, and a typical result will read 5555544321. This is known as the "paretic" reaction. In other forms of neuro-syphilis the tendency is towards maximal precipitation in the middle zone of the series, as 3455443210. This type of result is known as the "luetic." It has been found that an abnormal gold curve may also occur in many cases of disseminated sclerosis. Here again it may be of some diagnostic value taken in conjunction

with the other tests. An abnormal curve, together with a positive Wassermann, spells syphilis. With a negative Wassermann it should in itself suggest disseminated sclerosis.

A cerebro-spinal fluid containing an excess of protein, from whatever cause, may give an abnormal colloidal curve.

DISEASES OF THE NERVES

Lesions of the cranial and peripheral nerves differ in certain respects from those of the central nervous system, and especially in regard to the degree of recovery which may occur after a lesion which is anatomically and physiologically complete. This, no doubt, depends upon the presence throughout the peripheral nervous system (including the cranial nerves) of the neurilemmal sheath which permits complete regeneration of the nerve, even after transection, by downgrowth from the central end. The cranial and peripheral nerves also, being comparatively avascular structures, are more resistant to the effects of pressure as from chronic inflammation or new growth than the tissues of the brain and spinal cord.

Although the term *neuritis* properly implies inflammation, it is widely used in a clinical sense to describe the symptoms which result from all kinds of disease of the peripheral nerves and nerve roots, including such diverse causes as infection, intoxication and trauma.

Of these *trauma*—whether from a single severe blow, from repeated minor injuries or from stretching—will produce a local effect involving damage to the nerve sheath and more or less damage to the nerve fibres. Local injury to a nerve fibre which stops short of destruction results in temporary disturbance or loss of function with rapid recovery. Local destruction, on the other hand, leads inevitably to secondary descending degeneration followed by the downgrowth of new fibres from above—a process which must occupy a considerable period of time, varying with the length to be traversed by the new fibres from site of injury to periphery.

New growths of other parts frequently compress, and sometimes infiltrate, nerves in their vicinity, and there are in addition certain tumours which may arise from the nerves themselves. Of these the commonest and most important is the neurofibroma, which may grow from the sheath of cranial or peripheral nerves, the auditory nerve being a favourite site. Often these tumours are multiple and are associated with von Recklinghausen's disease (*see* p. 980). Plexiform neuromas are of the same pathological type as the neurofibromas, but are softer and more diffuse. They are commonly confined to a single area of the body, where they form a nodular mass of interlacing cords. The malignant tumours arising from nerve sheaths are, as a rule, sarcomas, spindle or round-celled.

Local infection of a nerve may occur as the result of direct spread from inflammation in neighbouring structures—bone, muscle, fascia, etc.

In such instances of local damage the nerve is affected in its whole thickness, and, since the connective tissue elements comprising the nerve sheath bear the brunt of the injury, the process is sometimes called an *interstitial* neuritis to distinguish it from cases in which the neuro-fibrils themselves are directly injured by a selective poison. This latter variety is sometimes called *parenchymatous* neuritis.

Bacterial or chemical poisons which have a selective incidence upon the nerves, are, as a rule, conveyed thither by the blood stream. Their action, therefore, is as a rule symmetrical, often multiple.

In certain cases, however, bacterial poisons emanating from an infective focus may travel up the perineural lymphatic sheaths, and gain entrance to the neural elements at the point where the posterior nerve root enters the spinal cord. The work of Orr and Rows in this connection has already been mentioned, as

also the evidence for supposing that the initial neuritis of diphtheria is due to a lymphogenous intoxication of this kind. Occasionally one meets with other examples such as an ulnar or median neuritis developing after a septic finger.

Damage to nerve fibres, whether due to injury or disease, causes disturbance of sensation, muscular power and bulk, and vasomotor control. The injury to the lower motor neuron results in wasting, weakness and flabbiness of the muscles supplied. The tendon jerks of the affected muscles are diminished or lost owing to the loss of tone, and damage to the reflex arcs concerned. The disturbance of sensation takes the form at first of uncomfortable tingling (pins and needles) in the sensory distribution of the nerve, followed by anæsthesia. There may also in the early stages be cramp-like pains in the muscles. The trophic and vasomotor changes have already been referred to. In addition to these symptoms in the distribution of the nerve, there are in cases of local damage, pain, tenderness and sometimes swelling at the site of the disease. In severe lesions of motor nerves the electrical reactions are altered (*see* p. 627).

In recovery from injury to a nerve, or after reunion of a divided nerve signs of returning function should appear within three months. With the return of sensibility pin prick and extreme degrees of heat and cold are appreciated before cotton wool touches. The return of power in the paralysed part generally precedes any decided improvement in the electrical reactions. In severe lesions with extensive atrophy of muscle, R.D. persists for some time, but after some weeks the irritability of the muscle to galvanism also diminishes, and finally becomes extinct.

OLFACTORY NERVE

A diminution or loss of the sense of smell (*anosmia*) arises from altered conditions of the nasal mucous membrane, such as excessive dryness, or coryza, and in affections of the base of the skull involving the olfactory bulbs, such as injury, tumours, caries of the bone, and meningitis. It sometimes occurs in tabes dorsalis, and is not uncommon in hysteria, as a part of hysterical hemianæsthesia. It should be remembered that loss of smell may affect the power of appreciating flavours, which really requires the combined action of the sense of taste and the sense of smell through the posterior nares.

Morbid subjective sensations of smell occur in the insane, and sometimes as an aura in epilepsy.

The primary cause of these defects must be treated, if possible.

OPTIC NERVE

The main points of anatomical importance in connection with this nerve and the methods of investigating its functions have already been referred to (pp. 612 and 621, Fig. 71).

Affections of the Optic Nerve. With the ophthalmoscope it is not always possible to distinguish between *optic neuritis* and *papillœdema,* but it should be borne in mind that, despite their similarity, these two conditions are the result of quite different pathological processes (*see* Plate 50).

Papillœdema is the term used to denote swelling of the nerve head (or papilla) due to the mechanical conditions produced by increased intracranial pressure, from whatever cause. The increased pressure, being transmitted to the sheaths of the optic nerves by way of the cerebro-spinal fluid in the subarachnoid space, gives rise to compression of the veins, with resulting transudation through the vessel walls at the point of least resistance, which is the nerve head; the same factors cause a blockage of the paths whereby this transudate might naturally be absorbed, so that the condition is a progressive one, and the papillœdema may increase until the highest point on the nerve head stands out 2 or 3 mm. in front of the general retina.

Optic neuritis, as the term implies, is an inflammatory condition of the nerve which may be caused by various infective or toxic agents. It is a comparatively uncommon condition. It may or may not involve the nerve head. If it does so, the appearance on ophthalmoscopic examination resembles that seen in papillœdema, and it should strictly be called *papillitis*. If it does not, the condition is spoken of as a *retrobulbar neuritis*, and at first gives rise to no changes recognisable with the ophthalmoscope, though later on the disc may show the pallor of optic atrophy from spreading degeneration of the nerve fibres and their replacement by fibrous tissue.

The causes of *papillœdema* are those which give rise to increased intracranial tension, of which cerebral tumour is the commonest. The causes of *papillitis* are few. It may be encountered in renal disease, in disseminated sclerosis when a patch of the disease happens to involve the nerve head, and rarely in other infective or toxic conditions. The common cause of *retrobulbar neuritis* is disseminated sclerosis. Methyl alcohol poisoning, or combined poisoning with ethyl alcohol and nicotine are occasional causes.

Optic Atrophy. This may be produced as the result of various processes, of which the most important are :—

1. Degeneration of the nerve fibres as the result of *syphilitic infection ;* the disc is of a greyish pallor with clear-cut edges ; this is frequently seen in tabes and dementia paralytica.

2. Degeneration of the nerve fibres secondary to a *retrobulbar neuritis ;* this is most commonly seen in disseminated sclerosis, in which the disc shows a dead-white pallor, which is best marked on the temporal side.

3. Degeneration of the nerve fibres as the result of *pressure* upon the optic nerve or optic tract. In this case the disc presents an appearance of startling pallor with exceedingly clear-cut edges.

4. Degeneration of nerve fibres *secondary to papillœdema* or *papillitis* with organisation of the exudate. The nerve head is dead white, but may still show some swelling ; the edges are indistinct, the physiological cup is filled in, and there are whitish streaks of exudate along the course of the vessels.

Optic atrophy of the first three types mentioned above is often called *primary optic atrophy*, in order to distinguish it from the *secondary optic atrophy* following swelling of the disc from œdema or inflammation. Vision is very greatly reduced or abolished in optic atrophy.

THIRD, FOURTH, AND SIXTH NERVES

The lesions causing ocular paralysis may affect—

1. The trunks of the nerves. Here the lesions are syphilitic and so-called rheumatic inflammations and toxic neuritis ; the pressure of orbital or intracranial growths, or of aneurysms, and rarely tumours of the nerves themselves ; direct injury ; and inflammation or suppuration spreading from the middle ear.

2. The nerve fibres in the brain connecting the nerve trunks with the nuclei, the chief causes being hæmorrhage, softening, tumours, and disseminated sclerosis.

3. The nerve nuclei. Nuclear palsies may be caused by focal lesions of the same type as those just mentioned, or they may be due to the selective action of some poison upon the nuclei themselves, as in tabes. A focal lesion can usually be distinguished from primary nuclear disease by the implication in the former of neighbouring structures, leading to nystagmus or the signs of motor and sensory disturbance. In the case of the fourth and sixth nerves it may be impossible to distinguish between a lesion of the nucleus and the nerve trunk. The third nerve, however, supplies the pupil, the upper lid and several of the muscles which rotate the eyeball. In a lesion of its trunk all these functions are affected together, whereas a nuclear lesion is apt to affect them separately. A lesion, for instance, in the anterior part of the nucleus may result in ptosis, pupillary paralysis and failure of

upward movement of the eyeballs, without any affection of the other muscles. Apart from disease of the oculomotor nerves myasthenia gravis should be remembered as a not uncommon cause of ocular palsy.

Treatment of Ocular Paralysis. This must depend upon the cause, if it can be ascertained. Syphilitic cases—and they form a very large proportion—should be treated by salvarsan and potassium iodide and mercury. For cases of an inflammatory nature counter-irritation by a blister behind the ear or leeches to the temple should be tried. If the paralysis has appeared to follow after exposure to cold, hot fomentations should be applied, and salicylates may be given internally. The so-called rheumatic cases, however, tend to recover without treatment. Diplopia may be relieved by the use of a prism, which should not be strong enough to fuse the images, but only to approximate them, so that muscular efforts may be encouraged.

FIFTH NERVE

The fifth nerve may be injured in any part of its course. In the pons its origin may suffer from tumours or hæmorrhage; its trunk may be affected by tumours or meningitis at the base of the brain; in front of the Gasserian ganglion the first division is liable to pressure from aneurysm, tumour or meningitis; the second and third divisions may be injured by growths arising in the nose or pharynx. Injuries to the mouth or nose may involve various branches of the second and third divisions, and neuritis of these branches may be caused by neighbouring inflammations.

Symptoms. These must depend on the position of the lesion. If the *sensory* fibres are involved, the result is anæsthesia of the face, corresponding to the distribution of the nerve. The loss of sensation is often preceded by tingling and numbness or neuralgic pains. The conjunctiva and the nasal and buccal mucous membrane are, of course, involved as well as the skin. If the sensory root of the ganglion or its ophthalmic division be involved the corneal reflex is lost early, and, when corneal anæsthesia is complete, as the result of unheeded irritation from foreign bodies, inflammation (neuro-paralytic keratitis) often occurs and the eye may eventually be destroyed. When the third division is involved, in consequence of the mouth being insensitive on one side, food is not chewed on that side, and a thick fur collects on the tongue for want of the cleaning operation of mastication.

Herpes zoster occurs especially in connection with the first division (*Herpes zoster ophthalmicus*), and appears to arise from inflammation of the Gasserian ganglion.

If the *motor* portion of the fifth nerve is involved, which is only likely to happen in lesions near the origin of the nerve, the temporal, masseter, and pterygoid muscles are paralysed, and after a time atrophy of the temporal and masseter muscles may be recognised.

Lesions of the sensory root between the ganglion and the pons usually give rise to progressive numbness and anæsthesia without pain. In the case of lesions of the ganglion itself or its branches anæsthesia is preceded or accompanied by pain. Paroxysmal trigeminal neuralgia is described on p. 754.

Diagnosis. The presence of severe pain may give for a time a resemblance to neuralgia, but anæsthesia, diminution or loss of corneal reflex, or wasting of the muscles supplied by the motor root prove an organic origin. If one or other branch is alone affected the lesion is in front of the Gasserian ganglion; if all the branches, it must be near the origin. The association of other nerve paralyses, such as those of the ocular nerves, or of the motor tract, may also help to localise the lesion.

Treatment. Besides dealing with the cause where this is possible, relief from pain may be obtained by injection with alcohol of the Gasserian ganglion or its branches.

SEVENTH OR FACIAL NERVE

The pathological interest of the seventh nerve chiefly centres in its motor fibres, and its tortuous course from the pons through a bony canal to its distribution on the face renders it especially liable to inflammation and compression. A focal lesion affecting the seventh nucleus almost inevitably produces other symptoms from involvement of the neighbouring structures, especially the sixth nerve. In its course through the cerebello-pontine angle the seventh nerve is closely associated with the fifth, sixth and eighth nerves, so that one or more of these are usually involved with it by disease in this situation. In the first part of its bony canal it is in close contact with the eighth nerve. An isolated affection of the seventh nerve is therefore most commonly due to a lesion in the lower part of the facial canal, or after its emergence from the stylo-mastoid foramen.

Nuclear palsies may be caused by inflammation or growth. In its intracranial course the nerve is not infrequently affected by a tumour in the cerebello-pontine angle, or by syphilitic meningitis. In the upper part of its bony course it is commonly involved by an extension of middle ear disease in this direction.

The commonest variety of facial paralysis, however, is that in which this nerve is affected alone by what is presumably an infective or toxic neuritis. The condition is known as Bell's palsy.

Bell's Palsy. This may occur at any age and affects both sexes equally. The ætiology is unknown, but exposure to cold seems to play a part in the causation of some cases. The onset is usually acute, and may be preceded by complaint of pains about the site of the stylo-mastoid foramen. The patient finds himself conscious of loss of power in the facial muscles and often complains that his face is drawn up towards the opposite side. Mastication and articulation are interfered with, and the eye becomes sore owing to incomplete closure of the lids.

Within twenty-four hours of the onset the progressive stage of the affection is at an end. It is then possible to estimate the degree of paralysis. In a moderately severe case all the facial muscles will be found paralysed with the exception of orbicularis palpebrarum, in which power is seldom completely lost. After a variable interval power gradually returns, beginning with orbicularis palpebrarum, and in the majority of cases recovery is complete within two months from the onset.

In estimating the prognosis the electrical reactions are of great value. A fortnight should be allowed to elapse before these are tested. If at this date from the onset the facial muscles respond to faradism the prognosis is good. Cases showing R.D. are unlikely to make a complete recovery.

A partial recovery is often followed by contracture of the paralysed muscles. These are somewhat shortened, the eye is a little closed, and the angle of the mouth is slightly drawn up by the zygomatici; and if the muscles of the sound side are at rest, the first impression that one gets is that the paralysed side is active and that the sound side is paralysed. This idea is corrected at once when the patient speaks or smiles, or tries to shut the eyes. The contracted side can contract very little more, while the sound side has a wide range of movement. In this condition also the affected muscles cannot be moved independently—in closing the eye, the angle of the mouth is raised; in smiling, the eye is partially closed. This is called *secondary over-action.* In children facial paralysis is not so obvious as in adults, because elastic tissue plays a greater part in the facial expression of children, whereas in older people the muscles are all important.

Diagnosis. The recognition of facial paralysis is not difficult. Bell's palsy is by far the most common variety, and may be distinguished by its sudden onset and the absence of other signs. The presence of middle ear disease on the affected side should always be looked for. Facial weakness from an upper neuron lesion may, as a rule, be distinguished easily owing to the fact that in this

the lower facial muscles are much more affected than the upper, and there is usually an associated weakness of palate and tongue. The electrical reactions also are normal.

Prognosis. This will vary with the cause. The prognosis in Bell's palsy has already been discussed above.

Treatment. Apart from treatment of the cause, where this can be found, attention should be directed towards preserving the functions of the weakened muscles. Electrical treatment may usefully be employed so long as the muscles cannot be exercised by the will. When the muscles respond to faradism electrical treatment can easily be managed. If they do not the galvanic current must be employed. The patient should also be encouraged to practise the use of his facial muscles daily before a mirror. Massage may also be of value. In a severe case the flaccid muscles on the paralysed side may be supported in the position of rest by means of a piece of copper wire ensheathed in rubber tubing, the two ends being bent so that one fits over the ear and the other hooks into the angle of the mouth.

EIGHTH NERVE

Various cerebral lesions may involve the nuclei of the nerve in the pons, or its higher connections in the brain; the nerve itself may be injured by meningitis, aneurysms or tumours; and the expansion of the nerve in the labyrinth may be damaged by acute or chronic inflammation, by syphilitic disease, or degenerative changes.

The results of these lesions are *deafness*, *vertigo*, and various subjective sounds, especially *tinnitus*.

Deafness from the above cause is called "nerve" deafness, and has to be distinguished from loss of hearing due to interference with the conduction of sound through the middle ear and external auditory meatus (*see* p. 621).

When the conduction is found to be normal, deafness must be due to a lesion either of the nerve or of the labyrinth. Which of these is more likely to be at fault must be determined by associated symptoms. These may sometimes point to an intracranial lesion, but, as a fact, deafness is not a very common symptom in cerebral cases, unless the trunk of the auditory nerve is directly compressed by a tumour.

Tinnitus Aurium. This term includes the various subjective sensations of sound, generally of a hissing, whistling, ringing, or roaring kind, with which, in their slightest degrees, nearly every one is familiar. It is clearly due to irritation of the auditory nerve fibres, and may occur in almost any form of disease of the ear, whether of the external meatus, of the middle ear, of the labyrinth, or of the nerve or nerve centres. Thus it may result from cerumen in the external meatus, is not infrequently present in acute and chronic inflammations of the middle ear, and is a prominent symptom in cases of tumour involving the eighth nerve between the internal auditory meatus and the pons. The commonest cause of tinnitus, however, is disease of the nerve endings of the cochlear apparatus. These may be affected temporarily by the action of certain drugs, especially quinine and the salicylates, or as a result of defective blood supply, *e.g.* in the secondary anæmia following a severe hæmorrhage. More frequently the tinnitus is associated with progressive deafness and is due to irritation of the nerve fibres as a preliminary to destruction. The cause in such cases may be disease of the bony capsule of the cochlea (otosclerosis), degenerative changes in the arteries leading to a permanently defective blood supply, or primary degenerative changes in the nerve fibres themselves as in the common form of Ménière's syndrome, whose cause is unknown, and which is sometimes called Ménière's disease. In the last instance the vestibular nerve endings are also affected with resultant attacks of vertigo.

Treatment. The cause of the tinnitus must be first considered. Disease of

the external or middle ear should be directly treated. In the cases of obscure origin the symptom may be alleviated by the avoidance of fatigue, especially of the mental order, and the prescription of sedatives such as bromide and luminal in small doses taken regularly.

Vertigo. The complaint of giddiness is a common one, and it is of the greatest importance in diagnosis that one should ascertain what are the actual sensations of the patient who uses this word to cover them. Disease or disorder of the vestibular nerve endings or their central connections gives rise to characteristic symptoms for which the term vertigo should be reserved. These may take the form either of sudden and transitory attacks or of a more continuous sensation. In the former instance the patient has a false sensation of movement of surrounding objects, of himself, or of both. The movement may be in any direction and is often rotary. Thus surrounding objects may appear to revolve in a clockwise or counter-clockwise direction, the ground may seem to come up towards the patient's eyes, or the ceiling fall ; or again he may appear to himself to be spinning or falling in one direction or another. In a severe attack he may fall. The after effects of such an attack may last for minutes, hours, or days, depending upon its severity, and during this period the patient has sensations of vertigo on movement, especially any quick movement of the head. At the height of the attack vomiting is a common symptom and may be severe and prolonged.

Vertiginous sensations of the milder degree may occur without any initial attack, the patient complaining of a continued state of unsteadiness which is aggravated by movement of the eyes or head.

Vertigo may be caused by an inequality of pressure upon the two sides of the tympanic membrane as from a plug of wax in the meatus, or a blocked Eustachian tube ; by acute or chronic otitis media ; by chronic degenerative disease affecting the middle and internal ear ; by syphilitic and arterial disease of the latter ; by tumour or syphilis involving the eighth nerve ; and by vascular lesions, syphilis, tumour or disseminated sclerosis affecting the central connections of the vestibular nerve in the brain-stem and cerebellum. Vertigo may also occur as the aura of an epileptic attack from disease of the cerebral cortex.

The first question to be asked when vertigo is encountered is whether it is associated with deafness or tinnitus, if so the lesion is almost certainly in the middle or internal ear or the eighth nerve. Affections of the latter are usually associated with involvement of other cranial nerves, especially the fifth, sixth and seventh. By a process of exclusion, therefore, the situation of disease in the ear can be inferred when present.

Lesions of the brain-stem or cerebellum are not necessarily associated with deafness or tinnitus, but give rise to other symptoms and signs (inco-ordination, paralysis, anæsthesia) which are of localising value. Vertigo as an epileptic aura is followed by disturbance or loss of consciousness. The aura may occur without any subsequent attack, but it is brief and is not followed by any aftermath in the shape of vertiginous sensations.

In the great majority of cases vertigo is due to that form of degeneration affecting the internal ear whose cause is unknown and which is sometimes called Ménière's disease.

Treatment. Vertigo is to be regarded as a symptom rather than a disease, and treatment must, therefore, be directed to the underlying cause when this has been ascertained. In cases due to chronic otitis media surgical treatment is required. In some instances syphilis is the cause of a destructive labyrinthitis and should be treated by the appropriate remedies. In those cases in which the pathology is obscure, potassium bromide appears to be of value in diminishing the frequency and the severity of the attacks, and should be given in doses of from 15 to 20 grains three times a day. Luminal, in doses of ½ grain thrice daily, or 1 grain night and morning, is perhaps even more valuable. When the

cause of the vertigo can be localised with certainty to the labyrinth and the disease is unilateral, relief may be offered by means of operation. Either the labyrinth is exposed and destroyed by injection of alcohol, or the eighth nerve is cut within the skull. Such procedures should be reserved for patients whose attacks are severe and disabling, but are then well worth consideration in that they afford the only means of permanent relief.

Ménière's Syndrome and Ménière's Disease. It has already been pointed out that the commonest cause of both tinnitus and vertigo is disease of the labyrinth from whatever cause, these two symptoms being then associated with deafness. This triad of symptoms is known as Ménière's syndrome, after the French physician who first described it and correctly inferred its labyrinthine origin. In one of the first cases which Ménière observed the symptoms came on acutely. The patient died, and the appearances suggested a hæmorrhage into the labyrinth. In all probability this was a case of acute streptococcal infection. Such cases are extremely rare. Commoner causes of labyrinthine disease are chronic otitis media, arteriosclerosis, head injury, and syphilis. It must be remembered also that Ménière's syndrome may be reproduced by disease affecting the eighth nerve, in particular the so called acoustic neurofibroma.

But in the great majority of patients who present Ménière's syndrome none of these causes are to be found. The story is usually that of a gradual onset of tinnitus and deafness, which begins in one ear, and after a considerable interval, usually of years, affects the other, the whole period being punctuated by attacks of vertigo. There may be long remissions in the course of the disease, and the state of the hearing may vary from time to time. Nerve deafness is always present but may be associated with middle ear deafness. For this large group of cases of uncertain cause Mygind and Dederding propose the term Ménière's disease, defining this as " a disease which so far as the ear is concerned shows itself by a varying function both of the acoustic and the static part, and with regard to which it has been possible to exclude any specific ætiology." Ménière's disease in this sense is a term which may be used with advantage provided that its implication of an undiscovered cause is remembered. The writer has observed in a series of patients with Ménière's disease that 9 per cent. also suffered from typical attacks of migraine (see p. 747).

NINTH OR GLOSSO-PHARYNGEAL NERVE

The nerve is rarely affected alone, but may be involved in tumours at the base of the skull together with the other nerves which pass through the jugular foramen. Its destruction results in anæsthesia of the mucous membrane covering the tonsillar region, and the posterior part of the tongue and soft palate on the affected side. The glosso-pharyngeal nerve may also be the seat of paroxysmal neuralgia, the pain being referred to the parts just mentioned and to the region of the ear drum and Eustachian tube. It is excited by movement of the fauces or tongue or contact of food with these parts, occurs in bouts of progressive frequency and severity, and is relieved only by section of the nerve.

TENTH, OR VAGUS NERVE

The motor nuclei of the vagus besides being responsible for the innervation of a considerable extent of the smooth muscle of the thoracic and abdominal viscera, supply motor fibres to the voluntary muscles of palate, pharynx and larynx. The sensory nucleus is concerned with visceral sensation only. The vagal nuclei in the medulla may be affected by thrombosis, hæmorrhage, new growth, syringomyelia, poliomyelitis or degenerative change (progressive bulbar palsy). At the base of the skull the nerve may be compressed by new growth or chronic inflammation (syphilitic, tuberculous or suppurative) of meninges or skull. In

the neck and chest the trunk of the nerve or its recurrent laryngeal branch are not infrequently involved by aneurysm, new growth or enlarged glands.

The symptoms to be looked for in a lesion of the vagus are those which result from paralysis of palate, pharynx and vocal cord.

The *palate* on the affected side fails to rise on phonation, the uvula being drawn over to the unaffected side. The posterior wall of the *pharynx* on the affected side is drawn laterally over to the unaffected side on phonation (curtain movement of pharynx).

The *vocal cord*, following a lesion at any point between the nucleus and the recurrent laryngeal nerve, is completely paralysed and lies in the cadaveric position. With this there is usually some hoarseness and difficulty in coughing. A lesion of the recurrent laryngeal nerve results in abductor paralysis only, and phonation and coughing are unaffected. The vomiting, irregular respiration and slow pulse rate, which occur as the result of increased intracranial pressure, are presumably due to the effects of the pressure upon the vagal nuclei. (*See also* p. 208.)

Treatment must be conducted on the lines indicated in the case of other nerves. (*See also* Diseases of the Larynx.)

ELEVENTH OR SPINAL ACCESSORY NERVE

The external portion of this nerve arises by a series of roots from the cervical part of the spinal cord, and is really a motor spinal nerve directly connected with the anterior cornua. It is distributed to the sterno-mastoid and trapezius muscles.

In addition to cerebral and intracranial lesions, like those which may involve the vagus, the spinal accessory may be injured by caries of the cervical spine, by enlarged glands or abscesses in the neck, or by blows and strains. If the lesion is in the posterior triangle, the sterno-mastoid will of course be spared. Paralysis of the sterno-mastoid is shown by the want of prominence due to contraction of this muscle, and by deficient power of rotation of the head to the opposite side. In paralysis of the trapezius, the natural slope between the neck and the shoulder is converted into a deep hollow, which is exaggerated when the shoulder is raised, as it still can be by the action of the levator anguli scapulæ. The point of the shoulder lies lower than normal, and the posterior border of the scapula is inclined from below upwards and outwards. Elevation of the hand above the head is, however, difficult or impossible, because the trapezius does not fix the scapula for the use of the deltoid, nor does it assist in that rotation for which the serratus magnus is chiefly employed. With a persisting lesion atrophy and electrical changes naturally follow.

Treatment. Here we must deal, when possible, with the causative lesion and with the muscular failure by electrical stimulation, and massage.

TWELFTH OR HYPOGLOSSAL NERVE

The commonest cause of a muscular lesion is motor neuron disease (progressive bulbar palsy), both nuclei being affected together. Unilateral destruction of the nerve fibres in their intramedullary course occurs in occlusion of the postero-inferior cerebellar artery. At the base of the brain the nerve may be involved by new growth or syphilitic meningitis, and outside the skull by malignant glands, inflammation or injury. When one side of the tongue is paralysed the organ is pushed over to the affected side on protrusion. When the paralysis is bilateral the tongue lies motionless in the mouth and deglutition and articulation are seriously affected. Wasting of the muscles results in a wrinkled appearance of the mucous membrane, which is especially apparent when the affection is unilateral. Fibrillation is usually to be seen in the wasting muscles. This again is easily

recognised when the paralysis is unilateral, but in the case of bilateral palsy may be confused with the fine irregular tremor often seen in the protruded tongue of a normal person. In such cases it is best looked for with the tongue lying at rest in the open mouth.

Treatment. This must follow the causal indications.

LESIONS OF SPINAL AND PERIPHERAL NERVES

The spinal nerves may be injured or diseased at the roots, or in the plexus or nerve trunks beyond them.

Lesions of the nerve roots arise in connection with diseases, injuries and tumours of the spinal cord or spinal column, and the symptoms may be combined with those of the central affection, as, for instance, in the case of a tumour growing from the dura mater, syphilitic meningitis or tuberculous caries. Lesions of the spinal nerve trunks are mostly from new growths, aneurysms, and abscesses in or near the spinal column. The roots emerging from the intervertebral foramina may also be affected in the course of a rheumatic fibrositis (radiculitis). Effusion into the nerve sheaths may also occur as the result of comparatively slight trauma, or excessive stretching, especially if this is often repeated. Inflammation of the nerve sheaths sometimes results from poisons gaining access from the blood stream, and these may be either of bacterial origin or by-products of faulty metabolism. Owing probably to their more exposed position and greater liability to stretching the nerve fibres of the brachial and sciatic plexuses are those chiefly affected by these causes.

Since the spinal nerves contain both motor and sensory fibres, the symptoms of their lesions are both loss of muscular power and anæsthesia, determined by the distribution of the nerve fibres to muscles and skin respectively. If the lesion is persistent, atrophy and altered electrical reactions (*see* p. 627) of the muscles will ensue, and perhaps trophic changes in the skin.

Treatment. The results of these lesions which require treatment are paralysis and muscular atrophy on the one hand, and pain or other sensory symptoms on the other. In either case a removable cause, such as pressure by abscess or tumour, should, if possible, be dealt with ; or, if a toxic neuritis is the presumed cause, all possible sources of infection or intoxication in the body should be investigated and remedied as far as may be, *e.g.* pyorrhœa alveolaris, septic tonsils, chronic infections of the alimentary tract. Atophan and aspirin may be given internally, and dietetic reform prescribed in cases suspected of a gouty origin. Massage, electrical stimulation and exercises are of use in dealing with the paralysis. For pain the local application of heat, or of the liniments of belladonna, aconite, turpentine, etc., may be valuable. *Rest* is also essential for a quick recovery ; the arm should be carried in a sling, or, if the leg is affected, the patient should lie in bed, and when necessary special splints should be employed to maintain paralysed muscles in the position of rest.

Some of the more important and frequent lesions of the spinal nerves are here shortly described.

UPPER CERVICAL NERVES

These may be involved in diseases of the upper part of the spine, especially in tuberculous disease of the atlas or axis. The posterior rami are often affected by neuritis of traumatic or toxic origin. The common " crick " of the neck is a familiar example of minor injury, and in persons predisposed to toxic neuritis cold appears to be a deciding factor in producing an attack (*e.g.* sitting in a draught). If the trouble is confined to the branches of the second cervical nerve the pain is felt in the occipital and sub-occipital regions and is frequently complained of as headache. Tenderness over the scalp and the points of emergence of the great occipital nerves are present during the paroxysms of pain and serve to distinguish these cases from those of intracranial disease.

use, *e.g.* hot water bottles or an electrically heated pad continuously applied to the painful spots.

As a counter-irritant a mustard leaf applied over the centre of pain with three or four layers of handkerchief between it and the skin is often valuable. Used thus it may be allowed to remain *in situ* for six or eight hours without raising a blister, and the application may be repeated as soon as the state of the skin will allow it. Diathermy and galvanism may also exert a sedative action.

As a rule the patient may be allowed to get out of bed to the lavatory or commode, but when, despite this degree of rest, after a few days the pain continues unabated, he should be nursed continuously in bed.

The motions should be kept soft by means of liquid paraffin.

Various accessory methods of treatment have been devised from time to time whose object is to stretch the nerve or its roots and so break down adhesions. These are best avoided in the acute stage, and will naturally be left alone at a later stage when progress is satisfactory. In some cases, however, a point is reached when the patient is free from pain except during or after certain movements, and it is in these that stretching may be of value. The methods in use are injection of saline into the nerve trunk below the sciatic notch, injection of saline under tension into the epidural space through the sacro-coccygeal foramen, or manipulation of the affected limb and lower back under general anæsthesia. In the writer's experience the last method has been the most successful, but it should be reserved for selected cases.

Most patients with sciatica will recover completely with rest, heat, sedatives and analgesics if they can be persuaded to persevere with this treatment. Rest should be strictly maintained until the patient has been reasonably free from pain for a few days before any liberty of movement is allowed, and it should then be remembered that movement of a kind which does not cause pain at the time may be followed by it afterwards. Great care, therefore, should be exercised in treading the path of convalescence. For some time stooping movements should be avoided and a cushion or rubber ring should be used to avoid pressure in sitting. In the final stage of convalescence massage and exercises are of use in restoring the function of the limb and correcting faulty posture.

The part played by focal sepsis in the causation of sciatica is doubtful. Infected teeth or tonsils are generally best left alone during the attack, but may be dealt with later with the object of preventing recurrence, and with the same end in view modifications of diet and *régime* may be advised.

Meralgia Paræsthetica. This is an affection, probably inflammatory, of the external cutaneous nerve of the lumbar plexus. The symptoms are *pain*, sometimes brought on by walking, at others when the patient is lying still or sitting, and abnormal sensations, such as numbness, pins and needles, cold feeling, burning sensation of tightness, felt on the front and outer part of the thigh within the distribution of the above nerve. Over the same area there is some modification of sensibility, either hyperæsthesia, or more often anæsthesia, or changes in the appreciation of pain, heat or cold. In most cases there is some tenderness on pressure below the anterior superior iliac spine, where the nerve comes through the fascia lata. It is more frequent in men than in women, and has been attributed in different cases to injury and to toxic and infective agents. Rest, warm baths, and counter-irritants should be tried for its treatment.

In chronic cases the nerve may be found constricted by fibrous contracture of the opening in the fascia lata, and the condition may be relieved by the minor operation of slitting up the channel in the fascia and so releasing the nerve from pressure.

MULTIPLE NEURITIS

(*Peripheral Neuritis, Polyneuritis*)

Ætiology. It is in only a minority of cases that the cause can be definitely traced. The known causes may be divided into: (1) Poisons introduced into

the body from without. Of these the best known are alcohol and arsenic. Carbon bisulphide, carbon monoxide and dinitro-benzol may also be responsible. Lead is often included in this category, but acts rather upon the muscle fibre directly and the anterior horn cells (p. 588). (2) Poisons arising within the body. Of these the commonest is hyperglycæmia in diabetes. Beri-beri may also be included in this class, as also certain rare instances in which polyneuritis and hæmatoporphyrinuria are associated. Probably a number of the cases of obscure origin are caused by toxins arising in the body as the result of faulty metabolism, and these are sometimes spoken of as "gouty" or "rheumatic." (3) Bacterial toxins. The common instance is diphtheria, but polyneuritis has been recorded as a rare complication of many other infective fevers. (4) There appears to be a special liability in cachectic states such as accompany malignant disease and tuberculosis.

Morbid Anatomy. The characteristic picture is of degenerative changes in the nerve fibres, without affection of the nerve sheaths. There is thus no abnormality visible to the naked eye, but microscopic examination by the Marchi method shows fragmentation and fatty degeneration of the myelin sheath. The axis cylinders are less affected. These degenerative changes are most marked in the peripheral nerve twigs, being slighter as one approaches the spinal cord, and the anterior roots are usually normal.

Symptoms. The clinical picture of polyneuritis varies somewhat with the cause in operation. The following description applies to the majority of cases.

The onset, as a rule, is gradual, with complaint of "tingling," or "pins and needles" in the toes and fingers. These subjective sensations of discomfort gradually spread upwards, but do not usually advance higher than the knees and wrists. They are commonly accompanied by occasional "cramps" of a painful nature in the muscles of leg and forearm. Motor symptoms as a rule follow the sensory disturbance. There is weakness, especially of the dorsiflexors of the feet with consequent foot-drop, and in walking the knees are lifted high in order that the hanging toes may clear the ground ("steppage gait"). The movements of the fingers are impaired so that the grip is weakened and fine movements, such as doing up buttons, become impossible. If the weakness extends higher in the arms the extensors of the wrists are usually next affected with the appearance of "wrist drop." The circulation in the affected extremities is often enfeebled so that they become cold and blue.

On examination it is found that cutaneous sensibility is impaired in the areas in which numbness and tingling are complained of, the degree of impairment being less as one proceeds upwards from the periphery. Deep sensibility is less affected, and the muscles are frequently unusually tender to pressure. The enfeebled muscles are flabby, and if the disease has been present for more than two or three weeks, show wasting, which is most evident in the small muscles of feet and hands, and the calves of the legs. The tendon jerks in the earliest phase of the disease are temporarily exalted. Later they are diminished or lost, the earliest to disappear as a rule being the ankle jerks; loss of knee jerks follows if the case is a severe one, and the supinator jerks also are affected if the upper limbs are extensively involved.

The symptoms are usually symmetrical, but may commence in one extremity before the others. The lower limbs are, as a rule, more severely affected than the upper.

The cranial nerves are not affected, and there is no loss of sphincter control.

In some cases, however, although the initial complaints are very much the same the clinical picture develops in a different form. Deep sensibility—including sense of position and passive movement, and the vibration sense—is extensively affected, and muscular weakness is more widely and more evenly distributed. The patient then has difficulty in estimating the extent and direction of his movements, and therefore staggers in his gait, flinging his lower limbs about in a

manner reminiscent of tabes. This clinical variety is known as *ataxic polyneuritis*, and is probably due to an extension of the toxic effect to the posterior columns of the spinal cord.

Polyneuritis is sometimes accompanied by a peculiar condition of mind, which is most frequent in alcoholic neuritis, but also occurs, as was first observed by Korsakow, in multiple neuritis from other toxic causes (puerperal septicæmia, typhoid, influenza). He therefore called it *psychosis polyneuritica*, and it is also known as *Korsakow's syndrome*. The patient suffers from loss of memory for recent events, is ignorant of his whereabouts, has false memory, and describes events which have never happened. Thus he will be unable to tell his name, age, the day of the week, or where he comes from; but, on the other hand, he may say that he has been for a walk, a ride, or has seen certain friends, in obvious antagonism to facts. There may be a stage of talkativeness, or even delirium; but in advanced cases the patients show extreme apathy, and complete indifference to surroundings.

In cases of known causation there occur variations from this description, which in some instances are characteristic. Those in the case of diphtheria and lead-poisoning are described on pp. 65, 588.

Alcoholic Neuritis occurs more often in women than in men, and commonly results from frequent slight excess. It is at present a rare disease in this country. Other signs of chronic alcoholism, such as dyspepsia and cirrhosis of the liver, may or may not be present. The lower limbs are more seriously affected than the upper and may be involved alone.

Complaint of painful cramp in the calves and tenderness of the same parts to pressure are prominent symptoms. Of the cranial nerves the vagus is sometimes affected, leading to persistent tachycardia, and (rarely) to laryngeal paralysis. Nystagmoid jerkings of the eyeballs are often present (due probably to slight weakness of the motor nerves), and the facial muscles may also be involved.

Arsenical Neuritis. This occurs occasionally as a result of continued full doses of arsenical preparations given medicinally. In the year 1900, in Manchester and some other towns in the north of England, a number of cases of neuritis, at first thought to be due to alcohol, were shown to be caused by the accidental impregnation of beer with arsenic in the process of brewing.

The distribution and character of the sensory and motor symptoms are much the same as in alcoholic neuritis, but there are in the arsenical form greater cutaneous hyperæsthesia, more frequent affection of the facial muscles and lower intercostal muscles, earlier atrophy, more frequent inco-ordination, and more rapid progress (Judson Bury), and extreme sensitiveness of the muscles to pressure (Reynolds).

Diabetic Neuritis. Although the complete clinical picture of polyneuritis may be met with in this disease, more commonly it is found that the ankle and knee jerks are diminished or absent without any sensory complaint or localised muscular weakness; in the latter case degeneration of the posterior columns has been found as in tabes.

Acute Febrile (or Toxic) Polyneuritis. This is a somewhat rare illness, in which preliminary symptoms of constitutional disturbance with or without pyrexia are rapidly followed by those of polyneuritis, without any discoverable cause. The cranial nerves are frequently involved, especially the seventh, and if, as often occurs, this affection is bilateral, a remarkably expressionless facies results. Superficial sensibility is little affected, nor is pain at all a prominent feature, but there may be considerable loss of the senses of position and passive movement. The weakness is more widespread and more evenly distributed than in most cases of polyneuritis caused by known poisons. In some cases the proximal rather than the peripheral groups of muscles may be involved. There is some risk to life from broncho-pneumonia in the early stages, if the muscles of deglutition

are involved, but after two or three weeks steady improvement sets in, and complete recovery may be expected.

Associated Conditions. As neuritis is frequently caused by poisons from without, such as alcohol, arsenic, and lead, its symptoms are often associated with others due to the particular poison concerned: thus in alcoholic cases cirrhosis of the liver may be present; in arsenical cases, various lesions of the skin, viz. pigmentation, keratosis or hypertrophy of the epidermis, erythema and herpes zoster. Cardiac failure with œdema occurs with the neuritis of beri-beri, and may be present in arsenical, alcoholic, and diphtherial cases.

Diagnosis. The early symptoms of polyneuritis bear a close resemblance to those of *subacute combined degeneration*. The peripheral numbness and weakness and loss of ankle and knee jerks are common to both. In combined degeneration, however, symptoms of spinal cord disease are usually present in the form of girdle pains, sphincter disturbance, or extensor plantar responses. Lesions of the lumbar enlargement of the spinal cord or cauda equina may also produce weakness of the lower limbs with absent tendon jerks, but here again sphincter disturbance and the segmental distribution of the anæsthesia are points of distinction. Some cases, especially those of the ataxic form of polyneuritis, need to be distinguished from tabes. But in the latter disease there is usually a history of lightning pains, quite unlike the sensory complaints of neuritis, the arms are rarely affected at the same time as the legs, and the calf muscles, so far from being tender, are unusually insensitive to pressure. Other signs of tabes, especially Argyll-Robertson pupils, are also of use in the differential diagnosis.

Acute febrile polyneuritis in a child may easily be mistaken for poliomyelitis, but in the former disease the distribution of the weakness is more symmetrical, its degree more uniform and its development more gradual. The afebrile or toxic variety, especially if the onset is relatively gradual and sensory disturbance is slight, may need to be distinguished from motor neuron disease (progressive muscular atrophy).

A point which is sometimes of value in differential diagnosis is that in cases of polyneuritis, especially the acute or rapidly progressive forms, there is usually a considerable excess of protein in the cerebro-spinal fluid without any corresponding increase in the number of cells.

Prognosis. Alcoholic cases may be fatal either in an early stage where the cause is not promptly removed, or after months from emaciation, or bedsores, or phthisis. In many cases the symptoms develop rapidly in the first six or eight weeks, and then the condition of the patient may remain stationary for months, or very slowly improve. After years recovery may be only partial. But in alcoholic and in other cases where the disease is not too far advanced, and the cause can be completely removed, the prognosis is more favourable, recovery taking place slowly in the course of from two to six months. In the cases of unknown origin complete recovery is the general rule, although relapses may occur. The duration of the illness varies with its severity. When the paralysis is widespread and severe it may be a year or more before recovery is complete.

Treatment. If any external poison such as alcohol or arsenic is the cause, it must be henceforth kept from the patient. In diabetic cases the cause should be treated. In acute and severe cases complete rest is sometimes necessary, at first on account of the muscular pains. As soon as possible massage and active and passive movements should be commenced: in milder cases these measures should be employed from the beginning. In very slight cases it is not necessary that the patient should go to bed, but he should be warned against fatiguing the affected limbs. Splints are frequently necessary to prevent contractions. In severe cases these must be worn continuously. At a later stage of the illness, or in less severe cases, it will suffice that they should be worn at night only. The

electric current should be used to stimulate muscles which cannot be exercised by the will.

Of drugs, aspirin is useful for the pains of onset: atophan may be given in cases suspected to be of gouty causation: and a strychnine mixture should be prescribed during convalescence. (*See also* treatment of fibrositis.)

LOCALISED MUSCULAR SPASM

Involuntary spasm of muscles may occur as a part of the response to disease or injury in any part of the body, being a simple protective reflex designed to prevent movement and confer rest. Tonic or clonic spasm may also be encountered in a variety of nervous diseases described in other parts of this volume. In some instances, however, localised muscular spasm may occur as an isolated symptom. Two of these, facial spasm and hiccup, will be discussed here.

Facial Spasm. This is a condition of obscure origin occasionally seen in persons past middle age. The spasm, which is mainly of the clonic variety, first affects the orbicularis palpebrarum, but is apt with time to spread to the other muscles supplied by the seventh nerve. The frontalis and obicularis oris, however, usually escape. At rest there may appear to be some tonic overaction of the side of the face affected, but on voluntary movement to request this side is seen to be slightly the weaker. The clonic spasms are intermittent and irregular, and are increased by fatigue and nervousness. They are quite painless, but may give rise to worry and discomfort. The condition is always in the first phase, unilateral, but may ultimately involve the other side.

Diagnosis. This must be made from such gross causes of irritation of the seventh nerve as tumour or meningeal inflammation within the cranium, bony disease, or the pressure of an enlarged gland. True facial spasm may be distinguished from these by its protracted painless course and the absence of other physical signs.

Treatment. In an early or mild case relief from mental stress, together with sedatives, such as bromide or luminal in small doses, may bring about improvement. Many persons, even if the condition is severe or continuous, learn to ignore it. For those who are willing to accept a facial palsy instead of the spasm, the nerve may be injected with alcohol as it emerges from the stylomastoid foramen. The effect, however, wears off and the injection needs to be repeated every six to twelve months.

Hiccup. This is due to a spasmodic contraction of the diaphragm, causing an abrupt inspiration which is cut short by a sudden closure of the glottis. Hiccup is usually due to some recognisable cause in the way of visceral distension or irritation, either below or above the diaphragm. It may also be caused by irritation of the phrenic nerve, and sometimes by disease or poisoning of the nervous centres in spinal cord or medulla. It may also occur from excessive laughter, and sometimes for no apparent cause. It may in rare instances persist for several days and in itself demand treatment. It may often be stopped by holding the breath. In more obstinate cases a paroxysm of sneezing, induced by tickling the nose, or a whiff of snuff or pepper, may be effective. Other remedies which have been advocated are atropine $\frac{1}{100}$ grain, hypodermically, to be repeated in four hours if necessary, hyoscine hydrobromide $\frac{1}{100}$ grain, hypodermically, inhalation of a capsule of amyl nitrite, or a hypodermic of morphia. The passage of a stomach tube or inhalation of a mixture of carbon dioxide with air or oxygen may be successful in stopping a refractory attack.

DISEASES OF THE SPINAL CORD

For the proper understanding of this group of diseases an acquaintance with the principles of physiology and anatomy summarised on pp. 593 *et seq.* is essential.

Primary Disease of the Neurons. The several groups of neurons in the spinal cord may be separately affected by degeneration or disease. Such degeneration is the result of toxins, or is due to congenital want of vitality, or remains entirely unaccounted for. The lesions have been known as *tract diseases* or *system diseases*, and the following are instances: tabes dorsalis, in which the posterior columns are diseased; primary lateral sclerosis—pyramidal tracts; subacute combined degeneration—posterior columns and pyramidal tracts; Friedreich's disease—posterior columns, pyramidal tracts and spino-cerebellar tracts; progressive muscular atrophy—anterior horn cells; amyotrophic lateral sclerosis—anterior horn cells and pyramidal tracts.

Transverse Lesions. The spinal cord, having an elongated form, is naturally liable to lesions affecting its whole thickness, such as may occur from trauma, localised external pressure, the indiscriminate growth of tumour, the diffuse spread of inflammation, or the anæmia of vascular obstruction. In such cases grey and white matters are equally affected.

COMPRESSION OF THE SPINAL CORD

The spinal cord, on account of its soft consistency, is subject to compression as the result of disease or injury of neighbouring parts. The pathological changes which take place under such circumstances are the same whatever the actual cause. The symptoms, which are those of a transverse lesion, naturally vary with the level of the lesion. Other variations may be due to the rapidity with which the compressing force acts, and to the actual nature of the compressing cause.

Ætiology. The causes of spinal compression may be divided into: (*a*) disease of the vertebral column, (*b*) disease of the extra-dural space and meninges.

(*a*) *Disease of the Vertebral Column.* The spinal cord is frequently compressed suddenly as the result of *injury* with fracture dislocation. Of causes acting more slowly the commonest are *tuberculous caries* of the vertebræ or *new growths.*

(*b*) *Disease of the Extra-dural Space and Meninges. Injury* may occasionally result in hæmorrhage into the meninges, with subsequent cicatrisation and compression. Commoner causes of cicatricial constriction are a localised *syphilitic meningitis;* or a preceding *suppurative meningitis.*

New growths of various kinds may arise in the extra-dural space, in the meninges, or upon the nerve roots.

Morbid Anatomy. Sudden compression of the spinal cord, such as occurs from a fracture dislocation or the sudden collapse of a vertebra infiltrated by growth, results in acute necrosis of the part compressed from cutting off of the blood supply. With this are associated hæmorrhages from ruptured veins and capillaries. The dead tissues rapidly undergo fatty degeneration, with resultant softening, and this softening may spread in an upward or downward direction some distance beyond the level of the lesion.

Following the transverse lesion there is secondary degeneration of the nerve fibres which are cut off from their cells of origin (*see* Plate 51).

When the compression is more gradual the effect at first appears to be mechanical; the function of the compressed fibres is impaired, but rapidly returns if the pressure is removed. Later there is circulatory stagnation and œdema from compression of the veins, and finally obstruction of the arteries leads to necrosis and softening.

Compression of the spinal cord, whatever its cause, is likely also to produce obstruction of the sub-arachnoid space. This results in stagnation of the cerebro-spinal fluid below the blockage, with accumulation of protein, and to this is sometimes added a yellow pigment probably derived from extravasated blood.

Tuberculous caries of the vertebræ may cause compression of the cord in two different ways. The commoner mode is that in which the infective process makes its way through the posterior wall of the vertebra and forms a caseous abscess separated from the meninges by the extra-dural tissues. The formation of such

an abscess may occupy only a few weeks, and is quite commonly preceded by a history of injury to the diseased spine.

In the other form of tuberculous compression the infective process spreads directly to the meninges, causing a chronic localised meningitis, which in time constricts the cord. This process is very much slower than the other.

New growths in the vertebræ are usually of secondary origin, the commonest sources in the female being carcinoma of breast or uterus, and in the male the gastro-intestinal tract and prostate. The growth arises in the cancellous portion of the vertebra, which it erodes, until it finally bursts through the compact shell. The softening of the bone eventually leads to collapse of the walls of the vertebral canal with pressure upon the spinal cord. Often the vertebral column is much more extensively involved than may appear from the symptoms observed during life. Sarcoma may be primary or secondary in the vertebral column or the structures surrounding it, and results in changes similar to the effect of carcinoma. Myelomas in the vertebræ may also give rise to compression of the cord.

Paget's Disease of the spine may also cause compression of the cord.

The space between the vertebræ and the dura mater may occasionally be the site of tumours, usually of a sarcomatous nature, and may be a resting place for hydatid cysts. It is also sometimes invaded by Hodgkin's disease or lympho-sarcoma originating in the mediastinum.

Chronic syphilitic meningitis may result in very great thickening of the meninges, in the midst of which the spinal cord is compressed. This is frequently associated with syphilitic disease of the arteries, which accelerates the process of necrosis.

Of *new growths of the meninges* the majority are small encapsuled tumours of benign type arising from the inner surface of the dura, the arachnoid, or the nerve roots. According to their microscopic appearance they are classified as endothelioma, psammoma, fibroma, fibro-myxoma and neurofibroma. This is the group of tumours which lend themselves readily to surgical removal.

The other type of growth met with in the meninges is of a diffuse sarcomatous nature, with a tendency to spread upwards and downwards, of malignant type and irremovable.

Meningitis serosa circumscripta is a title given to a condition in which the meninges are found matted together with inclusion of cyst-like spaces containing clear fluid. This may follow injury (often after a long latent interval) or may occur as a late result of suppurative meningitis, or it may be found without apparent cause.

Symptoms. The symptoms of spinal compression are those already described of a transverse lesion of the cord, varying with the level affected (*see* p. 607). To these must be added the symptoms due to compression of nerve roots when these are also involved.

When the compression occurs suddenly, as from fracture dislocation, or the collapse of a diseased vertebra, there is, in addition to the loss of sensibility, power, and sphincter control, an initial period of spinal shock during which all reflexes are abolished below the level of the lesion. With this there is often fever, and the clinical picture at first may resemble that of an acute myelitis.

When compression occurs gradually the first symptoms are often due to pressure upon posterior nerve roots. These take the form of pain, which is usually of a severe aching character, and is referred to the segmental distribution of the roots affected. As a rule it begins by being unilateral, but may later spread to the other side. Hyperæsthesia of the skin may sometimes be found in the area supplied by the irritated roots. Pressure upon anterior roots may also give rise to muscular wasting and weakness, which may be an important localising sign in compression of the cervical or lumbar enlargements.

It must be remembered, however, that in the thoracic region the vertical length of the segment is such that the cord may quite well be compressed without

involvement of nerve roots, and that in any case the compressing cause may act upon the anterior surface of the cord. In these cases the characteristic symptom of " root pain " is lacking from the history.

Of the structures within the cord the pyramidal fibres are usually the first to suffer, with resultant weakness and spasticity, increased tendon jerks, diminished or lost abdominal reflexes, and extensor plantar responses. Sensory disturbance is not as a rule evident for some time after weakness has been noticed. Careful examination is at first required for its detection. A level will be found below which pinprick is less painful, cotton wool touches are less constantly appreciated, and the difference between hot and cold tubes is less certainly distinguished.

Examination of the senses of positive and passive movement will reveal diminished accuracy, and the vibrating tuning-fork may be less keenly appreciated below a certain level.

As the disease progresses the sensory loss becomes more and more pronounced, until as a rule a definite border line may be distinguished between the healthy and the affected parts. This line, although it is not usually sharply defined, indicates fairly accurately the level of the lesion. It will occasionally be found that with a lesion in the upper region of the cord some of the fibres from the lowest segmental areas—and especially those conveying impression of deep sensibility —may escape, so that sensation to deep pressure is preserved over the sacrally supplied areas.

As the paralysis of the lower limbs increases control of the sphincters is impaired. with at first precipitate micturition and dyschezia.

Finally the compression, if not relieved, will lead to complete motor paralysis and sensory loss with abolition of sphincter control.

The details of the clinical picture will necessarily vary with the level of the lesion.

Additional evidence of spinal compression may be obtained by (1) examination of the cerebro-spinal fluid ; (2) X-ray examination after the intrathecal injection of lipiodol.

(1) The cerebro-spinal fluid obtained from below the level of compression as a rule contains an excess of protein. This varies from a slight increase above the normal (0·025 per cent.) to amounts as high as 3 per cent., according to the degree and duration of the compression. When the protein content is extremely high the fluid often contains fibrinogen, and therefore may coagulate in the test tube. In addition, it sometimes exhibits a golden yellow tinge, due probably to the hæmolysis of blood transuded through the walls of obstructed veins.

If a manometer be employed to register the pressure of the fluid Queckenstedt's test should be employed (see p. 631). Under normal conditons compression of the jugular veins by an assistant will cause an immediate rise of pressure in the manometer. Absence of this rise indicates blockage of the subarachnoid space.

(2) The practice of injecting lipiodol introduced by Sicard is sometimes of value in confirming the clinical diagnosis of spinal compression and determining the upper level of the lesion. Lipiodol is a compound of iodine and fat, which is opaque to the X-rays, of a specific gravity higher than that of the cerebro-spinal fluid, and with little injurious effect upon the tissues.

One or two c.c. of this substance are injected into the cisterna magna with the patient in the sitting posture ; immediately after the injection, while still in the erect position, he is X-rayed, and pictures taken both at the level of the presumed compression and of the lumbo-sacral spine. The X-ray examination is repeated half an hour later, and if necessary again after an interval of a few hours. Under normal conditions the lipiodol falls within a few minutes to the bottom of the thecal sac, where it is visible upon the X-ray plate at the lower border of the first sacral vertebra. It has been found that the irritative effect of lipiodol may cause an exacerbation of root pains, and may even lead to a temporary

increase in the signs of spinal cord compression. It should therefore be employed only when the diagnosis or localisation cannot be arrived at with sufficient accuracy upon clinical grounds (*see* Plate 52, Fig. 1). If the subarachnoid cavity is blocked, as must occur in an advanced case of spinal compression, the lipiodol is held up. In the illustration shown (Plate 52, Fig. 2) the block is at the upper border of the second lumbar vertebra. The cauda equina below this level was compressed by a large meningeal tumour of a fibromatous nature.

A more recent, safer and better method of employing lipiodal involves the use of an X-ray table upon which the patient can be tilted into a vertical position head downwards. The lipiodol is injected by lumbar puncture and its passage watched on the screen. By this means partial arrest can be observed.

These special methods of investigation are of great value, but it is not to be supposed that they will yield positive results until the degree of compression is considerable. There may therefore be a period in the early stages of the disease during which the clinical history and symptoms are the only guide to the nature of the case.

To the symptoms described above, which are common to all cases of compression, may be added those which belong to the compressing cause.

Disease of the vertebræ is commonly—but not always—associated with complaint of *local pain*, accompanied by rigidity and aggravated by any circumstance which tends to strain or jar the affected parts, such as stooping, jumping downstairs, or jolting over rough roads in a motor car. *Tenderness* and *deformity* of the diseased vertebræ are sometimes present. Finally the X-ray plate as a rule serves to demonstrate the presence of bony disease.

Chronic inflammation of the meninges as a rule involves several pairs of nerve roots. Root pain, therefore, is usually a prominent symptom and is often associated with reflex spasm of the back muscles leading to local rigidity of the spine.

New growths of the extra-dural space or meninges may cause no symptoms beyond those of simple compression, with or without root pains; they may, however, give rise to some tenderness of the overlying vertebra and reflex spasm of the muscles.

Diagnosis. This includes (1) the differentiation of spinal compression from other cases of transverse lesion; (2) the differential diagnosis of the causes of compression.

(1) Spinal compression of acute onset, as from a malignant growth, has to be distinguished from *acute myelitis;* here the chief points in favour of the former diagnosis are the presence of malignant disease elsewhere, and the characteristic changes in the cerebro-spinal fluid already described.

The more gradual cases of compression have to be distinguished from *intramedullary tumour, disseminated sclerosis, syphilitic myelitis, amyotrophic lateral sclerosis, syringomyelia,* and *subacute combined degeneration.*

From intra-medullary tumour the differential diagnosis may be possible only at operation; in disseminated sclerosis the presence of scattered lesions as shown in signs or history usually gives the clue, but in certain cases the problem can be solved only by an exploratory laminectomy. Syphilitic myelitis will be recognised if the Wassermann reaction in blood and spinal fluid be included in the routine examination. The absence of sensory changes in amyotrophic lateral sclerosis and the presence of characteristic disorders of sensation in syringomyelia and subacute combined degeneration serve to distinguish these. Finally, the examination of the cerebro-spinal fluid and X-ray examination with lipiodol are often of differential value.

(2) The exact cause of compression can be discovered only by systematic investigation; in the absence of clinical or X-ray evidence of vertebral disease, and with negative Wassermann reactions in blood and spinal fluid, exploratory laminectomy should be undertaken.

The **Prognosis** depends chiefly upon the cause of compression. In cases of injury the cord itself as a rule is so severely damaged by the impact that decompression has little effect in producing amelioration of symptoms.

In most cases of tuberculous caries the prognosis is good with adequate treatment provided there is no active tuberculous disease elsewhere. In those cases, however, in which the gradually progressive history indicates a chronic tuberculous meningitis, the outlook is less hopeful. Malignant growths of the vertebræ may continue for months or years before finally causing death from bedsores and cystitis.

The progress of syphilitic meningitis may be arrested by suitable treatment. In meningitis serosa circumscripta division of the adhesions relieves the compression, but the condition is apt to recur. Intrathecal growths of the benign type may be completely removed.

In all cases in which the compressing cause can be removed, whether by means of rest in tuberculous disease or by operation, the degree of recovery which may be expected is proportional to the severity and duration of the symptoms. Total loss of power and sensibility in the lower limbs, provided it has not lasted more than a few weeks, is compatible with complete functional recovery. Once sphincter control is lost the chances of recovery are diminished owing to the complicating factor of urinary sepsis.

Treatment. The object of *radical treatment* is to relieve the compression. In the case of new growths this can be achieved only by surgical intervention. Benign tumours can be completely removed, and in some cases of malignant disease decompression may relieve pain.

Tuberculous caries is best treated by means of absolute rest in hygienic surroundings. The patient is laid upon a firm bed and extension maintained by traction upon the feet and chin ; or he may be fitted from the first with a plaster jacket. Complete rest in the horizontal position should be maintained for at least a year. Subsequently the patient may be fixed in a plaster jacket and allowed gradually to resume the erect posture. Improvement in the signs of spinal compression may be delayed for several months, but as a rule these cases do well eventually.

Compression from syphilitic meningitis must be treated energetically with the anti-syphilitic remedies (*see* p. 666). If after a sufficient course there is no improvement, operation may be performed in the hope of dividing a cicatricial constriction. The meningeal adhesions resulting from trauma or suppuration should be treated in similar fashion by operation.

Palliative treatment in cases of transverse lesion of the spinal cord, whether due to compression or other causes, is directed towards preserving the anæsthetic skin from ulceration, draining and irrigating the bladder, providing relief from pain and discomfort, and preventing or remedying the contracture of spastic muscles.

For preservation of the skin the patient should be laid upon a water bed. The back should be washed night and morning, and whenever any soiling occurs ; after washing and drying, the skin covering the bony prominences (including the heels) should receive a firm and prolonged rubbing from the palm of the hand. A dusting powder of chalk and boric acid should then be used. Care should be taken to avoid sodden or wrinkled sheets likely to produce excoriation, and the patient's position should be changed from time to time during the day in order to avoid constant pressure upon the same bony points. To move the patient two nurses are necessary if he is to be rolled, not dragged.

Should bedsores develop they should be dressed at suitable intervals ; stimulant lotions and ointments may be used in succession ; of the former Eusol (1 in 2,000) and Lotio Rubra are satisfactory ; of the emollients equal parts of Ol. Ricini and Ung. Zinci or of Ol. Ricini and Tinct. Benzoini Co. are the most useful. Should the bladder be paralysed and retention of urine occur, cystitis almost

inevitably follows. It may, however, be kept in check by the following measures:

Either a catheter should be passed at six-hourly intervals or the instrument should be tied in and changed at intervals of three or four days. Before the catheter is passed not only should the glans penis be scrupulously cleaned, but the anterior urethra should be washed out with an antiseptic solution. The bladder should also be irrigated night and morning with an antiseptic fluid. Oxycyanide of mercury (1 in 4,000) is satisfactory, or if the urine is strongly alkaline a saturated solution of boric acid with an equal part of water may be used. In such cases also urotropin and acid sodium phosphate should be given by the mouth.

During irrigation care should be taken that sufficient fluid is not injected to cause over-distension, the correct amount being not more than 6 oz. When automatic emptying develops the irrigating fluid should be introduced under the least possible pressure and the bladder allowed to expel its contents if the reflex is evoked. It is not safe, however, to discontinue catheterisation until the bladder appears able to expel its contents completely without residual urine (**2**). Evacuation of the bowels should be managed with an enema every forty-eight hours, which minimises soiling; if necessary, a carefully timed aperient of senna pods may be given beforehand.

Reflex spasms of the limbs, which are not only uncomfortable in themselves, but tend to produce bedsores from friction, may be relieved to some extent by a cradle over the lower limbs to prevent contact with the bedclothes. The temperature within this cradle should be maintained at a constant level by means of hot-water bottles. If these measures are of no avail, sedatives, such as luminal, in doses of 1 grain thrice daily, may be employed, or a larger dose may be given at night time.

The onset of contractures should be guarded against by daily passive movements and splinting so long as there is any hope of ultimate recovery.

The electric current should be reserved for such muscles as are wasted and paralysed from involvement of their lower motor neuron supply.

In old standing cases, when spontaneous improvement can no longer be expected, spasticity of the lower limbs may be relieved by section of the posterior nerve roots (Förster's operation). Laminectomy is performed and alternate roots are divided from the second lumbar downwards. This is necessarily a severe operation, and should not be undertaken except in especially favourable circumstances. Adductor spasm of the thighs may be treated by the simpler operation of cutting the obturator nerves, which sometimes gives great relief from discomfort.

TUMOURS OF THE SPINAL CORD

(*Intra-medullary Tumours*)

Tumours arising from the meninges and nerve roots have already been considered in the preceding pages, as causing compression of the spinal cord. Tumours within the substance of the spinal cord are relatively uncommon.

Pathology. They are more commonly found in the cervical and lumbo-sacral enlargements than at other levels. The usual type is the glioma. Sarcoma tuberculoma and gumma may also occur.

Symptoms. The symptoms of an intra-medullary tumour are those of a gradually progressive transverse lesion of the cord (*see* p. 607). In contradistinction to cases of spinal compression root pains are absent, and the early symptoms, therefore, are complaint of numbness and weakness in the extremities. Other symptoms vary with the level of the lesion. When this lies in the cervical or lumbar enlargements muscular atrophy from destruction of the anterior horn cells is a prominent feature. Partial destruction of the pain-conducting fibres sometimes causes complaint of painful paræsthesiæ below the level of the tumour. In

the early stages the subarachnoid space remains free, the cerebro-spinal fluid shows no increase of protein, and lipiodol injected into the cisterna magna is not held up. Eventually, however, the tumour may produce sufficient swelling of the cord to produce obstruction, and these tests will give positive results.

Diagnosis. The differential diagnosis presents much the same problems as that of spinal compression (*see* p. 659). It may be impossible to distinguish clinically between an intra-medullary tumour and syringomyelia, an accurate diagnosis being achieved only as the result of exploratory laminectomy.

Prognosis and Treatment. Some relief may be obtained from decompression, but the growth being as a rule of an infiltrating character is irremovable, and the ultimate prognosis bad.

Deep X-ray therapy should be tried when an accurate diagnosis has been made. Palliative treatment is the same as for other cases of transverse lesion, and has already been described under spinal compression.

MYELITIS

This term is used to denote an inflammatory process occurring within the substance of the spinal cord and involving all the constituents—blood vessels, nerve cells and fibres, and neuroglia—of the part affected.

Ætiology. It is assumed that in every instance the process of inflammation is due to bacterial agents, but in a number of the cases the causal organism remains unidentified. The spirochæte of syphilis, however, is responsible for a large majority, as proved by the history of primary infection, by the Wassermann reaction in blood and cerebro-spinal fluid, with increase of lymphocytes in the latter, and by histological examination of the spinal cord *post mortem*.

Apart from syphilis, several of the acute specific fevers may be complicated by the occurrence of myelitis, which is usually accompanied by signs of encephalitis. Of these the most important are measles, small-pox and chicken-pox. Myelitis may also occur together with encephalitis after vaccination.

In cases of this type the infective agents are presumably carried to the spinal cord by way of the blood stream. In other instances it is possible that organisms may reach the cord from some peripheral focus of sepsis through the pathway afforded by the perineural lymphatics.

To these may be added a group of cases in which the invasion of the cord by micro-organisms is secondary to an affection of the meninges. A greater or less degree of myelitis of such an origin may occur in meningitis due to tubercle bacillus, or to various other organisms, such as the pneumococcus, streptococcus and staphylococcus. In some cases the inflammatory process may spread directly from neighbouring structures, involving the meninges *en route*, as in the case of an ulcerating bedsore.

From the pathological standpoint it is convenient to differentiate between *acute infective myelitis* and *syphilitic myelitis*.

Morbid Anatomy. In *acute infective myelitis* the cord is softened and bulges on transverse section, or may be quite diffluent; but previous to section it may seem hard, from mere tenseness of the membrane containing the swollen cord.[1] To the naked eye the section is congested, minute vessels are visible, especially in the grey matter, and this itself is darker than usual, and its outline is indistinct. Patches of grey tint may be present in the white column, or the whole surface is confused. Under the microscope, in early stages, are found perhaps capillary hæmorrhages, and leucocytes in the lymphatic sheaths and around the vessels. The nerve fibres suffer by breaking up of their myelin sheaths, and here and there occurs a fusiform enlargement of the axis cylinders, which in its thickest part is five or six times the diameter of the normal fibre; this may

[1] Any cord may become soft from decomposition, or may be reduced to a pulp by clumsiness in extracting it from the spinal column.

be due to imbibition of fluid. The nerve cells are swollen, granular, with perhaps fatty globules, and some of them undergo vacuolation. Subsequently both nerve cells and fibres undergo fatty degeneration, and the degeneration products are removed by scavenging cells of neuroglial or vascular origin. There is at the same time an increased growth of neuroglial fibres, so that the end result is a sclerosis of the parts affected.

The lesion may be confined to a few segments (*transverse myelitis*), it may be quite diffuse, affecting a considerable length of the cord (*diffuse myelitis*), or there may be several areas of inflammatory softening, separated by areas of healthy tissue (*disseminated myelitis*).

Syphilitic Myelitis. In this condition the spinal cord may be affected in different ways. On the one hand, syphilitic disease of the vessels may lead to thrombosis and so to softening of the nervous substance, while, on the other hand, gummatous thickening of the meninges may eventually cause compression of the spinal cord, with consequent degeneration of the part encircled. In most cases the condition found is a combination of these two processes, which should be spoken of more correctly as a *syphilitic meningo-myelitis*. Probably the specific toxins of the syphilitic virus also play a part in causing the degenerative changes.

The process is generally limited to a few segments, thus resulting in a transverse lesion of the cord. The blood vessels may show cellular infiltration of the adventitial sheath, together with thickening of the intima, which has sufficed to occlude the lumina. In this case there is complete disintegration and liquefaction of the area supplied by them. Or the appearance may correspond more nearly with that of an inflammatory lesion. There may be no endarteritis in this case, but the vessels are completely surrounded with cellular exudate, which may extend into the surrounding tissues, and is accompanied by degeneration of the nerve elements, apparently of a toxic nature. The leptomeninges are in almost all cases infiltrated with mononuclear cells, and in some instances the dura mater is also involved and may be greatly thickened, so that the whole cord is surrounded by a band of dense fibrous tissue, which in its turn may lead to occlusion of blood vessels by pressure, and so to central softening. Where the meninges are extensively affected the nerve roots become involved in the inflammatory mass, with resultant degeneration of their fibres.

Symptoms. These depend rather upon the localisation of the lesion than upon its pathology. It is useful, however, to distinguish between an *acute* and a *chronic* form of the disease.

Acute Myelitis may be either of syphilitic or of general infective origin. The *syphilitic* variety of acute myelitis occurs more commonly in males than females, generally in young adults with a history of primary syphilis a few years previously. The symptoms are probably due in most cases to the sudden occlusion of thickened vessels with consequent softening of the spinal cord. The onset, therefore, is frequently sudden, paralysis and anæsthesia occurring without warning and without pain, unless, as sometimes happens, the vascular disease is associated with extensive meningeal involvement, in which case there will probably have been previous complaint of pain in the distribution of the posterior roots affected. There is little or no constitutional disturbance. Examination of the cerebro-spinal fluid reveals an excess of cells and albumin with a positive Wassermann reaction. The Wassermann reaction is as a rule positive also in the blood.

Acute infective myelitis may occur at any age without especial relation to sex, but is most often seen in young adults. It is a comparatively rare disease. At the onset there are usually signs of constitutional disturbance, such as headache, pains in the limbs, anorexia and general malaise, with pyrexia of varying degree, and occasionally rigors.

The nervous symptoms may develop suddenly with paralysis and anæsthesia

below the level of the lesion, but more usually some days elapse before the acme of the disease is reached. The early symptoms are numbness and tingling in the extremities and slight degrees of motor weakness, together with impairment of sphincter control. Pain is but slight as a rule, but there may be complaint of a dull ache in the back, or a girdle sensation around the chest or abdomen. With the further development of the disease paralysis and loss of sensation generally become complete up to the level of the lesion, and this may progress in an upward direction (*acute ascending myelitis*). There is complete loss of control over the sphincters, bedsores rapidly develop, the pyrexia continues, and the illness progresses after a variable time to a fatal issue, or more rarely it may become arrested with some degree of recovery.

Acute Disseminated Myelitis is a comparatively rare and fatal variety of the infective form, characterised by the simultaneous occurrence of symptoms referable to lesions scattered throughout the cerebro-spinal axis, together with signs of severe constitutional disturbance, and in a number of cases optic neuritis, retro-bulbar neuritis or papillitis.

In all forms of infective myelitis examination of the cerebro-spinal fluid may show an excess of cells, comprising lymphocytes, polymorphs, or a mixture of both. In many cases, however, the fluid shows surprisingly little abnormality.

The **physical signs** in a case of acute myelitis naturally vary with the level of the lesion and with its extent (*see* p. 607).

Death in cases of acute myelitis or softening takes place (1) from pulmonary complications following upon paralysis of the respiratory muscles; (2) from bedsores intensifying exhaustion, or leading to pyæmia; (3) from vesical complications; (4) from intercurrent affections, such as pneumonia or bronchitis. The bladder is extremely liable to cystitis, partly from trophic disturbance, partly from retention of urine; and the use of the catheter may be responsible for the introduction of organisms which set up septic inflammation. When cystitis occurs the urine rapidly decomposes and becomes ammoniacal, unless it is repeatedly removed by the catheter; it contains pus or muco-pus, and readily deposits crystals of ammonium-magnesium phosphate on standing. Almost at any time the septic condition of the bladder may extend up the ureters to the kidneys, and suppurative pyelitis and nephritis will then occur, and the patient may die with uræmic symptoms.

Cases which escape these dangers generally lapse into a chronic condition, which may be of indefinite duration, but sometimes recovery slowly takes place after many months. A small number of cases get well comparatively quickly, and these are more common among the milder cases of myelitis following infectious disorders.

Cases of syphilitic origin frequently recover under proper treatment, but there is usually a more or less serious degree of residual paralysis with imperfect control over the sphincters.

Chronic Myelitis is almost always of syphilitic origin. The process is one of gradual compression of the spinal cord and its vessels by gummatous thickening of the meninges, together with a certain amount of toxic degeneration of the nerve cells and fibres due to the syphilitic poison. The symptoms therefore are those of a localised spinal meningitis with involvement of nerve roots, to which are added those of compression of the spinal cord. The main feature of these cases in their early stages is the pain due to involvement of the posterior roots. This is of a shooting nature, and if, as frequently occurs, the lesion is in the mid-dorsal region, the pain, as a rule, begins in the back and radiates around the trunk on one or both sides; if the cervical region is affected, the pain will be experienced in the length of one or both arms, and will be accompanied by muscular paralysis and atrophy due to involvement of the motor nerve roots (*see* Internal Pachymeningitis). These symptoms of root irritation and destruction may exist for some

months before the spinal cord is seriously involved. The symptoms of a transverse lesion of the cord appear gradually, beginning with a transient weakness or numbness of the lower extremities, together with a difficulty in controlling the sphincters, progressing in a few weeks to a condition of spastic paraplegia with increased tendon jerks and extensor plantar responses. The loss of power and sensibility is not as a rule complete.

If the lesion is situated in the lumbo-sacral enlargement, the most prominent symptoms are pain in the distribution of the sacral nerve roots together with disturbance of sphincter control.

It is not possible to draw any hard and fast line between cases of acute and chronic syphilitic myelitis of the types described above : disease of the vessel walls is an almost constant feature, so that in a case which has begun with symptoms of gummatous meningitis the signs of a transverse lesion of the cord may develop rapidly as the result of thrombotic softening.

Another somewhat rare form of syphilitic myelitis is that in which the pyramidal tracts alone are affected by the specific toxins, resulting in a gradually progressive motor paralysis of the lower limbs with increase of the deep reflexes, extensor plantar responses and spasticity. This is known as *Erb's syphilitic paraplegia.*

Another rare and obscure disease, known as *toxic myelitis,* is especially associated with pregnancy. The symptoms are those of a gradually progressive transverse lesion of the cord, which is not complete, and the tendency is towards spontaneous recovery. The condition may clear up completely after confinement and recur with subsequent pregnancies.

Diagnosis. The recognition of the acute infective form of myelitis is as a rule not difficult in view of the pyrexia and constitutional disturbance. It must be recognised, however, that such signs of general illness may be present in cases of tuberculous caries or malignant growth of the vertebræ, in which sometimes the onset of signs of compression of the spinal cord may be quite sudden. Careful examination of the vertebral column, together with an X-ray picture of that part of the bony canal which encloses the affected segment, suffices as a rule to differentiate these cases. Acute poliomyelitis and Landry's paralysis may be distinguished by the absence of sensory loss and sphincter involvement.

Both the acute and especially the chronic forms of syphilitic myelitis have to be distinguished from compression of the spinal cord by tumours of the membranes or the vertebræ or by spinal caries. Here again the X-ray plate will help to exclude vertebral disease, whilst in the syphilitic cases the cerebro-spinal fluid constantly shows an increase of cells and albumin, together with a positive Wassermann reaction. The latter is positive also in the blood. Myelitis may sometimes be confused with peripheral neuritis, but in the latter condition there is no disturbance of sphincter control, the weakness involves both upper and lower limbs before it affects the trunk, and the sensory disturbance, when present, has a peripheral nerve distribution.

An extensive patch of disseminated sclerosis may produce all the signs of an acute myelitis, but there is no severe constitutional disturbance such as occurs in the acute infective conditions; examination of the cerebro-spinal fluid serves to exclude syphilis ; and a careful review of the history with perhaps the presence of other signs, such as nystagmus, will make clear the diagnosis.

Prognosis. Complete recovery is the exception, except in those cases which follow measles or chicken-pox, in which the prognosis is very favourable. Most of the syphilitic cases make considerable improvement under proper treatment, but there is always a residue of paralysis, usually associated with impairment of sphincter control. Many of the cases of acute infective myelitis progress to a fatal issue either in the early stages from the severity of the initial illness or later from urinary sepsis or bedsores.

Treatment. The general treatment of a case of myelitis is the same as that

of any transverse lesion of the cord, and has already been described under the heading of compression lesions (p. 660).

Treatment of Syphilitic Myelitis. In cases due to syphilis, salvarsan should be given, and a course of mercury and potassium iodide should be instituted, and continued over a long period. There is some diversity of opinion as to the dosage of salvarsan which should be employed. It appears, however, that for the efficient treatment of syphilis of the nervous system larger doses are required than in the case of syphilis elsewhere, and that patients suffering from this form of the disease are relatively tolerant of the drug.

The following course is recommended: The initial dose of novarsenobillon for an adult male should be 0·45 gramme intravenously, followed after a week's interval by 0·6 gramme, and subsequently by six further doses of 0·6 gramme at weekly intervals. An interval of eight weeks should then be allowed to elapse before any more novarsenobillon is given in order to guard against the dangers of delayed arsenical poisoning. During this period a weekly dose of bismuth (*e.g.* stabismol 2 c.c.) should be given by intramuscular injection. The intravenous injections are then begun again with a dose of 0·6 gramme followed by six further doses of 0·6 gramme at weekly intervals. Throughout this course of treatment mercury and iodide should be given by the mouth. A mixture containing 1 drachm of the liquor hydrarg. perchlor. and 15 grains of pot. iod. t.d.s. p.c. is suitable. The patient should be instructed to take particular care in cleaning his teeth while under this treatment on account of the liability of persons taking mercury or bismuth to develop septic conditions of the gums and mouth. If symptoms of this kind arise treatment by these drugs must be suspended for the time being.

One month after the completion of the course the Wassermann reaction may again be tested in the blood and cerebro-spinal fluid, but even if this is negative the patient should not be considered "cured"; if the progress of the disease appears to have been arrested, he may discard treatment for the time being, but whether the Wassermann reaction is positive or negative, he should submit himself annually to a short course of further treatment, which may consist of four weekly injections of novarsenobillon 0·6 gramme, together with the mercury and iodide mixture thrice daily during the month.

In any case in which, at the end of the initial course, symptoms appear to be actively progressing, treatment should be recommenced on the same lines after a suitable interval, while a careful watch should be kept for any symptoms of arsenical poisoning. The dosage of novarsenobillon described above is that recommended for a healthy adult male. In the treatment of individual cases the dose to be employed must be carefully considered in relation to the general condition of the patient, and it should be remembered that some persons are intolerant of arsenic in much smaller quantities than those recommended. The early signs of poisoning to be looked for are severe constitutional disturbance within twenty-four hours of each injection, continuous malaise and gastro-intestinal irritability, jaundice and skin disturbances such as erythema and exfoliative dermatitis. The occurrence of any such symptoms is a warning to discontinue arsenical treatment at once (*see* p. 117).

HÆMORRHAGE INTO THE SPINAL CORD

(*Hæmatomyelia*)

This is a very rare occurrence, and contrasts remarkably with hæmorrhage into the brain, which is one of the most common causes of cerebral paralysis.

Ætiology. It is in almost all cases the result of injury, either from direct violence applied to the spine, or less directly from a fall upon the feet or head. In the last instance, when associated with symptoms of cerebral concussion or contusion, its symptoms may easily escape recognition. The cervical region of the

cord is the part most commonly affected, and the hæmorrhage is generally confined to the grey matter. Rare instances of "spontaneous" hæmatomyelia have been recorded, and hæmorrhage may also occur into a pre-existing syringomyelic cavity.

In the great majority of the traumatic cases the lesion is in the lower part of the cervical enlargement, and the injury has been caused by force applied to the top of the head with violent flexion of the neck. It is probable that in most of these cases the spinal cord is damaged by momentary compression from a fracture-dislocation of the cervical spine. The contusion which results from such injury has its maximal disruptive effect in the central grey matter of the cord.

Symptoms. The symptoms of a severe hæmatomyelia in the early stages are indistinguishable from those of a transverse lesion of the cord, for the hæmorrhage, though confined to the grey matter, compresses the longitudinal fibres around it. When the effect of this has passed off the results of the damage to the grey matter are evident in the form of wasting and weakness of the muscles supplied by the anterior horn cells of the segments involved and a dissociated anæsthesia below this level, sensibility to pain and temperature being affected without loss of the tactile or postural senses.

Diagnosis. The diagnosis in traumatic cases has to be made from a compression lesion of the cord. The presence of deformity of a degree sufficient to cause compression may be determined by clinical and X-ray examination, and evidence of sub-arachnoid block, obtained from lumbar puncture, will clinch the point. In the rare spontaneous cases the sudden onset suffices to distinguish the condition from that of syringomyelia and the dissociated nature of the sensory loss from a transverse myelitis.

Prognosis. Death is rarely caused by the primary lesion if the patient survives the first few hours; later urinary sepsis or bedsores may lead to a fatal issue. Some degree of recovery may be expected in almost all cases, and the final prognosis may be gauged in some measure by the rate of progress in the early stages. If improvement in power sensibility and bladder control manifest themselves within a week or two of the injury, the outlook is good. If there is no return of power at the end of three months, the paralysis is likely to remain permanent. In all cases affecting the cervical enlargement the atrophic paralysis of the hands due to destruction of anterior horn cells is likely to persist in some degree as a permanent disability.

Treatment. Absolute rest is the first consideration. The patient should be laid flat, preferably on a water mattress, and the greatest care should be taken to avoid unnecessary movement. Provided that the respiratory function is not impaired, morphia should be administered freely during the first forty-eight hours to control restlessness. Massage, exercises and electrical treatment should be prohibited for at least three weeks.

DISSEMINATED SCLEROSIS

(*Multiple Sclerosis, Insular Sclerosis, Sclérose en Plaques Disseminées*)

This disease is characterised by the development of numerous patches of sclerosis throughout the brain and spinal cord.

Ætiology. The disease is somewhat more frequent in females than in males. The symptoms are mostly noted for the first time in youth or early adult life, and in 170 cases observed by the writer the onset in 67 per cent. occurred between the ages of twenty and forty. In 8·5 per cent. the age of onset was between fourteen and twenty, and in the remaining 24·5 per cent. over forty, the latest age being fifty-five. Although the pathological and clinical evidence suggests a toxic or infective agent as the cause of the disease, experimental researches upon its nature have so far yielded negative results. In a small proportion of cases

the disease occurs in several members of the same family, which suggests that constitutional liability may play a part in the ætiology.

Pathology. Though little can be said with certainty as to the origin of the disease, it is probable that toxins carried to them by the blood cause degeneration of the myelin sheaths and eventually of the axis cylinders, and that simultaneously, or somewhat later, hyperplasia of the neuroglia occurs, resulting ultimately in sclerosis.

Morbid Anatomy. The surface of the spinal cord, medulla oblongata, pons, and the base of the brain presents a number of irregular patches of pinkish-grey colour, rather sharply outlined and contrasting with the natural white colour of the medulla, pons, and crura. On section the discoloration is found to extend inwards so as to form deposits of a round or oval shape, ranging in size from that of a pea to that of a hazel-nut, generally harder than the normal nervous tissue, and even leathery or cartilaginous, sometimes projecting above the level of the section, sometimes sunken below it. Recent patches are dark grey, older patches more yellowish grey, and less translucent. They affect the white matter more than the grey matter; thus in the spinal cord the greater part of the cornua is unaffected, and in the cerebrum they are best seen on section of the hemispheres, which are dotted with the grey areas, and the walls of the lateral ventricles are often invaded. The Sylvian aqueduct also is commonly surrounded by areas of sclerosis. They are not frequent in the cerebellum, but may invade the olfactory bulbs and the spinal and cranial nerve roots. Under the microscope the outline of the patch or nodule is much less distinctly marked than it appears to the naked eye. The nodule consists chiefly of fibrous or finely fibrillated tissue, developed by overgrowth of the neuroglia; within this area the nerve fibres have lost their myelin sheaths, but many axis cylinders persist. The earliest stage of the lesions appears to be degeneration of the myelin sheaths, which become swollen and are then broken up into fatty droplets. The products of myelin degeneration act as an irritant, the neighbouring vessels become congested and there is perivascular infiltration with lymphocytes, polymorphonuclear and plasma cells. In the next stage large mononuclear cells appear which engulf the fatty droplets and convey them towards the venules. There is at the same time a reaction on the part of the surrounding glia cells (comparable with the connective tissue cell reaction around inflammatory foci elsewhere in the body). The axis cylinders suffer less severely than the myelin but are always involved in some degree, those affected becoming at first swollen in an irregular manner and finally disappearing. Finally, when the products of degeneration have been completely removed, a dense patch of glial overgrowth represents the scar of the original lesion. Owing to the excessive glia reaction, neighbouring foci tend to be bound together in a common sclerotic plaque which is visible to the naked eye.

In sections obtained by the Weigert-Pal method the healthy fibres are stained black, while the plaques of glial sclerosis, being left unstained, stand out in sharp contrast against the dark background (*see* Plate 53, Figs. 1 and 2).

Symptoms. The most characteristic feature of the illness in its early stages is the variety, and often the transient nature, of the symptoms, depending as they do upon a random and haphazard distribution throughout the cerebro-spinal axis of minute foci of the disease, each of which in its initial stages causes a much greater disturbance of function than ultimately persists. As the disease progresses, with the accumulation and coalescence of repeated patches of sclerosis, the total area of permanent damage steadily increases, so that the symptom picture becomes more uniform and more constant.

The manner of the onset is itself variable; most frequently it is somewhat sudden, with symptoms referable to a small lesion of the longitudinal fibre tracts, the optic nerves or the substance of the brain-stem. Thus the patient may complain of a numbness in some area of trunk or limbs, a dragging of one foot, some

slight difficulty in controlling the bladder, double vision, or a mistiness before one or other eye. Examination at the time may reveal slight evidence of organic damage, such as impairment of sensibility, inequality or absence of the abdominal reflexes, or an abnormal plantar response, but these signs, together with the symptoms, commonly disappear in the course of a few days or weeks, to be succeeded after a variable interval of quiescence by the development of new troubles elsewhere or renewal and intensification of the old. In other cases the symptoms begin more gradually, perhaps with progressive weakness or stiffness of one or both legs or an increasing tremor of the hand. Even of these cases, however, the majority show remissions and exacerbations, so that the course of the illness is seldom continuous.

The nature of the earliest symptoms depends upon the situation of the first patches of the disease, and is therefore variable in the extreme. It is to be remembered, however, that the morbid process chiefly involves the white matter of the cerebro-spinal axis; that, owing to the great length of the main sensory and motor tracts, these are most likely to suffer damage; and that on account of their functional importance such damage is most likely to result in symptoms. Moreover, on account of their greater length the fibres going to and coming from the lower limbs are more vulnerable than those connected with the arms.

The optic nerves, however, are affected with a frequency which is quite out of proportion to the space which they occupy in the white matter, and are often involved in the earliest stage of the disease. The most characteristic form of this involvement is an attack of retro-bulbar neuritis, usually confined to one eye. The patient becomes suddenly conscious of defective vision, and on closing the sound eye finds that his sight is seriously impaired. The onset is usually accompanied by pain in the eyeball, especially on movement, and the defect of vision may be progressive over a period of days. On examination of the fundus at this stage no abnormality is detected unless the lesion has extended forward as far as the papilla, when a variable degree of swelling (papillitis) is to be observed. Examination of the visual fields reveals a central scotoma, and, if this be large, with a correspondingly severe diminution of visual acuity, the reaction to light of the pupil on the affected side will be ill-sustained. After a variable period there is improvement of the visual function, often with a return to normal. Within a few weeks of the onset the pallor characteristic of optic atrophy is to be observed in the optic disc, particularly on its temporal side.

In a series of 139 cases of disseminated sclerosis collected by the writer, such an attack of retro-bulbar neuritis occurred at some time or another in 28 per cent., and in two-thirds of these cases it occurred, either alone or with other symptoms, as the first evidence of the disease. The affection of the optic nerves, however, as of other parts, may be gradual and insidious, so that it is not uncommon to observe optic atrophy in one or both eyes in a patient who can give no account of any sudden or severe disturbance of vision, and may be unaware that it is affected. Permanent impairment of vision in both eyes of any serious degree is fortunately extremely uncommon.

Not infrequently the first symptoms take the form of paræsthesiæ—that is, sensations of numbness, tingling, tightness, coldness or heat—referred to various areas of the trunk or limbs. Careful examination may reveal diminished cutaneous sensibility, but of more common occurrence are signs of damage to the posterior columns, revealed by impairment of the senses of position and passive movement, diminution or loss of the vibration sense, and in the hands astereognosis. In the arms extensive damage of this nature may give rise to symptoms which are somewhat characteristic and by no means uncommon. The patient complains that the hand is useless: he is unable to employ it usefully for purposes of eating, buttoning his clothes, and so on. Examination reveals no loss of power, and as a rule little or no impairment of tactile sensibility, but there is gross loss of sense of position, with consequent ataxia and astereognosis.

The commonest form of motor disturbance is weakness of one or both legs of the type due to pyramidal damage. Thus the group of muscles earliest affected is that of the dorsiflexors of the ankle, so that the foot drags along the ground, and this in the early stages may only be noticed after excessive exercise, as at the end of a long day's walking. With the weakness, which in more severe cases affects the flexors at knee and hip joints also, is associated spastic rigidity of the extensors, so that the patient may complain of stiffness rather than paralysis. With this also there is sometimes complaint of "cramps" in the legs, or of involuntary flexor movements, described as "jumping upward" of the lower limbs, which are especially likely to occur in bed at night.

When symptoms of this nature are prominent they are associated with the signs of a pyramidal lesion, namely, loss of the abdominal reflexes, exaggeration of knee and ankle jerks, and an extensor plantar response, which are most marked on the side chiefly affected.

In connection with involvement of the brain-stem reference has already been made to diplopia from involvement of the oculo-motor nuclei or nerve. This is nearly always of a quite transitory nature, lasting a few hours or a few days, and occurs at one time or another in about a third of the cases. It is often one of the earliest symptoms, and may be neglected at the time and afterwards be forgotten by the patient, unless his attention is specially called to the point.

Nystagmus, from interference with the fibres connecting the vestibular with the oculo-motor nuclei, is seldom noticed by the patient, but is present in more than three-quarters of the cases, often at an early stage. It is usually obtained only on lateral deviation of the eyes, is most commonly bilateral, and at first irregular, being well marked at some times, hardly to be noticed at others. It is, however, one of the most characteristic signs of the disease.

Motor inco-ordination of cerebellar type, probably attributable to lesions of the superior cerebellar peduncles at or near the point of their decussation, is sometimes an early symptom, and is present in about half the cases at some time. It is shown most frequently in the form of intention tremor of the arms, and a disturbance of the speech which depends upon inco-ordination of the articulatory musculature. The intention tremor is so called because it is not as a rule present when the arm is at rest, but is observed when the patient attempts to take hold of an object, or in the performance of the finger-nose-finger test. One limb oscillates irregularly to the right and left, or up and down, without regard to the object aimed at, and there is a tendency to overshoot the mark. In addition to this, a nodding, to-and-fro tremor of the unsupported head is frequently observed. The speech has been described as staccato, or scanning, and is of the type already described under Disturbances of Cerebellar Function (*see* p. 617).

As has already been noted, the cerebral hemispheres are commonly riddled with sclerotic patches, and to this must be ascribed the mental changes which are present in the majority of cases before the end, and are often noticeable at an early stage. They are of the general type occurring in other organic diseases of the brain, and consist of emotional instability and lack of control, indifference to the serious nature of the malady, lack of judgment in practical affairs, and defective memory. It is the combination of slight mental changes of this type with a history of transient weakness, or vague sensory disturbances, which so frequently leads to an erroneous diagnosis of hysteria in the early stages.

In addition to those already described, the disease may be ushered in by a variety of other symptoms of less common occurrence. Thus lesions of the cerebral hemispheres may give rise to hemiplegia of sudden or gradual onset, patches involving the central connections of the vestibular nerves may lead to attacks of giddiness or vertigo, or a predominant affection of the cerebellum may cause symptoms of pure cerebellar disease. There are also cases in which the morbid process begins in the lumbo-sacral enlargement, and loss of control over the sphincters is a prominent and early symptom.

In rare instances also the grey matter of the anterior cornua is affected, with resultant atrophy of the corresponding muscles, usually those of the hands.

The *course of the disease* is also variable. In a majority of cases the illness begins in a subacute manner—the patient suddenly notices a numbness of the hand or dragging of the foot—and its progress is characterised by a succession of remissions and exacerbations. The latter may be manifested in the form of new symptoms or intensification of those already present. The duration of the remissions is variable, but may extend over months or years. The writer has notes of a case in which there was an interval of twenty-four years between one exacerbation and the next. In some cases, however, the disease runs what appears to be a chronic and progressive course from the beginning. It is doubtful whether one can separate a chronic from a remittent type, for, on the one hand, a case which has begun in the more usual manner with remissions may finally become steadily progressive, and, on the other hand, there may be subacute exacerbations in the course of a case which has for some time shown a chronic progressive character.

In the later stages the patient becomes bedridden from paralysis of the lower limbs, which commonly develop the position of spasticity in flexion. Control over the sphincters is lost, and bedsores frequently develop. Even at this stage, however, tactile sensibility often remains unaffected, though examination with the tuning-fork usually reveals loss of the vibration sense in the lower limbs. The knee and ankle jerks may now be exaggerated or absent, the plantar responses are extensor, and the abdominal reflexes are lacking.

Diagnosis. There is no disease in which a carefully elicited history is of greater value. The diagnosis rests upon the proof of *multiple* lesions of the central nervous system, and this may only be forthcoming from a consideration of the story of a retro-bulbar neuritis or of a transient diplopia, numbness, or weakness in conjunction with the physical signs. The danger of a mistaken diagnosis of *hysteria* has already been mentioned. As a rule the detection of some slight sign of organic disease, such as nystagmus, absent abdominal reflexes, an extensor plantar response, or pallor of the optic discs, will permit of the differential diagnosis, but there are cases in the early stages in which it may sometimes be wiser to suspend judgment. The combination of nystagmus with tremor and inco-ordination of the arms may give rise to suspicion of *cerebellar tumour*. In the latter condition, however, the symptoms are all referable to a single lesion, and in the later stages there are symptoms of increased intracranial pressure. The spasticity and weakness of the lower limbs need to be distinguished from similar conditions arising from *compression of the spinal cord* by tumour or spinal caries.

Syphilis of the central nervous system in certain of its forms may give rise to a picture closely resembling that of multiple sclerosis, and in any case in which there is a doubt as to the diagnosis the Wassermann reaction should be done with blood and cerebro-spinal fluid. In disseminated sclerosis this reaction is uniformly negative, and the cerebro-spinal fluid does not often show changes in its cell or protein content. The colloidal gold curve, however, is often abnormal, resembling that found in neurosyphilis. Some cases of *encephalitis lethargica* in which the spinal cord is extensively involved may at first be mistaken for multiple sclerosis ; this mistake is especially likely to occur with a case of encephalitis in which the illness is protrated with comparatively long remissions ; the differential diagnosis may be made as a rule by careful consideration of the history of the case, particularly the nature of the onset and the occurrence of pyrexia or drowsiness in encephalitis.

The **Prognosis** is unfavourable. If the patient be seen in an acute exacerbation it may generally be said that some improvement will follow, but the great probability is that by the accumulation of repeated patches of the disease

he will finally become crippled and bedridden. Remissions simulating recovery are not uncommon and may last for years, but only in very rare instances has the progress of the illness seemed to be arrested.

Treatment. There is at present no specific remedy for the disease. Arsenic is of traditional repute as a medicine for it, and its use has been provided with some rational basis by the suspicion that disseminated sclerosis may be due to a chronic protozoal infection akin to syphilis. It may be given either by the mouth or by injection, the latter method being chosen for an acute exacerbation. In such case the patient should be put to bed as soon as the nature of the symptoms is recognised, and kept at rest for a fortnight or until the symptoms begin to improve. Three doses of Stabilarsan, 0·3 gramme, or an equivalent dose of some other suitable arsenical compound may be given by intramuscular injection at weekly intervals, and should be followed up by a mixture containing 3 to 5 minims of liquor arsenicalis by the mouth thrice daily after food. This may be continued for six weeks and repeated at intervals, as a measure of treatment or prophylaxis. The patient who has once manifested symptoms of the disease should lead a life as free as possible from physical and mental stress and from risk of cold and exposure. A sedentary occupation is indicated, both for its freedom from physical fatigue and the opportunity which it affords for continuing at work despite some degree of disability. In women the stress of pregnancy and confinement carries with it a risk of exacerbation, and the diagnosis of disseminated sclerosis provides a sound reason for abortion.

There is no doubt that in cases in which ideal conditions can be obtained the remissions are on the whole longer than in the others, though the relapses, when they occur, may be equally severe. Many patients in whom the disease is recognised and treated early, and who are able and willing to lead quiet and sedentary lives, may go years without relapse. Massage and graduated exercises are valuable in the treatment of motor symptoms, especially in the stage of recovery from an exacerbation. Hot baths followed by passive movements are useful for the relief of spasticity. A mixture containing 5 grains of potassium bromide and 10 minims of the tincture of belladonna given thrice daily is helpful for patients with precipitate micturition.

Palliative treatment in the later stages of the disease must be conducted on the same lines as those already prescribed for transverse lesions of the spinal cord (*see* p. 660).

SYRINGOMYELIA

This is a disease in which elongated cavities are formed in the centre of the cord as the result of a combined process of new growth and degeneration. The symptoms depend in the early stages upon destruction of the constituents of the grey matter; in the later stages the fibre tracts are also involved from pressure.

Ætiology. The disease occurs more commonly in men than women, and begins as a rule between the ages of twelve and thirty. It is sometimes associated with spina bifida, with cervical ribs or other congenital deformity.

Pathology. The essential feature of the disease is a new growth of glial tissue with subsequent degeneration and cavity formation. This begins as a rule in one of the posterior horns of grey matter close to the central canal and extends forward into the anterior horns, occluding, or sometimes communicating with, the central canal. There is a tendency for the morbid process to spread upwards and downwards in the cord, but the lumen of the tube thus formed may exhibit great variations at different levels (*see* Figs. 85, 86). The portions of the cord chiefly affected are the cervical and upper dorsal regions, the lumbar region and the medulla (syringobulbia).

The **Symptoms** in the early stages are referable to destruction of (1) the anterior horn cells; (2) the fibres conveying sensations of temperature and pain which decussate in the grey matter; (3) the cells of the lateral horn of grey

TABES DORSALIS

(*Locomotor Ataxy*)

Tabes dorsalis is essentially a gradual progressive degeneration of the lower afferent neurons, first manifesting itself in the posterior columns of the spinal cord; this is accompanied or followed by an overgrowth of the neuroglia. Similar changes may occur in the optic nerve, and in the central portions of the afferent cranial nerves. Tabes is therefore a disease affecting the sensory neurons, the disorder of locomotion from which it was originally named being due to loss of sensations of position and passive movement, with resultant inco-ordination of the movements in walking. Later experience shows that the ataxia is often a very late phenomenon, and, indeed, may be entirely absent; while there are other disturbances in the realm of sensation which are more constant, and provide the symptoms for which the patient usually first seeks medical advice.

Ætiology. That the sole cause of the disease is syphilis is now generally accepted. This opinion is founded upon evidence of primary infection in the past history of the patient; positive Wassermann reactions in blood and spinal fluid; and the presence of other syphilitic lesions (such as aortitis) in the body after death. One or other of these proofs is seldom if ever lacking when searched for. Noguchi first demonstrated the *Treponema pallidum* in the spinal cord from a case of tabes, and the observation has now been often repeated. Cold and wet, injuries to the spine, excessive labour, and sexual excesses may possibly act by depressing the general vitality, and so precipitate the disease in a person whose nervous system is already infected.

The disease arises generally between eight and twelve years after syphilitic infection, and is therefore commonest in the middle period of life, between thirty and fifty, and it is noteworthy that tabetics comparatively rarely manifest other signs of constitutional syphilis. It is more frequent in men than women, in about the proportion of ten to one. In the juvenile form, however, which appears in a small proportion of congenital syphilitics during adolescence, the distribution between the sexes is more nearly equal.

Morbid Anatomy. The change constantly found in the spinal cord is a degeneration of the ascending nerve fibres, and sclerosis of neuroglia, in the posterior columns. It is seen as a grey discoloration of the white matter in the fresh specimen, whilst in sections stained by the Weigert-Pal method the pallor of the diseased columns stands out in evident contrast with the deep staining healthy tracts (Plate 54, Figs. 1—3). In ordinary cases it is the fibres entering the lumbo-sacral segments of the cord which are affected, and the degeneration is therefore most evident in the postero-external columns in this region (*see* Plate 54, Fig. 3), whilst in the cervical enlargement, owing to the displacement inwards of these fibres, it appears in the postero-internal columns. In cases involving the arms the postero-external fibres are degenerated in the cervical region. The association fibres in the posterior columns remain intact, the degenerative process being confined to those fibres which represent the direct continuation upward of the processes of the posterior root ganglia. Under the microscope degeneration and disappearance of the nerve fibres, increase of the glial tissue, which is fibrillated, and thickening of the walls of the arteries are observed. In advanced cases changes may also be detected in the grey matter, such as atrophy and degeneration of nerve cells or fibres in the posterior horns, in Clarke's columns, and even in the anterior cornua. The pia mater is often thickened over the posterior columns, or even over the lateral columns as well, or completely round the cord.

The posterior nerve roots are generally atrophied down to the spinal ganglia, which are mostly healthy, as well as the mixed nerves beyond them. In the optic nerves, in cases alluded to, are found atrophied nerve fibres and overgrowth of neuroglia. Atrophy or degeneration of the nuclei of the third, fourth, fifth sixth, eighth, and twelfth cranial nerves have in different cases been seen, as well

as of the Gasserian ganglion, but the lesion of reflex iridoplegia in tabes is not certainly known, though it is probably situated in the periaqueductal substance of the mid-brain.

Pathology. Little is absolutely known of the pathology of tabes beyond the fact, which has already been stated, that the disease is primarily a process of destruction of the posterior column nerve fibres due to the activity of the *Treponema pallidum* or its toxins. Since the action in tabes dorsalis and in general paralysis of the insane appears to be directly upon the nervous elements, these two diseases are often spoken of as *parenchymatous syphilis of the nervous system* to distinguish them from those forms of syphilis in which degeneration of nerve cells and fibres is secondary to affections of the meninges and blood vessels.

Owing to the chronic nature of the illness, opportunities for pathological study have been limited mainly to end results, but in early cases the point of initial lesion appears to be the point where the nerve fibres coming from the posterior root ganglion pass through the pia mater to enter the cord.

The delay between the original syphilitic infection and the onset of the disease has been variously explained. The probable sequence of events is as follows and has reference not only to tabes but other forms of neurosyphilis. In the stage of blood stream dissemination spirochætes find their way to the meninges and give rise to a mild inflammatory reaction. In the great majority of cases this causes no symptoms, but the cerebro-spinal fluid shows an increase of cells and protein, sometimes an abnormality of the gold curve. A positive Wassermann reaction is uncommon. Such changes are to be found in forty to fifty per cent. of all cases of untreated secondary syphilis. It is supposed that in most of these cases, with or without treatment, the meningeal infection dies out, but in a small percentage it continues and there is a chronic but clinically silent meningitis. This may eventually develop in the form of localised gummatous thickening with injury to the brain, cranial nerves or spinal cord, or it may continue as a diffuse leptomeningitis. After a lapse of many years it may then commence to invade the substance of the brain causing a diffuse meningo-encephalitis, which is the basis of general paralysis of the insane. Into the spinal cord it finds entry along the path followed by the afferent fibres as they pierce the pia mater, giving rise to the symptoms of tabes.

Symptoms. As might be expected from its pathological anatomy, tabes is essentially a disease of sensory symptoms, especially in its early stages. The significance of these is readily missed, and yet, seeing that the best we can hope for our treatment is to arrest the progress of the disease, it is most desirable that we should recognise it before gross defects of muscle and joint sensibility have led to a condition of disablement from ataxy. In the early (pre-ataxic) stage the characteristic symptoms are pains in the limbs, cutaneous hyperæsthesia of the trunk or limbs, loss of knee jerk, and loss of pupil light reflex. This stage may last for months or years.

The pains known as *lightning pains* occur in 95 per cent. of the cases; they are severe shooting, stabbing, or darting pains, as a rule in the lower extremities, sometimes in the arms. They come on suddenly, and, it may be, with such severity as to make the patient start up in bed, or cry out. Each pain lasts only for a few seconds, but they generally soon recur and continue thus coming and going in different parts of the limbs for several hours. They may then disappear, and not return till the next day, or till after an interval of days or weeks. They thus present the greatest irregularity both as to recurrence and duration. The patient frequently puts them down to "rheumatism," but if questioned gives a description so graphic as to be quite unmistakable.

The hyperæsthesia of the skin, usually that covering the upper part of the trunk or of the legs, is often noticed early by the patient, who complains that light-stroking contact, for instance putting on and off the underwear, gives rise to a peculiar, unpleasant sensation, which may also be aroused by extremes of

in the stage of arrest or quiescence, both blood and spinal fluid may be normal. Or again a positive blood may be found with a normal fluid.

Prevention. This consists in the prevention of syphilis in the first place, and in the early adoption of vigorous antisyphilitic measures if the disease is contracted.

Treatment. This may be considered under two heads, specific and symptomatic.

Specific. Of recent years it has become a universal practice to employ salvarsan or similar compounds in the treatment of all forms of syphilis, and cases of tabes are usually treated by such means. The principles to be employed are those laid down for the treatment of syphilitic myelitis (*see* p. 666). In the majority of cases symptoms may be alleviated and the course of the disease retarded or prevented by efficient treatment. As in the treatment of syphilitic myelitis, mercury and iodides are also given in tabes.

Symptomatic. For the lightning pains any of the analgesic drugs may be tried, singly or in combination. A powder containing 5 grains each of aspirin, phenacetin and veramon is useful. If other measures fail, opium or its derivatives in some form must be used. Five grains each of aspirin and phenacetin with one-sixth of a grain of heroin hydrochloride makes a useful cachet. Heat also is sometimes of value, and in some instances an attack of lightning pains may be aborted by an analgesic dose taken together with a bath as hot as the patient will stand. Hypodermic injections of morphia should be employed only as a last resort, but are sometimes necessary. As a general rule they should not be given except by doctor or nurse and should be reserved for the severe bouts of pain, for there is a considerable danger of habit formation.

A gastric crisis may sometimes be aborted by giving a bath as hot as the patient can stand it, and then putting him to bed with hot-water bottles and the administration of morphine, $\frac{1}{4}$ grain, hypodermically. At the height of an attack morphia may be necessary to relieve the pain. If the attack is of long duration, rectal feeding is necessary.

In cases in which repeated gastric crises have rendered the patient's life almost intolerable, a surgical procedure which has met with some success is exposure of the spinal cord and division of the antero-lateral ascending tracts in the upper thoracic region.

Attention to the bladder is very necessary, and the catheter should be used if any urine is retained. The expulsive power may be increased by strychnine or incontinence lessened by belladonna.

For the laryngeal crises inhalation of amyl nitrite may give relief.

Much may be done for the ataxia by means of graduated exercises (Fraenkel's exercises). This is essentially a process of re-education by which the patient is taught to compensate for his loss of sense of position by co-ordination of visual impressions with muscular movements. These exercises may be begun in bed, the patient being instructed to practise simple co-ordinated movements such as raising the leg to a certain height and then placing it nicely in contact with an object set up for the purpose. Thence he is led through movements in the sitting and standing postures to those of orderly progression, full use being made throughout of the visual sense. Thus he is taught to stand opposite a wall and raise the foot to touch various marks upon it, while supporting himself with his hands, to advance by placing his feet accurately upon footmarks outlined on the floor, and so on. In this way it is often possible to obtain for a bedridden patient some measure of ambulatory activity.

SUBACUTE COMBINED DEGENERATION

This is a disease *sui generis* characterised by progressive widespread degeneration of the fibres of the posterior and lateral columns of the spinal cord, usually associated with pernicious anæmia, and if untreated leading to a fatal termination.

Ætiology. This disease is most common between the ages of fifty and sixty, the extremes at which the onset has been recorded being twenty-six and seventy. Nothing is known of its true ætiology. Its association in the great majority of cases with pernicious anæmia, and its response to the same treatment, which is of value in that disease, suggests that subacute combined degeneration of the cord is at any rate partly dependent upon a failure of absorption from the diet of some substance essential to the health of the nerve fibres.

Pathology. In the great majority of cases evidence of pernicious anæmia is already present when the symptoms of spinal cord disease first appear. In a few cases, however, the spinal cord symptoms precede those of anæmia.

As in pernicious anæmia, gastric achylia is the rule. Subacute combined degeneration may also occur in association with carcinoma of the stomach, pellagra and ergotism.

Morbid Anatomy. Macroscopic examination shows the spinal cord to be of normal size, in contrast with the condition found in diffuse sclerotic processes. On cross section the degenerated areas in the white matter appear as greyish patches, which in the mid-dorsal region usually form a complete circle around the central grey matter. The degeneration of the longitudinal fibres is the essential feature of the disease. The Weigert-Pal staining method shows, in cases where death has occurred in the earlier stages, that this process commences in the centres of the ascending posterior and descending lateral columns of the lower thoracic region (*see* Plate 55, Fig. 2); thence it extends centrifugally until, in cases where the fatal termination has been delayed, there are no medullated fibres remaining except for the short association fibres surrounding the grey matter.

Similar patches of degeneration occur in the lumbar and cervical enlargements, and the disease process extends longitudinally by coalescence of these patches. The first sign of degeneration is swelling of the myelin sheaths, which then undergo fatty degeneration and break up into droplets which are stained black by the Marchi staining method. With this the axis cylinder breaks up and disappears. The degeneration products are subsequently absorbed, leaving a fine network of neuroglial and connective tissue elements containing empty spaces in place of the destroyed nerve fibres. There are no material changes in the walls of the blood vessels and relatively little overgrowth of neuroglia.

The nerve cells are not affected except as a secondary result of degeneration of their axons. Thus the cells of Clarke's column show vacuolation and chromatolysis consequent upon the degeneration of the spino-cerebellar fibres, and similar changes are found in the Betz cells of the pre-central cortex as a result of destruction of the pyramidal tracts.

In rare cases there are found scattered minute hæmorrhages in the cord, but these probably occur as terminal events, and cannot be considered as a cause of the degeneration of nerve fibres.

Symptoms. The illness is most commonly ushered in by paræsthesiæ of the extremities. These begin with numbness and tingling of the fingers and toes, extending to the hands and feet, and are soon followed by impairment of cutaneous sensibility of the same distribution. The nature of the sensory loss varies; sensibility to pin-prick is generally lost earlier than that to cotton wool, and with extension of the area involved the loss to pain precedes that to touch. In the earlier stages the glove and stocking distribution is retained, but as the anæsthesia progresses from the lower limbs on to the trunk the upper level follows a segmental line. Evidence of affection of the posterior columns is usually found at an early stage of the disease in the form of loss of sensations of position, passive movement and vibration in the extremities, and the knee and ankle jerks are lost. Other subjective sensory phenomena commonly met with are sensations of tightness around the waist and constriction or swelling in the lower limbs.

The signs of pyramidal disease usually follow those already mentioned, and are indicated by the complaint of weakness in the lower limbs and the appearance of

extensor plantar responses. In other cases the lateral columns may be affected first. The patient then complains that his feet feel heavy, and drag as he walks, especially when he is tired. Later the lower limbs become stiff, and the gait is that of a case of spastic paraplegia, though careful examination will probably reveal an ataxic element due to the loss of muscular and joint sensibility. As the posterior columns become more completely involved the spastic picture gives place to that of flaccid paralysis, and the gait resembles that of the tabetic. At this juncture the patient, relieved of his stiffness, may be led to the false hope that he is improving, but with the further development of the ataxy soon becomes bedridden. The paraplegia does not as a rule reach the upper limits of the regions supplied by the cervical enlargement, and even in the later stages of the disease the affection of the upper extremities remains limited to peripheral anæsthesia and weakness.

The sphincters are always affected in the later stages of the disease. At first there may be difficulty in starting the act of micturition, which is followed by loss of control, with the rapid development of complete incontinence of urine and fæces. At this period cystitis is likely to occur, with the sequence of pyelonephritis, leading to a fatal termination, and bedsores inevitably develop.

The mental state toward the end is one of lethargy, drowsiness and complacency, occasionally developing into a state of feeble delirium. The special senses and cranial nerves are not affected. The reflexes are variously affected at different stages of the disease. In the more usual type beginning with sensory disturbance the ankle jerks are lost early, loss of the knee jerks follows, and the plantar responses by this time are usually of the extensor type. In the type which begins with spastic weakness the plantar responses are from the first extensor, the knee and ankle jerks at first exaggerated, subsequently lost. The abdominal reflexes are as a rule retained until a late stage of the disease.

Anæmia is recognisable in about one-half of the cases when first seen. It is of the type met with in pernicious anæmia, see p. 432. The skin often shows a yellowish tint, against which the presence of a bright malar flush may give the face a characteristic aspect.

Although anæmia of this type appears in a great majority of cases before death, there are some which run a course typical of that described above to a fatal termination without ever developing the characteristic blood picture.

Gastric achlorhydria is the rule and may be present without anæmia.

The **Diagnosis** in the early stages is often difficult, but complaint on the part of a person between the ages of fifty and sixty of peripheral paræsthesiæ as described above should always arouse the suspicion of subacute combined degeneration, and lead to a careful investigation of the reflexes, a complete blood examination, and a test meal.

The flaccid type of the disease with absent tendon jerks and peripheral anæsthesia has to be differentiated from *polyneuritis*. The calves may be tender to pressure in both diseases. The main points of clinical value in distinguishing the two are the presence in the history of subacute combined degeneration of girdle sensations and defective sphincter control and on examination a predominant affection of deep rather than cutaneous sensibility with extensor plantar responses.

This type of the disease also has to be distinguished from tabes in which the pyramidal tracts may be occasionally involved with extensor plantar responses. The history of the illness, together with the frequent occurrence in tabes of pupillary abnormalities, are points of importance in this connection, and the examination of blood and spinal fluid will settle the question.

The spastic type must be distinguished from *disseminated sclerosis*, in which the presence of nystagmus and intention tremor and a history of transient disturbances of sensation, power, or vision are commonly present.

The manner of the onset is sufficient to distinguish the disease from acute

myelitis or a spinal tumour. The only other illness of note in which combined posterior and lateral column degeneration occurs is *Friedreich's disease*, from which subacute combined degeneration is easily differentiated by the age incidence and other signs.

The absence of free hydrochloric acid in the gastric juice and the macrocytic anæmia, which are characteristic of most cases of subacute combined degeneration, furnish positive evidence of a kind which usually suffices to decide the diagnosis in a doubtful case.

Prognosis. Until recently the prognosis was considered to be almost uniformly bad, the tendency being towards a fatal issue from cystitis or bedsores within two or three years of the onset, although in rare cases remissions might occur. With the advent of the liver treatment of pernicious anæmia the outlook in subacute combined degeneration became more hopeful, and it is now apparent that in cases of pernicious anæmia in which symptoms of spinal cord disease have not yet appeared they may be prevented; that when the spinal cord degeneration has already commenced its progress may be arrested; and that in many cases the symptoms and signs of subacute combined degeneration may be considerably improved. These results, however, are only to be obtained by means of adequate and persistent treatment.

Treatment. The treatment is that for pernicious anæmia and has already been described. For the treatment of subacute combined degeneration it is essential that liver extract, desiccated stomach, and iron should be given in doses sufficient to achieve and maintain a normal blood picture, and that over and above this an extra margin of maintenance dosage be allowed for the treatment of the spinal cord disease. In cases in which the disease has become arrested with treatment, but with posterior column damage, Fraenkel's exercises as recommended for tabes may be of great help.

FRIEDREICH'S ATAXIA

The characteristic feature of this disease is its congenital tendency and its appearance in several members of the same family. Thus a man may transmit it to his children, or it may appear in two or more brothers and sisters without the parents being affected. It affects males only a little more often than females, though males may be especially affected in one family, females in another; and it is generally first noticed at an early age, either about the seventh or eighth year, or at puberty. Non-familial cases also occur.

Pathological Anatomy. Degeneration is found in the posterior columns in the spino-cerebellar tracts and in the pyramidal tracts (Plate 55, Fig. 3). Both sides of the cord are affected symmetrically, and the degeneration is most marked at the mid-thoracic level. The cells and fibre network of Clarke's column show changes in association with the degeneration of the spino-cerebellar fibres. The cerebellum as a rule shows no pathological changes.

The cause of the disease seems to be a congenital want of vitality in the neuron systems or tracts involved.

Symptoms. The onset is as a rule gradual, and the disease is first manifested in a certain clumsiness of the gait and a tendency for the child to fall about when at play or when performing actions requiring a nice balance. These symptoms depend upon inco-ordination, which conforms to the cerebellar type and may be demonstrated by means of the various tests already described (finger-nose-finger and heel-knee tests, diadochokinesis). The arms are affected as a rule rather later than the legs. While at rest the patient may show irregular jerky movements of the limbs somewhat resembling those of chorea, and in particular there is to be noticed a nodding tremor of the head.

The inco-ordination is not confined to the limbs, but also affects the speech musculature, so that the utterance is hesitating and explosive. Nystagmus is usually present, but is not a prominent feature of the illness. The knee and

ankle jerks are lost comparatively early by reason of involvement of the posterior columns, and the plantar reflexes are extensor as soon as the pyramidal tracts are affected.

A peculiar feature of the disease is the almost constant presence of certain skeletal deformities. Of these the most characteristic is *pes cavus*, a condition in which the arch of the foot is greatly exaggerated and the toes are hyper-extended at the metatarso-phalangeal, flexed at the interphalangeal, joints. The other is *scoliosis*, or lateral curvature of the spine in the dorsal region, with which is usually associated some degree of *kyphosis* or forward curvature. The causes of these deformities are imperfectly understood.

Sensibility is not as a rule affected to any important extent, but in some cases diminution of both the superficial and deep forms of sensation may be discovered on careful examination. The sphincters are not affected. In patients who show signs of the disease before the age of puberty physical development is usually retarded, and the mentality also remains somewhat childish. The disease is slowly progressive over a number of years, but not directly fatal.

Diagnosis. This has to be made from *juvenile tabes*, in which the common occurrence of Argyll-Robertson pupils, optic atrophy and associated signs of congenital syphilis, together with the Wassermann reaction in blood and spinal fluid, serve to make the differential diagnosis certain. Friedreich's ataxy may also resemble *disseminated sclerosis*, which, however, is seldom fully developed at such an early age, and in which the tendon jerks are exaggerated, not lost. In *cerebellar tumour* the signs of increased intracranial pressure are usually evident, but apart from this there are cases of *hereditary cerebellar ataxy* which are distinguished with some difficulty from Friedreich's disease.

Prognosis. This is unfavourable. The patient tends eventually to become bedridden after a period of ten or fifteen years, and as a rule dies comparatively young of some intercurrent affection.

Treatment is of little avail, but some improvement may be effected by means of systematic and continued training after the manner of the exercises employed for the treatment of tabes dorsalis.

PERONEAL MUSCULAR ATROPHY

(Charcot-Marie-Tooth Disease)

The main features of this disease are the distribution of the muscular wasting, its slow progress, and the frequency with which a hereditary tendency is manifested by cases occurring in blood relations. As a rule it is transmitted directly to succeeding generations by persons themselves affected. Although isolated cases are reported, careful search often reveals unmistakable signs of the disease in supposedly unaffected members of the family.

Pathological Anatomy. Degeneration is found in the anterior horn cells corresponding to the wasted muscles, in the peripheral nerves, and in the posterior columns (3).

Symptoms. These usually commence in childhood, but in exceptional cases may first appear in middle life. The onset is gradual with wasting and weakness of the small muscles of the feet, and of the anterior tibial group, especially the peronei. This results in characteristic deformity and difficulty in walking. The toes become curled up owing to over-extension at the metatarso-phalangeal and over-flexion at the inter-phalangeal joints; the plantar arch is raised and shortened, producing a *pes cavus*, and the foot is dropped at the ankle joint and inverted. The patient, therefore, has difficulty in clearing his foot from the ground, and is apt to trip over his toes, especially when hurrying.

As the disease progresses the small muscles of the hands are often next affected. The progress of the disease is often extremely slow and may not extend further than this. When it does so the wasting gradually extends up the lower limbs in a

somewhat characteristic fashion, affecting first the calves, and then the lower parts of the thighs. Fibrillary twitchings may occur in the wasting muscles, and the electrical reactions in most cases show R.D.

There may be complaint of numbness and tingling in the feet at the commencement of the disease, but there is no objective sensory disturbance.

Loss of tendon jerks as a rule precedes muscular wasting, so that all the tendon jerks of upper and lower limbs may be abolished at a stage when wasting is confined to the feet. There are, however, exceptions to this rule, and in practice it is found that each family group of these patients, though remaining true to its own type, shows variations from others. The mental condition, special senses, cranial nerves and sphincters are unaffected.

Diagnosis. The differential diagnosis has to be made from Friedreich's disease. In both there are *pes cavus* and absent tendon jerks with a family history of the disease, but in Friedreich's ataxia there are signs of damage to the cerebellar and pyramidal fibres. The absence of such signs in peroneal muscular atrophy, together with the wasting of the anterior tibial group of muscles, as a rule makes the distinction easy.

The distal type of progressive muscular dystrophy is not so easily distinguished. The points in favour of peroneal atrophy are the occurrence of fibrillary twitchings, the early loss of tendon jerks, and reaction of degeneration in the affected muscles.

Prognosis. The course of the disease is so slow that the disability in many cases is slight, and the patient may continue to get about with the aid of special boots and orthopædic apparatus. In some cases, after a period of five to seven years, the affection seems to become spontaneously arrested.

Treatment. Special boots, night splints, and in some cases walking apparatus, are needed to correct deformities. Massage and passive movements are also useful.

MOTOR NEURON DISEASE

This title has been taken to include the diseases formerly described in this volume under the separate headings of progressive muscular atrophy, amyotrophic lateral sclerosis, progressive bulbar paralysis and primary lateral sclerosis. The pathological process, so far as is known, is the same in all these maladies, being characterised by a primary degeneration of the upper or lower motor neurons, or most commonly of both together. The exact clinical picture varies with the preponderance of upper or lower neuron involvement and the level of the cerebro-spinal axis chiefly affected.

Ætiology. Our knowledge of the origin of this disease is very incomplete. It is a malady of middle and late life, and it is more common in males than in females. A small proportion of cases appear to be due to syphilis, as proved by a positive Wassermann reaction in blood or spinal fluid, but in the great majority no cause whatever can be found for the degeneration.

Morbid Anatomy. Macroscopic changes are inconspicuous. The spinal cord may appear shrunken in the cervical and lumbar enlargements and the pre-central convolutions of the brain show similar atrophy. Under the microscope there is what seems to be a primary degeneration of the pyramidal fibres in the spinal cord frequently extending upwards to the internal capsule and cerebral cortex. The fibres of the antero-lateral tracts in the cord also appear to be thinned, so that in a Weigert-Pal stained section (*see* Plate 55, Fig. 1) the healthy posterior and postero-lateral columns stand out in marked contrast to the affected areas. Sections stained by the Nissl method show a great diminution in the number of motor cells in the anterior cornua. Of those that remain most are shrunken and degenerate. Similar changes may be seen in the nuclei of the brain-stem, especially the twelfth and the motor nuclei of the vagus, and in the Betz cells of the motor cortex.

The affected muscles show degeneration and atrophy with proliferation of the sarcolemma nuclei, and some replacement fibrosis, but no deposition of fat such as is seen in the myopathies.

Symptoms. The clinical picture varies with the situation of the cells and fibres chiefly affected. In the commonest type (*progressive muscular atrophy*) weakness and wasting of the upper limbs is the initial symptom. This begins usually in the small muscles of the hands, both being affected together or one after the other. The thenar eminences are flattened, the hollow of the palm is accentuated and the line of the ulnar border of the hand loses its contour from wasting of the hypothenar muscles. On the dorsal surface hollows or " gutters " appear between the metacarpal bones from disappearance of the dorsal interossei, the hollow between the index finger and thumb being conspicuous. If the muscles of the forearm retain their power the fingers tend to fall into the " claw " position, extended at the metacarpo-phalangeal and flexed at the terminal joints from unopposed action of the long extensors and flexors. The thumb, on account of weakness in its intrinsic muscles, falls back into line with the fingers with pad facing forwards—the ape hand. There is no particular order of spread to the other muscles of the upper limbs, but those of forearm and shoulder are often affected, while the biceps and triceps still escape. The muscles of the neck, trunk and lower limbs are subsequently affected. In the latter the thighs are usually involved first. Not uncommonly, the disease spreads to the bulbar nuclei. In other cases the disease begins in this part (*progressive bulbar paralysis*), and the patient presents himself on account of dysarthria, dysphagia, or more rarely hoarseness. The tongue is first and chiefly affected and the fibrillary twitching, which is a characteristic but inconstant accompaniment of the wasting in the other muscles affected, is hardly ever absent in this organ. The muscular atrophy also betrays itself early by the appearance of creases and hollows in the enveloping mucous membrane. Together with the tongue the muscles of the lips are usually involved, increasing the difficulty of articulation, so that often before there is any striking abnormality in the outward appearance, speech becomes thick and unintelligible. Involvement of the palate and pharynx lead to dysphagia, and of the vocal cords to hoarseness. The masticatory and upper facial muscles are not often involved, and the ocular muscles hardly ever. In rare instances the disease may commence in the lumbar enlargement with weakness and atrophy of the lower limbs, usually first apparent in the thighs.

As a rule, the wasting and weakness advance *pari passu*, but there are cases, especially when the disease is rapidly progressive, in which muscles of a considerable bulk are found almost powerless. Together with the atrophic palsy there is nearly always some evidence of upper neuron involvement. Despite the atrophy, the tendon reflexes are usually brisk or even exaggerated in the early stages, only disappearing with the muscles themselves. An exaggerated jaw jerk is characteristic of the cases with bulbar involvement. The plantar responses sooner or later take the extensor form.

Sometimes, but rarely, the upper neuron involvement precedes or overshadows the other, and the disease is characterised by spastic weakness, especially of the lower limbs. This may be accompanied by atrophic weakness of the hands or bulbar muscles (*amyotrophic lateral sclerosis*), or the degeneration may remain confined to the pyramidal fibres (*primary lateral sclerosis*).

There is no objective impairment of sensory function, but in some cases the muscular atrophy may be preceded by complaint of shooting pains and tingling in the limbs. The fibrillary twitching, if severe, may be a source of discomfort. Sphincter control remains normal unless the pyramidal fibres are severely involved. The mental condition is usually unaffected, but in cases showing much involvement of the pyramidal tracts above the bulbar level there is frequently some loss of control over the expression of the emotions, so that the patient laughs, or more usually weeps, with unusual readiness.

Prognosis. The course of the illness is gradually progressive. The rate of progress is variable. At the extremes death may occur within a year of the onset, or the patient may be living at the end of fifteen years. The rate of progress in the individual case tends to remain steady, so that some idea of the prognosis may be gained after a period of observation. Cases with early involvement of the bulbar or respiratory muscles are most likely to run a short course. Those in which the wasting remains confined to hands and forearms (*progressive muscular atrophy*) may progress very slowly, and the same applies to those in which the pyramidal tracts only are affected. Death is usually due to intercurrent infection of the respiratory tract. Bulbar involvement opens the way to an aspiration broncho-pneumonia.

Diagnosis. The form characterised by early wasting of the hands (*progressive muscular atrophy*) has to be distinguished from the effects of any focal lesion in the cervical enlargement of the cord, such as tumour or chronic meningitis or pressure from diseased bone. The presence of sensory loss below the segmental level of the lesion, together with alterations in the contents or pressure of the spinal fluid, will usually serve to distinguish these. The distinction from syringomyelia may be difficult on account of the tendency in both maladies for bulbar and hand muscles to be involved simultaneously with the pyramidal tracts. A careful sensory examination may be necessary to settle the doubt.

Lead palsy may be distinguished by the characteristic distribution of the paralysis and other evidence of lead poisoning.

Cervical ribs cause atrophy of the hand muscles and may be bilateral, but in these cases the wasting is strictly limited to the hands. An X-ray will help to settle the question. The wasting of an *ulnar or median neuritis* is accompanied by its appropriate sensory loss. The hands may be involved in *peroneal muscular atrophy*, but after the feet.

The cases with bulbar onset (*progressive bulbar paralysis*) have to be distinguished from the pseudo-bulbar paralysis (*see* p. 702) due to vascular lesions. The absence of wasting and the history of a sudden onset in the latter are the distinctive features.

The cases which begin with spastic weakness of the lower limbs have to be diagnosed from the various transverse lesions of the cord, which may produce a similar picture, such as disseminated sclerosis, spinal tumour, spinal syphilitic meningitis, and from subacute combined degeneration. It may be possible to arrive at a conclusion only after a considerable period of observation.

Treatment. Except for the rare cases in which a syphilitic origin can be proved, there is no treatment which has any power to arrest the progress of the disease. An examination of the blood and spinal fluid should be made in every case, and if either shows a positive Wassermann reaction a course of anti-syphilitic treatment should be instituted. Treatment otherwise is palliative. A good nutritious diet, exercise without strain, and avoidance of mental fatigue are desirable. In the way of local treatment massage helps to preserve the muscles by maintaining the circulation. The function of the affected muscles is improved by warmth, so that radiant heat of any kind may be helpful.

Although public faith in the efficacy of electrical stimulation may force the hand of the physician, its effect, if any, is probably harmful.

LANDRY'S PARALYSIS

In 1859 Landry described cases of paralysis commencing in the lower extremities, rapidly ascending, and soon fatal, for which no pathological cause could be found on examination. Cases of the kind still occur in which the coarser lesions of myelitis and softening are entirely absent.

Ætiology. The disease affects males more than females, and is most frequent between the ages of twenty and forty. It has occurred after exposure to cold, in convalescence from acute diseases, and in patients addicted to

alcohol; and a few cases have been recorded after cystitis or other forms of urinary sepsis. In the majority of instances, however, no adequate predisposing causes are to be found.

Pathology. In some rapidly fatal cases the spinal cord, nerves, and muscles have been found completely free from disease. In others there have been varying degrees of degenerative change (chromatolysis and displacement of the nucleus) in the cells of the spinal cord, especially those of the anterior cornua, and of Clarke's columns, with more or less vascular engorgement, but no hæmorrhage or perivascular infiltration of leucocytes. There may be changes in the myelin of the anterior roots and of the white columns of the cord, but none in the peripheral nerves. Occasionally, when the fatal termination has been delayed, the Marchi method reveals the presence of degenerative changes in the peripheral nerves, which are probably secondary to those in the anterior horn cells. It is clear from the above account that the histological picture in Landry's paralysis is quite distinct from that of an ascending myelitis, peripheral neuritis or anterior poliomyelitis. Micro-organisms, but not always the same, have been found by different observers in the nerves, spinal cord, meninges, and blood.

Symptoms. In some cases there are premonitory symptoms, such as malaise, pain in the head and back, and numbness and tingling, but usually the disease begins with weakness in the legs, often one before the other. This soon increases to definite paralysis, and invades successively, and within a few days (or in acute cases in a few hours), the thighs, trunk, abdomen and arms; and these, like the legs, are not always affected simultaneously. The diaphragm and the muscles of the neck, of the palate, and those subserving articulation are subsequently paralysed. Very rarely other cranial nerves are affected; thus diplopia, paralysis of accommodation, dilatation of one pupil, and facial paralysis have been noticed. As a rule cutaneous sensibility is normal, though there may be some loss to light touch in the peripheral areas of the extremities. The sensations of passive movement and position are unaffected. In rapidly fatal cases the muscles have not wasted, and the electrical reactions have appeared to be normal; but in some cases of longer duration both atrophy of muscles and modifications in electrical properties have been observed. Control over the urinary and rectal sphincters is not lost, and there is no tendency to bedsores; the cerebral functions are perfect, and there is no fear except in a few cases at the very onset. The tendon jerks and skin reflexes are lost as the corresponding muscles become paralysed.

Diagnosis. This has to be made from acute ascending *myelitis*, from infective *poliomyelitis*, and from *multiple neuritis*. The first of these is distinguished by the pronounced loss of sensation, and the early implication of the bladder. In poliomyelitis there is more general disturbance—fever, headache, pains, perhaps convulsions—and the paralysis is rarely quite uniform or symmetrical. In multiple neuritis symptoms come on gradually, paralysis appears in the peripheral parts of the arms and legs almost at the same time, and the nerves and muscles are tender.

The mortality is high—*e.g.* 58 per cent. in cases collected by Ross; these, however, probably included some cases of peripheral neuritis. The duration of the disease is from two days to two or three weeks in fatal cases, and death occurs mostly from paralysis of the diaphragm and intercostal muscles. On the other hand, the symptoms persist from two to six or seven months in cases which recover; but recovery is generally complete.

Treatment. This may be the same as that of multiple neuritis or acute myelitis.

SENILE PARAPLEGIA

In people of advanced age the lower limbs may become weak and unsteady, and walking slow and difficult, without any of the physical signs characteristic of

the diseases of the spinal cord which have already been described. The term senile paraplegia, sometimes applied to such cases, has probably been used to cover a number of different conditions in which such symptoms may occur. In the majority the lesion is cerebral rather than spinal, being due to arterial thickening with consequent softening of the brain substance. Pathological examination shows a tendency for such areas of cerebral softening to be symmetrical, with frequent involvement of the basal ganglia, although other parts may be involved. A careful neurological examination will reveal in these cases some defect of function of a Parkinsonian, pyramidal or cerebellar type, which, though it chiefly affects the lower limbs, also involves the arms and trunk. The condition is slowly progressive. Adequate rest, with massage, passive movements and educational exercises, may be of some help.

MENINGITIS

In the cerebral as in the spinal meninges, we have to distinguish an inflammation of the dura mater, or *pachymeningitis*, and inflammation of the arachnoid and pia mater, or *leptomeningitis*.

The pia mater appears to be much more subject than the dura mater to the influence of micro-organisms, and to these bodies nearly all forms of lepto-meningitis can be traced.

The organisms most often concerned are—

1. The *pyogenic organisms* (streptococci, staphylococci) which may invade the meninges in pyæmia and septicæmia, after injury to, and operations on, the cranial bones, and in diseases of the ear, nose, and frontal sinuses ; these cause a *suppurative* meningitis.
2. *Tubercle bacilli*, secondary to a tuberculous focus, either in the brain itself or in some other part of the body.
3. The *pneumococcus*, often in association with pneumonia, as part of malignant endocarditis, or as a primary affection.
4. The *meningococcus*, or *Diplococcus intracellularis* of Weichselbaum, which causes cerebro-spinal fever, or epidemic cerebro-spinal meningitis, including its posterior basal variety.
5. *Syphilis* is a frequent cause of meningitis, which is, however, generally subacute or chronic in its course.
6. The bacilli of *influenza*, *typhoid fever*, the *gonococcus*, the *Bacillus coli communis*, and other organisms have been found in some cases.

The results of bacterial invasion are seen in the effusion of lymph or of pus on the surface of the brain, often with an increase in quantity of the cerebro-spinal fluid.

There is a general resemblance to what has already been described under the head of cerebro-spinal fever and tuberculous meningitis.

SUPPURATIVE MENINGITIS

Ætiology. If we exclude cases of cerebro-spinal fever, a purulent meningitis is in the majority of cases the result of invasion by the pyogenic or septic organisms, and arises in circumstances similar to those which lead to abscess of the brain ; that is, its common cause is a focus of disease in the immediate neighbourhood. Thus it may follow injuries to the head, or be set up by extension of inflammation in neighbouring parts, such as otitis media, mastoid suppuration, disease of the nasal cavities, syphilitic caries or necrosis of the skull, suppurative phlebitis, or abscess of the brain. But it occurs also as a complication in some general diseases of an acute, febrile, or infective nature—pyæmia, septicæmia, pneumonia, and malignant endocarditis.

Pathology. The inflammation chiefly affects the pia mater and arachnoid (*leptomeningitis*). When it has spread from a diseased bone of the skull, the dura

mater itself may show localised inflammation, but the extension of the disease over the brain is by means of the other membranes. Commonly the convex surface of the brain presents a more or less extensive layer of bright yellow or green pus, which may be on both sides, or confined to one side, the side of the lesion in secondary cases. The pus frequently follows the course of the larger vessels, and dips down with the pia mater into the sulci. Though mostly affecting the upper surface of the hemispheres (meningitis of the convexity), it usually extends to the base, and into the spinal canal. The brain tissue beneath it is commonly softened, and may present ecchymoses or minute abscesses.

Symptoms. While there is a general resemblance to the symptoms of tuberculous meningitis, the course of acute meningitis is usually much more rapid, and there is much diversity as to the prominence of particular symptoms. Where meningitis supervenes upon other acute illnesses, its features may be more or less masked. In cases without apparent cause, and in cases caused by chronic inflammatory lesions, like otitis, the symptoms often commence acutely with chill or rigor, and acute pain in the head. This is generally very severe and constant and aggravated from time to time. The patient becomes feverish, shuns light and noises, and may lie curled up in bed, resenting interference, as in the tuberculous cases. Vomiting often occurs at the commencement. There may be rigidity of the muscles at the back of the neck, and the head is drawn back. The pupils are often contracted. Kernig's sign is usually present. Convulsions also may occur quite early, and may be followed by active delirium, or by drowsiness accompanied by delirium; and in later stages there is often paralysis, with repeated attacks of convulsions, generally bilateral. The paralysis is very variable, corresponding to the situation of the effusion; from its frequent occurrence at the vertex it less often affects the cranial nerves than does tuberculous meningitis, though there may be squint; but an arm or leg is often paralysed, or there may be complete hemiplegia. Sometimes there is rigidity of the paralysed limbs, or of their fellows. The pupils become dilated, and the ophthalmoscope sometimes reveals optic neuritis, which may develop rapidly under observation. The temperature is high, varying from 102° to 104°, the pulse is mostly rapid, respiration is sighing, irregular, or of Cheyne-Stokes type, and in some cases the abdomen is retracted. The drowsiness passes into deep coma, and, finally, the evacuations are passed involuntarily, the breathing and circulation fail, mucus accumulates in the chest, and death terminates the scene. The disease is often fatal within two or three days of the first symptom, and sometimes even less. The cerebro-spinal fluid by the time that clinical suspicions have led to lumbar puncture is usually hazy or turbid, but in the early stages of an acute meningitis the fluid may be clear to the naked eye. On examination it contains an increase of cells, of which the large majority are polymorphs. The protein also is increased and the chlorides diminished as a rule in proportion to the cell increase. Microscopic examination and cultivation will often reveal the causal organism.

Diagnosis. Where there is a primary source, such as otitis media, the diagnosis is generally easy. In the other cases the initial symptoms may resemble those of any acute infection. Headache, however, is usually a prominent symptom, or when the spinal cord is first involved, pain in the back. The routine employment in all cases of obscure pyrexia of the tests for *neck stiffness* and *Kernig's sign* will as a rule ensure an early diagnosis. In some cases, however, in which the anterior parts of the cerebral meninges are chiefly affected, as for instance in a meningitis secondary to frontal sinusitis, neck stiffness may be late in developing, severe and persistent headache being the prominent feature. Lumbar puncture is the final test, and by this means the diagnosis of meningitis may usually be made at the bedside from naked eye inspection of the fluid, which is hazy or turbid. The nature of the meningitis can be determined only by bacteriological examination.

Prognosis. The majority of cases of suppurative meningitis are fatal, but a fair proportion of the milder cases, such as may be seen complicating otitis media, recover. The most important criterion in these cases appears to be the presence or absence of bacteria in the spinal fluid. If the causal organism can be seen in direct smears, or grown easily on culture, the prognosis is almost invariably bad.

Treatment. Where a primary focus, such as mastoiditis or frontal sinusitis, is present this should be dealt with surgically as soon as possible. Lumbar puncture should be performed daily, and the spinal fluid, which is usually under considerable pressure, should be allowed to drain until the rate of flow appears normal. This procedure is frequently successful in relieving headache and neck stiffness, and in the milder cases already referred to may lead to complete recovery, the fluid gradually becoming normal. Morphia is often necessary to relieve pain and allay irritability. In syphilitic cases treatment with neo-salvarsan should be instituted at once. If the streptococcus be identified as the causal agent anti-streptococcal serum should be given subcutaneously, or intravenously.

SYPHILITIC MENINGITIS

The syphilitic virus may in rare instances give rise to the symptoms of an acute leptomeningitis (*see* p. 690). These cases occur shortly after the primary infection during the stages of general dissemination of the spirochætes. Much more common than this is a chronic inflammatory process of syphilitic origin occurring at a later period, from one to five years or even later, after the initial infection which affects both pia-arachnoid and dural membranes in a widespread manner, and gives rise to symptoms both by strangulation of the cranial nerve roots and by causing an increase of intracranial pressure.

Morbid Anatomy. The appearances are very similar to those already described in connection with syphilitic meningomyelitis (*q.v.*). As a rule pia-arachnoid and dural membranes are affected together and become welded into a dense fibrous mass, which may be as much as $\frac{1}{8}$ inch in thickness and envelop the whole of one or both hemispheres. At the base of the brain the leptomeninges alone may be affected, but are usually adherent to the dura. The interpeduncular space is a common situation for this form of meningitis, from which may result compression of the upper cranial nerves, particularly the third and sixth pairs, and also interference with the arterial branches of the circle of Willis. As in the case of syphilitic involvement of the spinal meninges, there is always a certain amount of vascular disease accompanying the meningitis. This takes the form of endarteritis and perivascular sheathing with lymphocytes. With this is associated some degeneration of the underlying nervous substance itself. Thrombotic occlusion of the narrowed vessels may lead to the additional feature of patches of cerebral softening.

Symptoms. The symptoms of the rare form of acute syphilitic meningitis occurring in the early stages of the disease are similar to those met with in other acute inflammatory affections of the leptomeninges, and have already been described.

The main clinical features of the chronic variety are intense headaches, together with vomiting and other signs of increased intracranial pressure, and multiple paralyses of the cranial nerves. In the early stages the symptoms are very frequently intermittent. Thus the cranial nerve palsies—and it is the third and sixth nerves which are most often affected—are commonly transient; and the headache may come on in paroxysmal attacks, lasting a few hours or a few days, which are followed by relatively long intervals of quiescence. Papillœdema may be present, or a gummatous mass pressing upon the optic chiasma may lead to optic atrophy with alterations in the visual fields similar to those met with in pituitary tumour.

The cranial nerves are picked out in a random manner indicative of the wide-

spread distribution of the inflammatory process. Localised patches of thickening upon the surface of the hemispheres may give rise to attacks of Jacksonian epilepsy (*q.v.*), which may be followed in turn by paralyses of monoplegic or hemiplegic distribution. As the disease progresses the headaches become more continuous, and the cranial nerve palsies more constant.

Mental deterioration is a frequent symptom resulting from the combination of increased intracranial pressure with syphilitic disease of the blood vessels. The syphilitic endarteritis also may lead to additional symptoms of cerebral thrombosis with sudden onset of paralysis of one or more limbs.

Diagnosis. The chronic form of syphilitic meningitis has to be distinguished from other conditions which give rise to signs of increased intracranial pressure with paralysis of the cranial nerves. Of these the most important is cerebral tumour. Points in favour of a syphilitic origin are a relapsing tendency and scattered cranial nerve palsies. A strongly positive Wassermann in the blood and cerebro-spinal fluid is the rule in cerebral syphilitic meningitis, but occasionally the reaction may be negative in one and positive in the other. It follows that an examination of both is necessary to exclude syphilis in a doubtful case. There is frequently an excess of cells and protein in the cerebro-spinal fluid. In cases of cerebral tumour the Wassermann reaction is negative in both blood and fluid.

Some cases of syphilitic meningitis with mental deterioration, headaches, and epileptic attacks may closely simulate general paralysis of the insane, especially if the Wassermann reaction is positive in the cerebro-spinal fluid. The diagnosis in such an instance may usually be arrived at by observing the results of anti-syphilitic treatment. When the disease is mainly confined to the meninges the symptoms as a rule disappear, and the Wassermann reaction often becomes negative under treatment, whereas neither of these results is obtained in general paralysis.

The **Prognosis** is good in cases which are diagnosed and effectively treated in the early stages, but, as in the case of syphilitic disease elsewhere in the body, there is a tendency to relapse, and it is well, therefore, for the patient to submit to a short course of treatment annually as a preventive measure against recurrence.

Treatment. This is the same as for syphilis elsewhere, with the provision, however, that it is best not to commence with intravenous injections of arsenical compounds, such treatment being liable in some cases to provoke an initial reaction in the inflammatory tissue with increased symptoms of intracranial tension. It is, therefore, wise to begin with potassium iodide, which should be given in large doses (45 to 90 grains daily) for the first fortnight, after which treatment should be continued on the lines already indicated (*see* p. 666).

PACHYMENINGITIS INTERNA HÆMORRHAGICA

This is a condition in which a mass of blood and partially organised blood clot is found upon the surface of the brain between the dura and the arachnoid membrane. This is usually surrounded by adhesions by which it is encapsuled.

Ætiology. The condition is found most commonly in association with chronic alcoholism and chronic insanity and in old persons. Two views have been put forward as to its causation, (1) that the initial process is inflammatory (of toxic origin), with subsequent extravasation of blood from engorged capillaries; (2) that the effusion of blood is of traumatic origin and that the subsequent encystment results from the reaction of the meninges to the mass of blood clot. In favour of the second explanation Trotter has put forward the arguments that the condition in no way differs from that known to occur as a delayed result of head injury, and that the insane person or alcoholic is quite likely to sustain a head injury and subsequently forget its occurrence. According to Trotter, then, the effusion is due to oozing from the veins passing from the surface of the brain to the longi-

tudinal sinus, and the laceration of these vessels is due to an unrecognised head injury. Sudden displacement of the brain, especially in a forward or backward direction, may be supposed quite readily to cause such laceration, and may possibly result from a trivial blow. If this view is correct the condition is identical with that described in surgical text-books as *chronic subdural hæmatoma.*

Morbid Anatomy. The inner surface of the dura mater is covered with one or more layers of membrane, soft and friable when recent, tougher and more fibrous when old, in colour brownish red, brown, brownish grey, yellow, or even white, and often presenting punctiform ecchymoses; while between the layers may be considerable quantities of blood clot more or less altered by age, or collections of serum containing cholesterin crystals. The deposits are usually situate over the parietal region, near the middle line, and are bilateral in about half the cases. They may be mere membranes, or 2 or 3 mm. in thickness, and if much blood is extravasated, the surface of the brain is depressed. Micro-organisms have been looked for but have not been found.

The **Symptoms** are very variable. Often the condition has been found *post-mortem* without any symptoms which would be explained by it; sometimes, on the other hand, it is fatal as the result of a large hæmorrhage between the membranous layers, which compresses the brain. The symptoms are those of increased intracranial pressure—headache, drowsiness, papillœdema and mental deterioration, and those due to pressure upon the cerebral hemisphere—unilateral weakness with spasticity, increased tendon jerks and an extensor plantar response. If the effusion be left-sided aphasia may be a prominent symptom, and in the bilateral cases there may be a progressive double hemiplegia. It is somewhat characteristic of the condition that the symptoms both of pressure and paralysis vary from day to day. The patient may lapse into coma for a day or two and revive, and the process may be repeated, and the parietic signs also may fluctuate from day to day. Twitching of the limbs may occur but true epileptiform convulsions are uncommon. The cerebro-spinal fluid pressure may be increased as in cerebral tumour, but is sometimes normal. Its constituents usually show no abnormality but may include altered blood pigment.

Diagnosis. This has to be made from cerebral thrombosis and from causes of increased intracranial pressure, such as tumour and syphilis. A history of symptoms appearing gradually after a head injury is of the greatest value, but the latent interval may be one of weeks or even two or three months, the injury may have been a slight one, and in the alcoholic or senile patient it may have been forgotten. The progress of symptoms is, as a rule, much slower and more uneven than that of a cerebral thrombosis. Syphilis may need to be excluded by examination of blood and cerebro-spinal fluid. The distinction from cerebral tumour is more difficult, and is often achieved only with the aid of an exploratory craniotomy. Indeed, in many cases the unsuspected hæmatoma has been exposed by an operation designed to discover a cerebral tumour.

Treatment. If the diagnosis can be made correctly the proper treatment is surgical decompression with evacuation of the mass.

SPINAL MENINGITIS

The membranes of the spinal cord may be involved, together with those enveloping the brain, in acute meningitis of any cause. The pathological appearances and symptoms of this condition are described elsewhere in this volume (*vide* Meningitis). The inflammatory changes due to syphilis (p. 108) and tubercle (p. 88) have also been referred to.

There is one other condition which deserves separate mention. *Meningitis serosa circumscripta* is the name given to a condition in which over a circumscribed area adhesions are formed between the cord, the leptomeninges, and the dura. Cerebro-spinal fluid may be enclosed within the meshes of the

newly formed tissue, so that a cyst-like appearance is produced. The ætiology in some cases is obscure, but in a considerable number the origin, as it appears from the history, is traumatic, although the pathology of the condition has not been satisfactorily explained. The symptoms, which are due to compression of nerve roots and spinal cord, may follow upon those of a definite traumatic lesion of the cord or an injury to the back without spinal symptoms at the time, and develop after a latent interval of weeks or months. Their nature depends upon the level affected and the degree to which the roots or the spinal cord itself are relatively involved. Thus the early symptoms may consist of root pains and muscular twitchings, followed by sensory loss and wasting of segmental distribution and signs of spinal cord compression only as a late development, or the clinical picture may be that of a gradually progressive transverse lesion of the cord from the first without root involvement. The diagnosis has to be made from other transverse lesions such as may be caused by tumour, syphilis or disseminated sclerosis. X-ray evidence of former injury to the vertebral column may be a valuable point when there is a doubtful history of trauma. An exploratory laminectomy may be necessary to settle the diagnosis. The symptoms may be relieved by incision of the membranes with release of the localised collection of fluid, but the condition shows a tendency to recur.

DISEASES OF THE BRAIN

CEREBRAL HÆMORRHAGE

In dealing with diseases of the brain prominence must be given to vascular lesions, which are responsible for the majority of cases of cerebral paralysis. Rupture of the vessels, with escape of blood (*hæmorrhage*) into the brain, and obstruction of the arteries by *embolism* and by *thrombosis*, are the forms of acute vascular lesion which have to be considered.

Ætiology. Cerebral hæmorrhage occurs more frequently in men than in women, and more in advanced life than in youth. The cause, as a rule, is arterial disease, almost always in association with a high blood pressure. Thus it is a common event in diffuse hyperplastic sclerosis and chronic Bright's disease, but may also occur in cases of senile arterial degeneration with a normal blood pressure. Syphilitic arteritis, though commonly leading to thrombosis, is a rare cause of cerebral hæmorrhage. Hæmorrhage into the brain may occur in any one of the blood diseases in which there is a liability to bleeding, such as scurvy, purpura and hæmophilia. It also occasionally happens that a congenital aneurysm of one of the cerebral arteries ruptures into the cerebral substance instead of into the subarachnoid space as is more common, and this should be remembered as a possible cause of cerebral hæmorrhage in young persons with normal arteries and blood pressure. Hæmorrhage may also occur into a vascular tumour of the brain such as an angeioma.

Seats of Hæmorrhage. Scarcely any part of the brain is exempt from the risk of hæmorrhage, but it is much more frequent at the base in the neighbourhood of the corpus striatum and optic thalamus, which are mainly supplied by the branches of the middle cerebral artery, to which reference has already been made (*see* p. 605). Vessels may also burst in the lateral ventricles (*ventricular hæmorrhage*), or on the surface of the brain (*meningeal hæmorrhage*); but when blood is found in these situations, it has often proceeded from a hæmorrhage primarily in the cerebral substance.

Morbid Anatomy. In different circumstances the blood effused may be small in quantity or amount to several ounces. In the latter case it tears up the cerebral tissue, destroying, for instance, the great ganglia and the internal capsule, and extending thence into the centrum ovale, or it may burst through the optic thalamus or caudate nucleus into the lateral ventricle. Thence the

blood flows by the aqueduct of Sylvius into the fourth ventricle. Such cases are rapidly fatal, and post-mortem examination reveals a mass of dark red clot, filling the ventricle and occupying much of the hemisphere, surrounded by brain substance, which is ragged and discoloured by blood. In cases which have lasted a few days there is the same black-red clot, and the tissue around is soft and discoloured yellow, from absorption of hæmoglobin. The effect upon the parts of the brain not immediately destroyed by the hæmorrhage varies with the amount of the effused blood, and is due to pressure upon and consequent anæmia of the surrounding parts. This effect at first is local, but in the case of a large effusion rapidly becomes generalised, with consequent flattening of the convolutions and obliteration of the sulci. In cases which survive the clot gradually shrinks and becomes softened and yellow, this change proceeding inwards from the periphery, and is eventually absorbed. Meanwhile, the destroyed nervous elements in the surrounding brain tissue are broken up and destroyed by scavenging cells, and proliferation of the neuroglia proceeds to the formation of a wall surrounding the cavity or of strands which intersect it. The cavity may thus finally be obliterated with the formation of a puckered neuroglial scar, or it may remain in the form of a single or multilocular cyst containing serous fluid. The scar tissue frequently retains a yellow discoloration from the altered blood pigment. Destruction of the descending nerve fibres or their cells of origin leads to secondary degeneration, which is most easily followed in the course of the pyramidal tracts.

Symptoms. Cerebral hæmorrhage may be preceded for days or weeks by occasional giddiness, numbness or twitching of the fingers, headaches, insomnia, or some diminution of mental capacity; but these are not so much indications of the severe attack to come as evidences of existing disease of vessels, and perhaps due themselves to slight hæmorrhages. On the other hand, it may come on without any warning whatever. Sometimes it seems attributable to a definite cause, such as emotional excitement, muscular effort, violent coughing, or straining at stool; but at others it occurs when the patient is perfectly quiet, or even during sleep. In numerous cases cerebral hæmorrhage causes a group of symptoms known as *apoplexy*—that is, the patient is struck down suddenly unconscious, or he quickly becomes so (ἀποπλήσσειν, to strike to earth). Patients have died in five or ten minutes from the first symptom. More often the symptoms come on slowly. The patient is seized with intense pain in the head, becomes faint or slightly collapsed, may be sick or have a slight convulsion, and then, after half an hour or more, gradually sinks into a condition of coma. Or the first symptoms may show themselves in the motor system: the patient mumbles in his speech, or his arm drops powerless, and he gradually leans over to one side, falling if not supported, and then lapses by degrees into coma. Or the coma may be developed in a few hours through stages of increasing drowsiness, or the attack may begin with convulsions. In some cases the collapse is extreme, and the pulse is barely perceptible; but after an hour or two it improves and becomes full and bounding as the patient assumes the condition described below with complete coma and paralysis. Cases in which some hours elapse before the coma is complete have been called *ingravescent apoplexy*. When the patient is found by the friends alone, or is picked up in the street unconscious, or is unable to be roused in the morning from sleep, it is of course impossible to say what the onset has been. But undoubtedly cerebral hæmorrhage may occur without apoplexy; a very slight bleeding into the motor tract alone may give rise to paralysis without loss of consciousness, but this is uncommon.

The patient suffering from hæmorrhagic coma lies completely unconscious, and cannot be roused by shouting or any form of stimulation of his skin. The face is flushed; the pulse is full and tense; the breathing is *stertorous*, a loud, snoring noise being made in consequence of the palate or tongue falling back

and impeding the passage of air into the chest. The condition of the limbs varies: both legs and arms may be quite flaccid, falling at once when raised, or it may be obvious that the leg and arm on one side are more flaccid than those on the other. The muscles of the face share in the paralysis, and the cheeks are puffed out and sucked in with the processes of respiration; this may also occur only on one side. Sometimes, however, the limbs of one or both sides are in a condition of rigidity (*early rigidity*), the muscles contracted and resisting extension or flexion. The deep reflexes are commonly increased, and the skin reflexes are absent. The plantar responses are the first to return and are then usually extensor. The pupils are variable: they are sometimes contracted, at others dilated or unequal. Conjugate deviation may occur. The temperature shows a slight fall, which may continue till death, or if life is prolonged it rises a little above the normal. A greater or persistent fall of temperature, like a rapid or excessive rise of temperature, is of ominous significance. The latter is often associated with rupture into the lateral ventricles. Sugar is occasionally found in the urine, from pressure on the medulla oblongata. A trace of albumin is commonly present in association with primary contracted kidneys. In very severe cases the pulse and breathing are rapid, there is profuse sweating, and intense flushing of the face and skin generally; then after a time, two or three hours or more, the patient becomes livid, râles occur in the larger bronchi and trachea, the pulse gets weaker, the breathing slower, and finally death takes place. The fatal termination may, however, be delayed for several days, during which the lungs are very apt to suffer from œdema or pneumonia; and the occasional passage of particles of food or fluids through the glottis probably contributes to the inflammation of these organs. In more favourable cases, the patient lies simply comatose, with but little disturbance of his pulse or respiration, and gradually regains his senses in the course of a few hours or two or three days. In a large proportion of cases, the patient is then found to be suffering from *hemiplegia*, which may itself slowly recover or be permanent.

Diagnosis. This has to be made from other conditions, causing a sudden onset either of coma or the signs of a cerebral lesion, and will best be considered after cerebral thrombosis and embolism have been described.

Prognosis. This is generally unfavourable in proportion to the extent of severity of the first symptoms. That apoplexy is often fatal is well known, and death may take place at different intervals after the onset. The cases are grave in which the coma is profound, with much stertor, flushed or congested face, full bounding pulse, and complete relaxation of all the limbs. A temperature which rises steadily during the first thirty-six hours is usually a sign of hæmorrhage into the ventricles and a fatal issue.

If, after recovery from the first coma, headache continues, and the patient again becomes drowsy, the result is likely to be serious.

Treatment. If the case is seen early and the diagnosis is certain venesection is theoretically the correct treatment, for the fall of blood pressure thus produced may arrest the flow from the ruptured vessel and give time for coagulation to occur. Practical experience, however, shows that cerebral thrombosis, as well as cerebral hæmorrhage, may occur in a person with a high blood pressure and hypertrophied heart, and the differential diagnosis is largely a matter of conjecture. Venesection is, perhaps, as likely to do harm in thrombosis as to help in hæmorrhage. As a general rule, therefore, it is perhaps better avoided. In the case, however, of a person of middle age previously known to have a systolic pressure over 200 mm. Hg. without signs of cardiac failure, the chances of hæmorrhage as opposed to thrombosis are high, and prompt removal of a pint of blood is the right course.

The essential part of treatment in all cases is complete rest until such time as it may be assumed that the ruptured vessel has healed. The patient should be

put to bed with as little disturbance as may be. If he is unconscious he should be laid on his side, care being taken that his head does not drop forward and impede the circulation in the large veins of the neck. The skin should be carefully tended. The patient should not be allowed to remain on one side too long, and if he is heavy a water-bed is advisable. He may be incontinent, but if there is retention catheterisation is necessary. During the first twenty-four or forty-eight hours purgatives are better avoided. Their administration to an unconscious patient is difficult and their action disturbing. If the patient is known not to have had his bowels open recently an enema may be given at the end of twenty-four hours. If he is in a restless semi-conscious condition sedatives should be given. Chloral hyd. gr. xv. with pot. brom. gr. xxx. in a single dose, to be repeated if necessary, is suitable by the mouth. If the patient cannot take this and is restless morphia should be given, for although it has a depressing action on the respiratory centres rest is most important, and restlessness itself an indication that the degree of pressure upon the vital centres is not dangerous. If the patient is conscious he should be laid upon his back with head and shoulders supported on a pillow. The room should be darkened and kept quiet and visitors forbidden. It is probably wise to starve the patient for the first twenty-four hours, water being given in sips from a feeding cup. After this fluid feeding can be commenced by the mouth if he is conscious, or per rectum after a preliminary enema to clear the bowel. A light diet should be enforced for some days or weeks. In a severe case the patient should be kept in bed for at least a month from the onset, and even in a slight case rest in bed for a fortnight is advisable. In the case of paralysed limbs massage and movements should not be begun until three weeks have elapsed, except that very gentle passive movements of the joints may be performed night and morning to prevent adhesions. At the end of this time, massage, passive movements and especially active movement, should be carried out daily. Electrical treatment in a case of hemiplegia is of no value. After an attack of cerebral hæmorrhage the patient's mode of living should be regulated according to the cause. (*See* Hyperpiesia.)

CEREBRAL EMBOLISM AND THROMBOSIS

Pathology. The usual cause of *embolism* is endocarditis. In ulcerative or infective endocarditis the embolus is formed by a fragment detached from one of the vegetations upon the valves. In chronic mitral stenosis with a dilated left auricle clot may form in the auricular appendix, and a portion of this being broken off and delivered into the blood stream may form an embolus. Embolism from mitral stenosis occurs as frequently without as with the association of auricular fibrillation. Another and much less frequent cause of central embolism is the passage of a clot from one of the systemic veins (*e.g.* saphenous, femoral or pelvic) through a patent foramen ovale. Occasionally after coronary thrombosis a portion of clot formed within the left ventricle may become detached and cause embolism.

The middle cerebral artery is more often affected by embolism than the others, and the left more often then the right.

Thrombosis is most frequently caused by disease of the vessel wall, such as atheroma, by which the surface is roughened, and fibrin is consequently deposited. Syphilitic disease of the arteries produces considerable narrowing of their channels, and thus favours thrombosis. In addition, thrombosis may occur from several conditions weakening the circulation, such as those resulting from enteric fever, typhus, cancer, phthisis, and other severe illnesses. It may also occur in erythræmia.

Embolism and thrombosis, by obstructing the circulation of the blood, alike lead to *softening* of the districts of the brain to which the vessels correspond, unless the vascular supply is maintained by means of anastomoses. These are

not abundant in the case of the cerebral vessels, and, indeed, the vessels going to the central ganglia are really terminal vessels, while those going to the cortex of the brain anastomose more or less. At least, this is true of the distribution of the middle cerebral artery—the vessel most often obstructed. A part of the brain in which softening has taken place has generally lost the smooth, glistening surface of a normal brain section, is more opaque, or grey, or speckled; it breaks down readily under a stream of water; or it is milky or diffluent. It shows under the microscope drops of myelin, portions of nerve fibres, large mononuclear phagocytes containing granular *débris*, and free fat globules. It sometimes has a yellowish or brownish colour from altered blood pigment; or minute extravasations of blood may be present in cases of sudden obstruction, and a form of *red softening* results. In cases of rapid death after embolism, the brain substance may look perfectly healthy, as there has not been time for any changes visible to the naked eye to take place. Occasionally an embolus sets up inflammatory changes in its neighbourhood; sometimes it leads to aneurysm and cerebral hæmorrhage, as already described. Rarely actual infarcts are formed. The later stages of softening consist in the absorption of the disintegrated tissue, and the formation of a cyst; or, if the softening is small, a cicatrix may be produced.

Thrombosis or embolism, involving the motor tract, are followed by the same secondary changes as are hæmorrhagic lesions.

Symptoms. The results of *embolism* are not very different from those of hæmorrhage; but it more often causes sudden hemiplegia without loss of consciousness than does hæmorrhage. Obstruction of a large vessel will cause sudden loss of consciousness, and death may take place soon after. Since the softening occurs only in the areas supplied by the vessel beyond the seat of obstruction, the symptoms are more likely to correspond with the distribution of the artery than in hæmorrhage, where the extravasated blood ploughs up the brain with little discrimination. If the middle cerebral be obstructed near its origin, there will be hemiplegia of the opposite side, and if the lesion is on the left side, aphasia also, since this artery supplies the internal capsule, Broca's convolution, the greater part of the motor area of the cortex, the first and second temporal convolutions, and the angular gyrus. Persistent hemiplegia is accompanied by the conditions already mentioned (*see* p. 607).

Thrombosis is usually less rapid in its effects, though with the same results—apoplexy and hemiplegia; but sometimes a sudden coma occurs, indistinguishable from that of hæmorrhage. There are often premonitory symptoms—headache, dizziness, loss of memory, drowsiness, numbness, or formication of an arm or leg, or of one side of the body.

Diagnosis of Cerebral Vascular Lesions. This may be divided into two heads—the diagnosis of apoplexy from other conditions simulating it and the diagnosis from one another of the different causes of apoplexy or hemiplegia.

1. In the former the history is of great importance. Causes of coma occurring in the course of severe illnesses, such as meningitis, cerebral abscess, cerebral tumour, typhoid fever, etc., may be readily excluded by the history; it is coma coming on suddenly or rapidly which may be confounded with apoplexy. In *pyæmia* a sudden coma has sometimes occurred closely resembling that of apoplexy. More commonly the conditions to be discriminated from it are coma from injury, poisoning by opium, alcoholic poisoning, uræmia, diabetes, epilepsy and heart-block. In hot countries it will be necessary to remember that coma arises from heat stroke and pernicious malaria.

Cases of *injury*, in the absence of history, may present the greatest difficulties, as, even with the external evidence of injury, it may remain uncertain whether the patient has fallen as a result of apoplexy, or has injured his brain in consequence of the fall. Even after death the problem may be insoluble. The position of a scalp wound in relation to the weaker side, if paralysis can be recognised,

may sometimes help; and the age of the patient, or other circumstances of his bodily health, may render a spontaneous lesion of the brain more or less likely. In cerebral concussion the patient is pale, with dilated pupils and low blood pressure. His limbs are flaccid. Recovery is usually heralded by vomiting. In sub-dural hæmorrhage there are symptoms of *compression*, with slow pulse; there is gradually deepening coma with remissions, during which the patient is quite conscious.

Opium poisoning is generally distinguished by the minutely contracted pupils, the slow pulse, and slow respiration; but it may be closely simulated by hæmorrhage into the pons Varolii. Evidences of a unilateral lesion, such as greater flaccidity or rigidity of limbs on one side, or unequal pupils, are in favour of hæmorrhage. In *poisoning from other hypnotic drugs*, such as chloral or the barbiturates, the respiratory rate and depth are often increased, and the pupils dilated and reacting sluggishly to light. The same may be said of *alcoholic poisoning*. The condition is one of profound coma, without any one-sided symptoms. Evidence of alcohol may, of course, be obtained from the breath, or from the stomach by means of emetics or the stomach tube. But a patient may have drunk freely or sufficiently just before an apoplectic attack, or if the attack has come on gradually he may have taken a glass of spirits as treatment.

Asthenic uræmia is accompanied by albuminuria, but the detection of albumin in the urine does not exclude cerebral hæmorrhage, for, in the first place, hæmorrhage occurs often in those who have granular kidneys; and, secondly, hæmorrhage may itself produce albuminuria in those who have healthy kidneys. In uræmia sometimes the coma is less profound; the patients are more easily roused for a time by shouting, to relapse again into coma. There is no paralytic weakness, no vasomotor disturbance, and no flush of congestion, such as occur in some cases of apoplexy. Addison used to call attention to the hissing nature of the breathing. Uræmia will be indicated by a large increase of urea in the blood (*see* p. 530).

Diabetic coma develops very slowly, and is not profound till near the end; it is often preceded by severe abdominal pain, so severe sometimes as to have led to a diagnosis of perforation of the intestine. The pulse is rapid and feeble, the breathing is often slow, deep, or sighing, and the breath has a sweet odour. The urine contains sugar and aceto-acetic acid; but here also a mistake is possible, for a hæmorrhage involving the fourth ventricle may produce glycosuria.

A *major epileptic attack* is commonly followed by coma, which is more like natural sleep than that of apoplexy; there are no unilateral symptoms, but both plantar responses may be extensor. Apart from a previous history of epilepsy, the presence of a recently bitten tongue, or of minute hæmorrhages beneath the skin, conjunctiva or mucous membranes may be of diagnostic value. If the onset of the attack has been witnessed by the patient's friends the story of tonic or clonic spasms at the onset is usually obtainable, and conclusive.

Hypoglycæmic coma, which may be accompanied by epileptic attacks, is usually the result of an overdose of insulin, but may occur as the result of other disease (*see* p. 479). Occasionally *hysterical* patients will lie unconscious for long periods, but the cases are generally distinguished by other characteristic symptoms.

The chief feature in *heart block* is the extremely slow pulse (*see* p. 232). There may be convulsions, and the breathing is deep and rapid.

Sub-arachnoid hæmorrhage is sometimes distinguished with difficulty from an intra-cerebral vascular lesion. In both cases the onset may be apoplectic, but in sub-arachnoid hæmorrhage, unless the effusion has torn its way into the brain, there are no unilateral signs, and as the patient begins to emerge from coma, neck stiffness and Kernig's sign are discoverable, and there is abundant blood in the cerebro-spinal fluid obtained by lumbar puncture.

2. In the diagnosis of the causes of apoplexy, one has to consider the nature of the attack and the associated condition of the patient. It will have been seen

that the nature of the attack often gives but little help. Hæmorrhage, embolism, and thrombosis may all produce a sudden or rapid coma. The more severe and prolonged the coma the greater the probability of hæmorrhage, whereas a pronounced hemiplegia, occurring without coma or with very transient unconsciousness, is more likely to be due to embolism or thrombosis. Age is in favour of hæmorrhage, and youth almost excludes it except from a congenital aneurysm; but in persons between forty-five and sixty years of age positive indications in one or other direction are often wanting. In ventricular hæmorrhage evidence of blood will be found in the liquid withdrawn by lumbar puncture.

The associated conditions of hæmorrhage are albuminuria and other evidences of renal disease, or arterial degeneration, with tense and rigid or thickened arteries, high blood pressure and a hypertrophied heart. Senile changes in the arteries may also be recognised in many cases of thrombosis. Hemiplegia in young subjects free from heart disease is often due to syphilitic arteritis, of which further evidence may be found in the history, or in the Wassermann test. In embolism there is generally a mitral or aortic murmur, or some evidence of dilatation of the left cavities of the heart, which serves as a source of the embolus, or there may be signs of embolism in other parts of the body, such as enlargement or tenderness of the spleen, blood in the urine, the characteristic appearances in the retina, or obstruction of an artery in one of the limbs. Other less common causes of apoplexy with hemiplegia are general paralysis of the insane, hæmorrhage into a cerebral tumour, infective encephalitis and the rupture of an intracranial aneurysm into the substance of the brain.

Treatment. If cerebral embolism or thrombosis can be certainly recognised, the treatment is similar to that of cerebral hæmorrhage; but venesection must not be thought of. Absolute rest, milk diet, ice to the head if there is pain, and gentle laxatives or enemas if the bowels are confined, are the main indications.

The treatment of the resulting hemiplegia is also the same.

CHRONIC CEREBRAL SOFTENING

Disease of the cerebral arteries, besides causing such relatively severe and sudden symptoms as have already been described, may lead to a gradual deterioration of cerebral function without any apparent seizure. This may result from the sum of repeated small vascular lesions or from a gradual and diffuse process of decay.

Pathology. Arterial thickening and decay of the varieties already described is the basis of the morbid condition. To the naked eye the brain may show multiple areas of softening or may simply appear shrunken. Under the microscope smaller areas of softening are apparent. In the affected areas the nerve cells and fibres are degenerated. The myelin is broken up into fatty droplets, which are removed by scavenging cells, and there is a variable amount of neuroglial reaction.

Symptoms. The symptoms vary according to the parts of the brain chiefly affected, but since the process of decay is usually widespread mental deterioration is often prominent. This takes the form of defective memory, especially for recent events, and difficulty in concentration. These symptoms are, as a rule, apparent to the patient, who will often complain of them. Loss of emotional control with short-lived moods of depression, irascibility and more rarely of elation, and disturbance of sleep, are other symptoms. Epileptic attacks may occur and may be of a generalised or focal type. Optic atrophy may occur with failure of vision as the leading complaint. Involvement of the pyramidal fibres on both sides of the brain not infrequently leads to loss of voluntary control over the muscles supplied by the cranial nerves, and of these the palate, tongue and pharynx are most often involved, with consequent dysarthria and dysphagia, the

condition being known as *pseudo-bulbar paralysis* to distinguish it from that form of bulbar palsy which is due to disease of the lower motor neurons, and has already been described. (*See also* Pseudo-uræmia.)

Sensory symptoms are uncommon, but the motor functions may be interfered with in various ways. If, as commonly happens, the pyramidal fibres are chiefly involved, the picture is that of a progressive double hemiplegia, the spasticity and weakness being usually more marked in the lower than in the upper limbs. Or the basal ganglia may be affected with consequent development of rigidity, weakness and tremor of the kind seen in paralysis agitans. The cerebellar functions also may be involved. In the case of pyramidal involvement the deep reflexes are increased, including, in the cases of pseudo-bulbar paralysis, the jaw-jerk, and the plantar responses are extensor. The history may be of an insidious onset, but careful enquiry will often elicit a story of attacks of giddiness or faintness, probably representing minute vascular lesions.

Diagnosis. The age of the patient and the condition of his arteries are as a rule the guides to a correct diagnosis. In a middle-aged patient a high blood pressure may be the important clue, and ophthalmoscopic examination of the retinal vessels will often provide valuable evidence of arterial disease.

The differential diagnosis has to be made from other causes of slowly progressive cerebral disease, such as syphilis and tumour, and from the neuroses.

Prognosis. This is necessarily bad, the symptoms tend to progress slowly and the patient with cerebral softening is always liable to an outspoken attack of cerebral hæmorrhage or thrombosis.

Treatment. This must be to a large extent symptomatic. The general *régime* should be that already laid down for patients suffering from arteriosclerosis (*see* pp. 301, 304), mental fatigue in particular should be avoided, and the patient advised to rest on his bed for an hour in the middle of the day. Sedatives and hypnotics should be given as required to control irritability and insomnia.

THROMBOSIS OF THE CEREBRAL SINUSES

The blood coagulates in the cerebral sinuses either as a result of some profound cachexia, or in consequence of infection from lesions of adjacent parts.

The former causes mostly an adhesive thrombosis, the sinus being obstructed by laminated clot, without any general infection of the system. It occurs most often in infants, especially those suffering from marasmus or chronic diarrhœa. It mostly affects the *longitudinal sinus*. Coma, rigidity of the neck, trunk or limbs, twitching of the muscles, and epileptic attacks are the main symptoms, and if there is recovery bilateral spastic weakness results which is most marked in the lower limbs.

The morbid appearances associated with thrombosis of the longitudinal sinus are highly characteristic. The large veins in the pia-arachnoid are thrombosed and stand out like dark cords. The veins on the inner surface of the dura as they enter the sinus are also distended.

Thrombosis from *local infection* is mainly caused by extension from disease of the ear, but the origin may be in the orbit, nose, mouth, pharynx, or other part from which the lateral or cavernous sinus can be reached.

Lateral sinus thrombosis is generally the result of otitis media and mastoiditis. The onset is usually marked by a rigor, which may be repeated at the peaks of a swinging temperature. The thrombosis may extend into the jugular vein, which is then felt as a hard swelling below the mastoid process in the neck.

Thrombosis of the cavernous sinus may be secondary to infection of the nose, cheek, eye or nasal sinuses. Rigors and fever are less constant and prominent features than in lateral sinus thrombosis. There is proptosis of the eye, œdema of the conjunctiva and eyelids, and frequently paralysis of the ocular muscles

from involvement of the third, fourth and sixth cranial nerves. Papillœdema may be present but is inconstant. The condition is usually bilateral and fatal.

In these infective cases septic particles are frequently conveyed into the right heart, and thence into the lungs, so that a fatal pyæmia is the result.

Treatment. In thrombosis dependent on general ill-health, this condition must be treated. If local lesions are the cause, they must be dealt with surgically. The spread of an infective thrombus down the jugular vein can be prevented by tying the vein below the clot and clearing out its contents, as well as those of the lateral sinus, if necessary.

SUB-ARACHNOID HÆMORRHAGE

Hæmorrhage in connection with the cerebral membranes may be between the bones of the skull and the dura mater (*extra-dural*), within the dura mater but outside the arachnoid membrane (*sub-dural*), or within the sub-arachnoid space (*sub-arachnoid*).

The first two are almost invariably traumatic and are dealt with in works on surgery. The symptoms of a chronic sub-dural hæmatoma which may present considerable difficulties in medical diagnosis are dealt with under the head of pachymeningitis interna hæmorrhagica (*see* p. 693).

Ætiology. Sub-arachnoid hæmorrhage may occur spontaneously as the result of rupture from any cause of a superficial vessel. The common cause in elderly persons is arterial disease with hæmorrhage either direct or with the preliminary formation of a small aneurysm. In young persons with healthy arteries the cause is usually the rupture of a congenital aneurysm. Such aneurysms are by no means uncommon, being found at the junctions of the circle of Willis or the bifurcation of its main branches, presumably as the result of a defect in development. They are often of minute dimensions and readily missed at a post-mortem in a case of sub-arachnoid hæmorrhage unless specially looked for. Aneurysm of the cerebral arteries with subsequent rupture may also result from embolism in infective endocarditis, and is another cause of sub-arachnoid hæmorrhage. It may also occur, though rarely, in the various conditions such as hæmophilia and purpura, in which spontaneous bleeding may happen.

Morbid Anatomy. In a fatal case the whole sub-arachnoid space is filled with blood, which extends in a thin sheet over the hemispheres, lies in greater depth in the basal cisterns, and wells up from the spinal sub-arachnoid space when the brain is removed. Patient search will usually reveal the source of hæmorrhage in the case of an aneurysm, but unless this is especially looked for it may be missed.

Symptoms. In elderly persons with disease of the cerebral arteries there are often preliminary symptoms of the same kind met with in cerebral hæmorrhage (*q.v.*). In others and in young persons with congenital aneurysms the onset is dramatic. If the rupture is a large one the patient may fall suddenly to the ground unconscious. More usually there is abrupt complaint of severe headache or pain in the back of the neck with subsequent loss of consciousness. The duration and depth of coma vary with the size of the effusion. If the rent is a large one the patient may die within a few hours without recovery of consciousness. In the case of a smaller leakage consciousness is regained and signs of meningeal irritation appear in the shape of pain and stiffness in the back of the neck and a positive Kernig's sign. The tendon reflexes at this stage are frequently lost and the plantar responses extensor. The optic discs are frequently engorged and sometimes show large retinal and sub-hyaloid hæmorrhages. If improvement continues these signs of meningeal irritation gradually pass away in the course of two or three weeks. During the earlier stages of this period there is irregular pyrexia and usually some delirium. In the case of a small hæmorrhage there may be no loss of consciousness at the onset, the leading symptoms from the first being headache and the evidences of meningeal irritation.

Lumbar puncture within a few hours of the onset will give spinal fluid mixed with fresh blood, which will clot in the test tube if allowed to stand, leaving a clear and colourless fluid above. By the end of twenty-four hours coagulation has begun to occur at the site of hæmorrhage and the red cells are disintegrating. The spinal fluid at this stage, if allowed to stand, shows no clot, but a sediment of red cells with a slightly golden-yellow supernatant fluid. During the subsequent few days this golden-yellow tinge becomes more evident.

Diagnosis. This has to be made in a severe case with prolonged coma from cerebral hæmorrhage and the conditions which may resemble it (*see* p. 696), and in the milder cases in which the signs of meningeal irritation predominate from meningitis. In meningitis, however, the onset is hardly ever so acute. The question, if in doubt, may be settled by lumbar puncture.

Prognosis. Recovery from a small leak is not uncommon. Leakage from a congenital aneurysm may occur on several occasions in a period of years, but is probably always fatal in the end. In hæmorrhage from other causes the prognosis depends largely upon the underlying condition.

Treatment. This is the same as for cerebral hæmorrhage, with the exception that lumbar puncture offers an opportunity of draining the effusion. This procedure is not without danger of provoking fresh leakage from a healing rent, and should therefore be undertaken only when persistent or deepening coma indicate a large or progressive effusion with danger to life from cerebral compression. A manometer should be used and the pressure of the spinal fluid should not be allowed to fall below 100 m.m. of water.

ENCEPHALITIS

The brain is, like other organs, subject to inflammation from the invasion of micro-organisms or their toxins, the condition being known as encephalitis. In the case of the pyogenic organisms this proceeds rapidly to the formation of a cerebral abscess. In other instances the inflammatory process may continue without suppuration towards a fatal issue from involvement of the vital nerve centres. The virus may be one with a selective action upon the brain, as for instance in encephalitis lethargica, or the encephalitis may occur as a complication or sequel of a more generalised infection, *e.g.* measles encephalitis. The brain may be affected alone or together with the spinal cord (encephalomyelitis).

Of the various diseases in which encephalitis may occur some have already been described. Thus it may happen, though rarely, that the brain is involved in poliomyelitis and it is constantly affected in disseminated sclerosis. The less common varieties of encephalitis will be briefly described in the succeeding paragraphs. Encephalitis lethargica will be described later.

Encephalomyelitis of Measles. This is a rare complication. The onset is usually on the fourth to sixth day of the disease after the fever has fallen and the rash has begun to fade. Drowsiness, headache, twitching and convulsions are the usual symptoms of onset. With these there is a recrudescence of fever, and the disease may go on to produce paralysis, of which the commonest form is a hemiplegia. The spinal fluid usually shows a moderate increase of lymphocytes. The mortality amounts to 10 per cent., and more than half of those that survive show residual symptoms in the form of weakness, ataxia, mental change or epilepsy. Pathological examination shows as the characteristic feature zones of demyelination around the small veins. With this may be associated perivascular exudation of lymphocytes and plasma cells.

A similar encephalomyelitis may occur as a late complication of *chicken-pox*. In these cases the prognosis appears to be good and records of pathological examination are lacking.

Vaccinal Encephalomyelitis. A number of cases of this disease have been

reported in this country and on the continent of Europe during the past few years. The clinical story is usually that of a successful and uncomplicated vaccination, followed about fourteen days later by the sudden development of signs of nervous affection. These are meningeal, cerebral and spinal, with a major incidence upon the pons and lumbo-sacral enlargement. The illness commonly begins with headache, fever, vomiting and drowsiness; diplopia and symptoms due to paralysis of other cranial nerves then develop, often together with paralysis of the lower limbs and loss of sphincter control. The cerebro-spinal fluid shows a moderate lymphocytosis. The mortality is high, the patient frequently dying comatose within a few days of the onset, but recovery when it occurs is usually complete. Pathological examination in fatal cases shows the presence of scattered areas of perivascular demyelination throughout the spinal cord, brain-stem and brain.

Other Forms of Encephalomyelitis. A number of other varieties of encephalitis or encephalomyelitis have been described and have been named after the distinguished physician who has described them (*e.g.* Strumpell's Encephalitis), or the part of the nervous system chiefly attacked (*e.g.* Polio-encephalitis acuta inferior). Such distinctions, however, would appear to have no real value, and in the present state of our knowledge we must admit the occurrence of sporadic cases, and from time to time small local epidemics, of what may be called acute meningo-encephalomyelitis. Such illness is, perhaps, commoner among children, but may be met with at any age. The leading symptoms may be those of a meningitis, encephalitis or myelitis, and the diagnosis can only be arrived at by a process of exclusion which frequently involves a period of prolonged observation. The cerebro-spinal fluid in these cases may show a moderate lymphocytosis, but is often normal. The prognosis on the whole is good, but in infants and young children a persistent hemiplegia is not uncommon and is sometimes associated with epilepsy.

ENCEPHALITIS LETHARGICA

(*Epidemic Encephalitis*)

This is an acute or subacute non-suppurative inflammatory process affecting the nervous system and meninges in a widespread disseminated fashion. It most commonly involves the structures of the mid-brain, giving rise in the first place to symptoms of lethargy and paralysis of the occulomotor nerves, and at a later stage weakness, tremor and rigidity of the type originally described by Parkinson in Paralysis Agitans. In a large number of the cases the inflammatory process becomes chronic and may progress slowly over a period of years.

The disease first appeared in epidemic form in Vienna in 1917; one year later it became widespread throughout the whole of Europe, and in the following year spread to America.

Persons of all ages are liable to infection. It attacks the population in a widespread random fashion; only in rare instances has more than one case been reported from the same household, and there is no evidence so far to show that it is directly communicable from one person to another. From the time of its first appearance mild outbreaks in epidemic form continued to occur every year in the winter and spring, with sporadic cases during the intervening periods. The greatest number of cases in this country occurred in the spring of 1924. Since 1925 sporadic cases only have been reported, and the disease in its acute form would appear at the present time (1935) to have died out.

Although the disease was not recognised as a specific entity until 1917, small epidemics of a similar nature were reported in Central Europe following the influenza epidemic in 1890, and it is probable that isolated cases have passed unrecognised since that time.

A number of investigators, Levaditi and Harvier in France, Macintosh and Perdrau in this country, and Strauss and Loewe in America, have recorded the

successful inoculation of animals with the disease by injection of material from the brains of fatal human cases. Levaditi and Harvier also obtained positive results from swabbings of the nasal mucous membrane in an acute case. The disease produced in animals from either source could be transmitted by inoculation through a series of animals from month to month. The organism has not been cultured and appears to belong to the group of filterable viruses.

Morbid Anatomy. On macroscopic examination the brain and spinal cord show in the majority of cases little abnormality beyond congestion of the capillaries, which is generally best marked in the grey matter of the basal ganglia, mid-brain and cerebral cortex. In some instances extravasations of blood are seen either in the subdural or subarachnoid spaces, or in the substance of the mid-brain.

Under the microscope in a case proving fatal within ten days of the onset there may be nothing more to see than intense capillary congestion. Later in the course of the infection, in addition to congestion, there appear other changes characteristic of the disease. The walls of the smaller vessels are seen to be infiltrated with small round cells, and the perivascular spaces filled with them, which leads to the appearance, on cross section of a capillary, of a cuff of lymphocytes surrounding the vessel. Among these small cells are seen occasional large cells containing granular pigment. The nerve cells in most cases show evidence of degeneration, but are attacked in a somewhat random manner, so that in a single nucleus of grey matter only a small proportion of the cells are affected. The changes seen are swelling and excentricity of the nucleus, breaking up of the Nissl granules (chromatolysis), and invasion by small round cells (neuronophagia). These changes are most constantly found in the grey matter of the mid-brain and pons and the basal ganglia, but may also be discovered in the cerebral cortex and the spinal cord. Capillary congestion and round-celled infiltration have also been described in the roots of the cranial and spinal nerves. No constant changes are found in the other organs of the body.

In cases of the chronic progressive variety exhibiting the Parkinsonian syndrome the maximal destruction is found in the substantia nigra of the mid-brain, where traces of an active inflammatory process may still be seen.

Symptoms. 1. *Early Stage.* These may be divided into those of general intoxication and those referable to localised lesions in the central nervous system. Under the former heading are included pyrexia, malaise, anorexia, vomiting, general pains, and occasionally an erythematous rash. The nervous symptoms are extremely variable, depending upon the localisation of the virus, which may involve any part of the nervous system or its coverings. In the large majority of cases, however, the main incidence is upon the mid-brain, and gives rise to characteristic signs. The disease as a rule commences insidiously with a feeling of lethargy and drowsiness. With this are frequently associated minor signs of meningeal irritation, such as headache (often suboccipital) and stiffness of the neck. In the course of a day or two the nuclei of the third nerves become affected, leading to dimness of vision for near objects due to paralysis of accommodation, ptosis, and weakness of the ocular movements; at this stage complaint is sometimes made of diplopia. Subsequently the drowsiness progresses, until the patient appears to be continually in a stuporous condition, from which he must be roused to take his food. When awakened, however, his mental condition is quite clear, and he is able to answer questions in a rational manner. At this period of the illness the picture presented is a very striking one. The face appears to be smoothed out and expressionless, and this, combined with the ptosis, gives rise to an appearance of inanimate stupidity, against which the lucidity of the mental state often stands out in remarkable contrast. Careful observation will often reveal the occurrence of irregular twitchings at this stage, affecting individual muscles or their fasciculi in random fashion, but seldom powerful enough to move the limbs. These may involve any part of the musculature, including that of the

trunk and face. The tongue is dry and coated, and frequentluy tremulos. The patient may complain occasionally of pains in the limbs.

The temperature at the onset is raised, and oscillates in an irregular manner between 99° and 101°, with corresponding alterations in the pulse rate. In a fatal case the temperature as a rule rises, the stupor deepens into coma, incontinence of fæces and urine follows, and death occurs in from ten to twenty-one days from the onset.

Physical examination when the disease is well developed may reveal additional signs. Thus the pupils are frequently unequal, and respond sluggishly to light. If the patient can be induced to co-operate in the examination, it is commonly found that the pupillary reaction in accommodation is lost, together with the power of convergence. Not infrequently there is paralysis of other ocular movements. Nystagmus is often present. The Argyll-Robertson pupil may occur.

The other cranial nerves are not affected as a rule. No anomalies of sensation are discovered beyond the complaints of pain already referred to. Examination of the motor system reveals general muscular weakness, combined sometimes with plastic rigidity, so that the limb will remain almost indefinitely in any attitude in which it is placed, however bizarre (catatonia). The reflexes vary from case to case; the tendon reflexes may remain unaffected; they may be increased; more frequently they are abolished; the abdominal reflexes seldom show any abnormality; the plantar responses are as a rule flexor.

If recovery ensues, the temperature begins to fall during the third week from the onset, and the patient gradually awakens from his stuporous condition. With the end of the third week the period of pyrexia terminates, but in a severe case lethargy persists, the cranial nerve palsies clear up slowly, and it may be three months or more before the normal functions of the nervous system are again fully established, if indeed complete recovery is attained.

Since the symptoms in a case of nervous disease depend almost entirely upon the localisation of the infective process, and since in the disease under consideration the distribution of the virus may be widespread, one must be prepared to find almost any combination of signs and symptoms in the course of an epidemic; with the extension of the inflammatory process from one part to another the appearance of a single case may change from time to time, and among half a dozen cases there may be no outstanding nervous symptom common to all. Thus, with regard to the onset, in addition to the common type already described there may be instances in which meningeal symptoms at first predominate; in other cases restlessness, irritability, or even a noisy delirium may take the place of the more usual lethargy; the illness may begin acutely with an apoplectiform seizure, or the picture may be entirely dominated by the presence of muscular twitchings (the so-called myoclonic type), usually associated with delirium. In another group of cases the disease may be ushered in by severe neuralgic pains of peripheral nerve or root distribution; these may be followed by wasting and weakness of isolated groups of muscles. Or, again, in some instances absence of tendon jerks and subjective sensations of numbness in the extremities may give rise to the appearance of polyneuritis.

This account by no means exhausts the symptomatology of the disease. Among signs of minor importance may be mentioned dysarthria, dysphagia, paroxysms of dyspnœa, hiccough, excessive salivation, excessive sweating, sensations of choking or stifling, retention of urine, and occasionally spasmodic contracture of the jaw muscles.

The extent and duration of pyrexia are variable; the temperature may have been raised during the initial stages, but on account of the insidious nature of the onset may have subsided before the patient comes under medical observation. In mild cases the signs of involvement of the nervous system are often fleeting, and special inquiry is necessary to elicit a history of transient diplopia, temporary

paralysis of accommodation, pain and stiffness in the back of the neck, neuralgic pains or muscular twitchings. In a great many patients presenting themselves with undoubted symptoms of the chronic progressive type no history of onset can be obtained.

The cerebro-spinal fluid is always clear; in about one half of the cases it shows no abnormality by the time it is examined, but in the other half there is an increase in the number of lymphocytes, which varies from ten to eighty cells per cubic millimetre; this lymphocytosis is more commonly observed in cases in which lumbar puncture is performed early in the course of the disease. There is, as a rule, no increase in the protein content, but the colloidal gold test may give curves of the paretic or luetic types. The Wassermann reaction in blood and cerebro-spinal fluid is negative.

2. *Late Stage.* In a large proportion of the cases after the acute stage has subsided further symptoms develop, as the result of a smouldering process of infection, which may continue to involve fresh areas of the brain for months or even years after the onset. In some cases the patient passes directly from the early into the late stage of the disease, but more often there is a latent interval during which he may appear to have made a satisfactory recovery—and this interval may be of several months' or even of several years' duration. The severity of his late symptoms bears no relation to that of the early stage, so that cases of a mild or ambulatory nature, which may not in the first place have been recognised, are often subsequently the victims of serious physical or mental disability. The commoner symptoms of the late stage may be grouped under the headings of (1) Weakness, rigidity and tremor of the paralysis agitans type, (2) Involuntary movements, (3) Mental changes.

(1) Symptoms resembling those of paralysis agitans probably develop in a high proportion of the cases which survive the early stage of the illness, and, as has already been stated, may appear without any history of initial infection. The most noticeable feature as a rule is the stiffness of the facial muscles with consequent loss of expression; the rigidity often involves also the muscles of trunk and limbs; the gait is then slow and shuffling, with bent back and bowed head, the arms are held stiffly with elbows slightly abducted and fingers semi-flexed. Automatic movements are diminished or lost, and the patient has difficulty in adjusting his centre of gravity, and his balance therefore is easily upset. Inhibition of the blinking reflex adds to the staring facial expression, and of the swallowing reflex to the dribbling of saliva. The voice is frequently monotonous and speech slow. Tremor of the paralysis agitans type may also be present, but is usually slight in comparison with the rigidity.

(2) Involuntary movements of all kinds may occur, but the proportion of cases in which they are a striking feature is small. Tremor of the paralysis agitans type has already been mentioned. Choreiform and athetoid movements are also seen. Perhaps the commonest type, however, is that in which there are rhythmic movements of relatively large amplitude and slow rate involving the musculature of the proximal joints (shoulder and hip), often affecting a single limb or the arm and leg on one side of the body. Another striking, and as a rule a late, sequel is the occurrence of forced upward movement of the eyeballs (oculogyric crises). These are paroxysmal, and as a rule without warning, lasting for minutes or hours at a time. Being beyond voluntary control they render the patient for the time being incapable of useful vision.

(3) Mental impairment of some degree is an almost constant sequel of the disease. In adults it is manifest in slight cases as an increased tendency to fatigue and diminished emotional control; in more severe cases symptoms of a neurasthenic character develop with constant complaint of headache, feelings of inadequacy and morbid anxiety. In the cases of the paralysis agitans type, on the other hand, profound apathy is often present. Children are often more seriously affected, the disease in them leading to deterioration of character

without any corresponding impairment of intellect. They are apt, therefore, to develop habits of lying, stealing and violence, which make it difficult to control them at home and lead not infrequently to the police court.

Insomnia at all ages is a common and distressing sequel. The patient is drowsy and apathetic during the day, but at night time becomes restless and agitated, often excited, and gets off to sleep only in the early morning.

Diagnosis. In cases of the common type beginning insidiously with drowsiness, low fever, and ocular palsies, this is comparatively easy, but may be a matter of extreme difficulty when the incidence of the infection is more widespread. The diagnosis of cerebral abscess has to be considered, and, with this possibility in view, the ears should be examined for signs of suppurative otitis. Cerebral tumours also, especially if situated in one of the silent areas of the brain, may produce signs resembling those of encephalitis lethargica, but in this case examination of the optic discs may clear up the diagnosis, papillœdema being seldom absent in cases of tumour, rarely if ever present in encephalitis.

Cases in which the illness is ushered in with meningeal symptoms may simulate meningococcal or tuberculous meningitis, but the neck stiffness is hardly ever so important a feature of encephalitis as in these illnesses. In the rare instances in which the onset is apoplectiform, the condition can hardly be differentiated from that caused by a cerebral hæmorrhage or thrombosis.

In the later stages, after the decline of pyrexia, the presence of signs of widespread involvement of the nervous system may suggest the possibility of syphilis, when the Wassermann reaction in blood and cerebro-spinal fluid will be of use in settling the point. Cytological and bacteriological examination of the cerebro-spinal fluid is always of value in making the differential diagnosis. In the later stages cases presenting the Parkinsonian syndrome have to be distinguished from paralysis agitans. Careful enquiry for a history of febrile illness, transient diplopia, or sudden lethargy or insomnia preceding the Parkinsonian symptoms, by months or years, may decide the diagnosis. In cases where such a history is lacking the age of the patient may settle the question, paralysis agitans being a disease of middle or late life, while encephalitis lethargica attacks young as well as old. When this method of distinction is not available the detection of anomalies of the pupillary reactions and ocular movements, especially a failure of convergence and of the pupils to contract on attempted convergence, may decide the diagnosis in favour of encephalitis lethargica.

Prognosis. The death rate appears to be about 20 per cent. if note is taken of the abortive cases. The notification returns show a considerably higher rate of mortality. The large majority of deaths occur within the first three weeks of the illness, and after this period the prognosis as regards life is good.

Signs of ill omen are a rising temperature (above 102·5°), deepening of stupor into coma, or noisy delirium with extensive muscular twitchings (the acute myoclonic form).

In the cases which recover the cranial nerve palsies as a rule clear up, relatively soon leaving, perhaps, inequality of the pupils with sluggish contraction in accommodation. Lethargy, weakness and slowness of movement may persist for many weeks and develop gradually into the clinical semblance of paralysis agitans.

Symptoms of the order already described as belonging to the late stage may continue to make their appearance for as long as two or three years after the onset, but it may be said as a rule that a patient who has recovered from the initial attack and has thereafter remained completely free from fresh symptoms for six months is unlikely to have further trouble.

Of the late symptoms the paralysis agitans group show a tendency to progress slowly; they eventually come to a standstill, and there may be a slight improvement, but the patient is left considerably disabled. The involuntary movements develop slowly (over a period of months) to their climax, and as gradually recede,

often with but slight residuum. The mental changes, both in adults and children, though there may be some remission, appear for the most part to be of a permanent nature.

Treatment. There is no specific treatment for the disease. Urotropin in full doses should be given in view of its possible antiseptic action, and symptoms should be attended to as they arise. In most cases the patient can be roused to take his food, which should be confined to a light and easily assimilable diet with plenty of fluids. Occasionally the stupor is so deep that tube feeding has to be resorted to, and this may also be rendered necessary by dysphagia, due to glosso-pharyngeal paralysis apart from stupor. The method of choice is by the nasal tube, through which an ample diet may be given in the shape of milk, beaten-up eggs, malt, and orange juice. The bladder should be watched carefully, since retention with overflow may occur, and if neglected lead to cystitis. In prolonged cases there is, as a rule, much emaciation, with probable development of bedsores, so that it is wise to have the patient upon a water-bed if the course of the illness appears likely to be protracted. For the insomnia, which is sometimes a distressing sequela, hot baths (for one hour before bedtime) and various drugs may be tried, of which the most useful are paraldehyde in full doses and the veronal compounds. For rigidity of the limbs after the acute stage has subsided passive movements should be carried out daily, preferably after a hot bath.

In view of the grave risk of a smouldering infection leading to further symptoms, convalescence should wherever possible be prolonged, and the patient advised not to resume his full round of activities for a period of six months after the progress of symptoms has ceased. During this period regular exercise should be prescribed for body and mind, but this should stop short of fatigue.

Drugs of the belladonna group are of considerable value in the treatment of the Parkinsonian group of symptoms of the later stages. The effect is to diminish rigidity and increase the possible range and rate of movement. Large doses are necessary, and much depends upon the amount the patient can take without toxic symptoms. The tincture of stramonium seems to be the most effective preparation, and in the case of an adult should be given in doses at first of ℥xv. t.d.s. p.c. in ½ oz. of chloroform-water. After a few days the dose is increased to ℥xx., and thenceforward at similar intervals by increments of ℥v. until the limit is reached of the patient's tolerance. This is shown by complaint of weakness in accommodation, dryness of the mouth palpitation and tachycardia. Of these the first symptom is usually the earliest to appear, and may be overcome by giving a solution of eserine sulphate ¼ per cent., one drop to be instilled into each eye every morning. The dryness of the mouth may be relieved by acid drops. Thus the patient may be enabled to continue with the larger doses. An alternative plan is to add to the mixture pilocarpine nitrate in the proportion one-tenth of a grain to thirty minims of the tincture of stramonium. If as much as ℥xl. can be taken t.d.s. a great deal of relief may be obtained, so that a patient for instance who, without the drug is unable to feed or dress himself, is enabled with its aid to do so. Unfortunately the effect is apt to pass off with continued use, but may be prolonged by withdrawal of the drug during one week in every six, or on one day during the week, during which none of the belladonna derivatives should be given.

Prevention. The Ministry of Health makes the following recommendations (1924) :—

" The other occupants of a house in which a case of encephalitis lethargica has occurred, or is being treated, may be assured that the disease is one of low infectivity, and that very slight risk is run by association with the patient. At the same time it is desirable that such association should be limited to what is necessary for proper care and nursing, and the patient should be well isolated in a separate room.

"School children in the affected household may be kept from school, as a precautionary measure, for three weeks after the isolation of the patient. There is no necessity to place restriction on the movements of other occupants, provided they are frequently examined and remain well. Those in contact with the case, however, may be advised to use antiseptic nasal sprays or douches and to gargle the throat with solutions such as those advised for influenza.

"For example, any of the following :—

(1) One per cent. solution of peroxide of hydrogen.

(2) A solution of permanganate of potash, 1 in 5,000, in 0·8 per cent. solution of chloride of sodium (common salt).

(3) Liquor sodæ chlorinatæ, 0·5 per cent.

"These solutions can be used as ordinary throat gargles or snuffed up the nostrils, or applied by an efficient spray.

"Any persons in the infected household who suffer from sore throat or other symptoms suggesting an abortive attack should be treated from this point of view and isolated as far as possible until they have recovered.

"The sick room should be thoroughly cleansed and disinfected at the end of the illness."

ABSCESS OF THE BRAIN

In the great majority of cases abscess can be shown to be the result of direct infection by pyogenic organisms. By far the commonest cause is suppurative otitis media. It may also follow infection of the frontal or ethmoidal air sinuses, and compound fractures of the skull. Indirect infection by way of the blood stream is rare, but may lead to the formation of a cerebral abscess in pyæmic conditions, and especially in cases of chronic suppuration within the chest, such as bronchiectasis or empyema. In these latter cases the cause is presumably the detachment of an infected thrombus which lodges in the brain.

The pathological appearances vary with the age of the abscess. The first stage is that of acute suppurative encephalitis. This may extend diffusely, and if so leads rapidly to a fatal issue. The abscess cavity is then found to be ragged, with purulent infiltration of the surrounding brain substance. As a rule, however, there is sufficient reaction on the part of the surrounding tissues to form a comparatively firm and smooth wall, which limits the spread of the infective process, and a chronic encapsuled abscess results. Abscesses arising from the middle ear are commonly situated either in the cerebellum or the temporal lobe. The cerebral abscess may be associated with an extra-dural abscess, or there may be adhesions between the dura and leptomeninges, showing the track of the infection, or as in many cases the meninges over the abscess may appear healthy with no evidence of the path of entry. The streptococcus is the organism most frequently found, but in the otitic cases the bacillus coli communis is sometimes met with, giving a characteristically foul odour to the pus. In the pyæmic cases the staphylococcus is sometimes responsible.

Symptoms. These depend partly upon the infective nature of the condition, partly upon the situation of the abscess. In those of otitic origin the initial symptoms are often slight and pass unnoticed in the course of a suppurative otitis media or mastoiditis. They consist of fever and headache, often associated with vomiting and drowsiness. If the suppurative process spreads unchecked these symptoms rapidly progress, the temperature remains high, signs of cerebellar or cerebral destruction appear, and the patient dies within a week or two. Much more frequently the abscess becomes encapsuled, the initial symptoms, which may have been slight, subside, and a chronic abscess results, whose symptoms depend almost entirely upon its situation. Thus the patient with a chronic cerebral abscess may continue at his work for weeks or months with few symptoms and without appearing to be seriously ill. Headache of a bursting or splitting character is the most constant symptom of the early stages of a chronic abscess,

but may be intermittent. The important signs of a cerebellar abscess on either side are nystagmus on looking towards the side of the lesion, inco-ordination of the limbs on the same side as shown, especially in the finger-nose-finger test, and a tendency to stagger to the same side in walking. In the case of a left temporal abscess in a right-handed person aphasia is the most important localising sign, and takes the form of verbal amnesia, so that careful testing will reveal the patient occasionally at a loss for the correct word in attempting to name a series of objects presented to him.

Further signs common to an abscess in either temporal lobe are a weakness of the lower part of the face on the opposite side, and a defect in the visual field. The latter commonly takes the form of an upper quadrantic defect from involvement of the inferior bundle of the optic radiation as it runs through the posterior part of the temporal lobe. As the abscess increases in size the signs of increased intracranial pressure, headache, vomiting, drowsiness and slowing of the pulse, become more apparent, and papillœdema develops. The temperature, as a rule, is normal or sub-normal.

The cerebro-spinal fluid is under increased pressure, and commonly shows a moderate increase of cells, consisting mainly of lymphocytes with a small proportion of polymorphs, and the protein is also increased. Any large number of polymorphs in the fluid is suggestive of an abscess leaking either into the ventricle or into the subarachnoid space.

Diagnosis. The development of cerebral symptoms in the course of an otitis media, especially if this is complicated by mastoid infection, will always raise the question of abscess. This, however, has to be distinguished from other complications, such as lateral sinus thrombosis, extradural abscess and meningitis, which may occur separately or may coincide with the presence of a cerebral abscess. A careful search for the signs already enumerated of cerebellar and temporal lobe disturbance may decide the question, but the right-sided temporal abscess in particular may give rise to few signs. Examination of the spinal fluid may help, but it should be remembered that lumbar puncture is not without risk of spreading the infection. The fluid, therefore, should be examined at once and an operation performed without further delay if the evidence is positive. The chronic abscess may present great difficulties in diagnosis. Whenever there is persistent complaint of severe headache in a person with a discharging ear the possibility of abscess should be considered and the patient examined in the manner already described. It must be remembered, however, that chronic otorrhœa is common and may exist together with cerebral syphilis or cerebral tumour.

Prognosis. Many cases have been cured by evacuation of the abscess; without the help of surgery recovery cannot be expected.

Treatment. Where an abscess can with reasonable certainty be recognised, and its locality accurately determined, the attempt to evacuate the pus should be made.

Apart from surgical interference, the treatment of abscess of the brain must be purely symptomatic; the relief of pain may be attempted by local anodynes, by ice to the head, and by aspirin or morphia.

CEREBRAL CONTUSION

As a result of violence directly or indirectly applied to the head the cerebral substance may suffer laceration and bruising. Such damage to the brain, although commonly associated with evidence of external injury to the scalp or cranium, may occur without this, and in any case, apart from such complications as an infected compound fracture or arterial hæmorrhage, the important symptoms are those due to the cerebral rather than the cranial damage.

Pathology. The anatomical changes underlying the symptoms to be described may be inferred from inspection of the brain in fatal cases. Rupture

of the capillaries and small veins is the essential feature of the injury, with resultant extravasation of blood. This may take the form of multiple petechial hæmorrhages scattered throughout the brain, or of larger extravasations commonly related to the point of impact in the case of a direct injury or to the point of *contrecoup*. In these larger areas of injury the brain substance is frequently torn asunder by the escaping blood. The anterior poles and under surface of the temporal and frontal lobes are especially liable to injury from indirect violence, probably as was first pointed out by Hilton, because the water-bed of cerebro-spinal fluid is shallow in these situations, and the irregularities of the cerebral cortex more closely applied to similar contours in the bone.

Symptoms. If the injury has been a severe one there will probably be a history of concussion—that is total loss of consciousness immediately following the accident. The symptoms of concussion being due to a transient cerebral anæmia without structural damage are themselves transient. The phase of cerebral anæmia may be followed by one of œdema, with consequent headache, vomiting and drowsiness, but these symptoms in a case of simple concussion, uncomplicated by structural damage, should have disappeared at the end of twenty-four hours. It follows that any symptoms of cerebral disorder persisting after this time must be attributed to organic damage. This damage—apart from the possibilities of infection and meningeal hæmorrhage—will consist of cerebral contusion sustained at the moment of injury.

The symptoms of cerebral contusion vary from a condition of persistent stupor or delirium at one extreme to occasional headaches at the other. For purposes of clinical description it is therefore of advantage to distinguish between a major and a minor degree of cerebral contusion, on the understanding that the line of division is arbitrary. The most convenient means of distinction is to include in the category of major contusion all cases showing clouding of consciousness or stupor, the remainder constituting the group of minor contusions.

Major Contusion. The injury will almost always have been of such a nature and degree as to have caused immediate concussion. Following this the patient partially regains his senses, but instead of making that rapid and complete recovery to the normal state which characterises a simple concussion, is found at the end of twenty-four hours to show some degree of mental clouding. In a severe case this will amount to a state of stupor in which the patient is commonly said to be unconscious. He will, however, respond to vigorous stimulation, usually with a show of resentment, and is apt, especially at night-time, to be noisy and violent, with hallucinations of vision and hearing. The temperature and pulse rate are commonly raised. This condition, known as cerebral irritation or traumatic delirium, betokens extensive cerebral contusion. In milder instances the clouding of consciousness may not be apparent unless carefully enquired for. The patient may behave normally but is imperfectly aware of his surroundings, his memory for the events of the day is defective and he is subsequently found to have little or no recollection of this phase of his illness. Physical signs of local cerebral damage are not an essential feature of the clinical picture, but in the early stages of a severe case the plantar responses are commonly extensor. Lumbar puncture gives a fluid which is often blood-stained from the rupture of superficial vessels, and sometimes shows an increased pressure. In the severest cases death may occur during the first week either from the exhaustion of delirium or involvement of the medullary centres. The general tendency is towards recovery, which is, however, often incomplete. Mental deterioration of a degree necessitating institutional care is extremely uncommon (*vide* " Organic reaction type " of mental disease, p. 769), but lesser changes are often apparent. These take the form of defective memory and concentration, loss of emotional control, and alterations in the personality. Pre-existing trends of a psychotic or psychoneurotic nature may be accentuated, and there is a general defect of inhibition. Other symptoms of the recovery stage are headache and

giddiness of the type presently to be described as characterising minor contusion. Under proper conditions improvement may continue for a year or eighteen months, but analysis of the end results in a series of head injuries collected by the writer showed that not more than one-third of those who had suffered major contusion had returned to full work one year after the accident.

The **treatment** of major cerebral contusion in the early stages consists of rest. Careful nursing is essential. Morphia, or morphia and hyoscine, may be necessary at first to control excitement. Subsequently chloral and bromide and paraldehyde, either by the mouth or in double doses by the rectum, are best employed, the object being to control restlessness as far as possible without inducing stupor. Feeding may be regulated by the patient's tastes and the exigencies of the moment. Alcohol should be withheld. Lumbar puncture should be performed and the pressure of the cerebro-spinal fluid measured with a manometer. If it is raised enough fluid should be withdrawn to bring the pressure down to normal (120 mm. of water), the patient should be propped up in the Fowler position, and mag. sulph. should be given by the mouth to the point of looseness of the bowels, or by the rectum in the form of a solution containing ℥iii of mag. sulph. in ℥vi. of water. In many cases, however, the pressure is found to be normal; in these no cerebro-spinal fluid should be withdrawn, and dehydration with mag. sulph. is unnecessary.

In the convalescent stage the treatment is the same as for minor contusion.

Minor Contusion. Symptoms of this order may follow upon those of concussion or may develop without any such prelude after an injury which at the time has seemed of no moment. There is quite commonly an interval of a day or two before the symptoms develop, during which the patient regards himself as completely recovered from his accident. The main complaints are of headache, giddiness and failure of the higher mental functions, expressed as loss of confidence, nervousness and difficulty in concentration.

The headache may be of two kinds. That which is most characteristic is an intermittent throbbing and bursting pain provoked or aggravated by coughing, stooping or straining, and by any unusual physical or mental effort. It is often referred to the site of the injury or the point of *contre coup*, but may be frontal or generalised. In response to questioning the patient will usually admit a relation to posture, the headache being as a rule worst when he is in the horizontal position. This type of headache resembles that met with in known cases of intracranial pressure and is probably due to this cause. The other variety is constantly associated with some or other of the mental symptoms to be described. It is described in terms of discomfort rather than pain—a sense of pressure, heat or numbness enveloping the head—is continuous rather than intermittent, and is aggravated by mental tension or distress.

The mental symptoms comprise slowing of the intellectual processes, which is not only complained of by the patient, but is noticeable in his speech and actions: indecision, timidity, and defective emotional control.

The giddiness is usually described as a general sense of unsteadiness with fear of falling, transient and provoked by stooping or quick movement of the head.

This triad of symptoms, when they are present together, constitutes an easily recognised clinical picture. Any one of them, however, may predominate. Physical signs are usually lacking, although a careful neurological examination will occasionally reveal an unsuspected extensor plantar response, absent abdominal reflex or nystagmus as evidence of focal damage.

With proper management most cases of minor contusion make complete recoveries. In the minority some of the symptoms continue indefinitely, the liability to headaches of the hypertension variety being the most persistent.

Prolonged rest and a properly graduated convalescence are the essential points in the **treatment** of minor contusion. The patient should at first be put to bed. The sitting posture is that which in theory and practice is most likely to relieve

intracranial pressure, but the patient should be encouraged to find the optimum position for himself.

Bright light and noise should be excluded as far as possible, visitors forbidden, and absolute quiet enjoined. Light reading may be allowed and tobacco is permissible, but alcohol should be prohibited. A mixture, containing pot. brom. gr. x.–xv. t.d.s., should be given to induce relaxation, and the patient encouraged to doze. Aspirin and phenacetin may be given at need for headache, and at night medinal grs. v.–x., if necessary, for insomnia. The bowels should be opened to the point of looseness every morning with the requisite dose of mag. sulph. This *régime* should be continued until the patient has been free from headache for three or four days. He may then be allowed, step by step, to take more liberties, commencing with permission to walk to lavatory and bathroom, and proceeding at two-day intervals to more and more physical and mental activity. The recurrence of symptoms such as headache or insomnia should be the signal for retiring a step and making a fresh start on the road to convalescence. It is particularly desirable that the final stage be well managed and the patient have an opportunity, in the shape of a holiday, of testing his capacity for mental and physical endurance before returning to work. It is impossible in the early stages to forecast the duration of the illness, which must depend upon the results of treatment.

Differential Diagnosis. The symptoms of cerebral contusion in its later stages or minor degree may closely resemble those of an anxiety neurosis. Hence the term "traumatic neurasthenia," which is often used to cover all conditions of minor mental disorder following upon injury without discrimination between the organic and the psychoneurotic elements. The distinction, however, is important, both from the therapeutic and the medico-legal aspects. A neurosis—arising usually out of the desire to exploit illness for purposes of compensation—may follow an accident to the head as well as to any other part of the body. It needs to be treated by means of psycho-therapy, and may be assessed as a condition which is completely recoverable. The mental symptoms of contusion depending upon organic cerebral damage, besides needing different treatment, carry the possibility of a permanent impairment of wage-earning capacity. In the absence of physical signs the differential diagnosis may be very difficult.

Points in favour of cerebral contusion are: *objective* difficulty in concentration, defect of memory and slowing of the intellectual processes; the association with other contusion symptoms such as headache of the hypertension variety and vertigo; and a history of prolonged clouding of consciousness following the injury. The most difficult cases are those in which the symptoms of an anxiety neurosis—a not unnatural development in a disabled workman—are added to those of true cerebral contusion.

INFANTILE CEREBRAL DIPLEGIA

(*Infantile Spastic Paraplegia, Diplegia Spastica, Congenital Spastic Paraplegia, Birth Palsy*)

This title includes all cases of bilateral spastic weakness of the extremities, of cerebral origin, occurring in infancy or early childhood.

These cases may be further divided into two groups according to their pathological and clinical features (**6**).

Group I. comprises those cases in which the symptoms are due to lesions of both cerebral hemispheres resulting from injury or infection, at or after birth. Of such causes the commonest are meningeal or cerebral hæmorrhages as the result of birth injury, and acute encephalitis (*see* p. 704).

The brain in such instances provides post-mortem evidence of injury or inflammation in the shape of meningeal scarring and cyst formation in the traumatic cases, and perivascular scarring in those of infective origin.

Clinically in many cases no definite history of injury or infection may be obtained, but a series of convulsions occurring shortly after birth is suggestive of meningeal hæmorrhage, or a history may be elicited of an acute febrile illness in infancy.

The symptoms are as a rule asymmetrical, one limb or one side of the body being more involved than the other. Actually the paralysis often escapes notice until the child proves backward in sitting up, walking and talking.

The damage in these cases is of an irreparable nature, but a great deal may be done for these children by means of carefully planned remedial exercises and drill. There is almost always some degree of mental impairment, which is irremediable. Nevertheless these children are much more educable than may appear at first sight and will usually repay patient instruction.

Group II. comprises the majority of cases of cerebral diplegia, and consists of cases in which as the result of some obscure cause acting as a rule in utero, but sometimes after birth, the development of the cortical cells is arrested or retarded.

In a severe case of this kind the brain is small and atrophic, with wide sulci and wrinkled convolutions, and is sometimes compared to a walnut kernel. Microscopic examination reveals a diminution in the numbers of the cortical nerve cells with secondary overgrowth of neuroglia. The process is symmetrical in the two hemispheres and frequently includes the cerebellum. The optic nerves also are frequently degenerated.

Clinically these cases are distinguished by the remarkable symmetry of the spasticity and weakness. Nothing may be noticed at birth, although a history is often obtained of premature, sluggish, or precipitate labour, which is possibly due to the same cause affecting the reproductive mechanism of the mother as is responsible for the disease in the child. After birth the child may suck feebly, but often nothing is noticed until he proves backward in sitting up and slow at learning to walk, owing to the stiffness of the lower limbs. Ultimately the condition is much like that seen in the spastic paraplegia of adults. The limbs are extended and rigid with increased tendon jerks and persistent extensor plantar responses. Sometimes spasm of the adductors is extreme and the legs are crossed over one another, in spite of which the child manages to walk—*crossed leg progression.* The arms are never as rigid as the legs, and may escape entirely. The picture may be complicated by the addition of cerebellar ataxia and nystagmus, and optic atrophy is of frequent occurrence. Some degree of mental impairment is usually present.

In the cases which are of congenital origin (and these are in the majority), although the development of some nerve cells would seem to have been arrested in other cells it is merely retarded, and as the result of suitable treatment by means of remedial exercises and patient education considerable improvement may be expected.

Treatment. In cases of both groups this is the same, and must consist of regular exercises and drill with suitable educative measures. Deformities must be treated by manipulation, splinting, and tenotomies when necessary. A small proportion of cases of Group II. are of syphilitic origin and should be treated accordingly.

Amaurotic Family Idiocy (*Tay-Sachs' Disease*). This is a familial disease of infancy affecting chiefly the Jewish race and depending upon a progressive degeneration of the nerve cells in the retina and throughout the nervous system. The affected cells become swollen, subsequently degenerate, and are finally absorbed. The symptoms, as a rule, commence within the first year of life and consist of mental enfeeblement, convulsions, and spastic weakness, together with failing vision. The ophthalmoscopic picture is characteristic. The retinal degeneration is maximal at the macula and the choroid showing through it in this region appears as a cherry-red spot. The optic discs show primary atrophy.

The disease is steadily progressive and ends fatally as a rule within a year of the onset. In the terminal stages the paralysed limbs become flaccid.

Cerebro-Macular Degeneration (*Juvenile Form of Tay-Sachs' Disease, Vogt-Spielmeyer Disease*). This disease resembles amaurotic family idiocy in having a familial incidence and depending upon a simultaneous degeneration of the nerve cells in the brain and retina. It is, however, commonly encountered among non-Jewish people, and begins in childhood rather than infancy. The ophthalmoscopic appearance also differs from that of amaurotic idiocy. The earliest change is a white circle with red margin in the macular area. Subsequently in the same area minute white spots and specks of pigment appear, giving a pepper-and-salt appearance. The optic discs show a waxy pallor. The retinal degeneration ultimately becomes widespread. Clinically there is progressive failure of vision with mental deterioration and epileptic attacks, and the physical signs of cerebral and cerebellar disease. The progress of the disease is slower than in amaurotic idiocy, but death usually occurs before the age of fifteen.

The age of onset, as well as the ophthalmoscopic appearance, serves to distinguish this disease from amaurotic family idiocy. From infantile cerebral diplegia, as already described, it may be distinguished by the progressive nature of the symptoms and the retinal involvement.

Schilder's Encephalitis (*Encephalitis Periaxialis Diffusa*). This disease was first described by Schilder in 1912, although an unpublished case had been recognised by Collier at the National Hospital, Queen Square, in 1902. It would appear to be at least as common as the two diseases just described, and to account for some proportion of the cases of progressive diplegia seen in children and young adults. It is characterised pathologically by a degeneration of the white matter in the cerebral hemispheres, the sub-cortical or arcuate fibres alone being spared. This may commence in any part of the brain and is usually symmetrical. The optic nerves are not infrequently involved. The cause of the degeneration is obscure. A few cases have been recorded of familial incidence. The age of onset varies, but appears usually to be in infancy or childhood. The symptoms depend upon the parts of the brain chiefly affected. Involvement of the occipital lobes has led in several cases to the gradual development of blindness with normally reacting pupils and normal fundi. Bilateral involvement of the temporal lobes may lead to progressive deafness, of the parietal lobes to sensory loss, and of the pyramidal fibres to a double hemiplegia. Mental deterioration is a part of the clinical picture, epileptic attacks may occur, and primary optic atrophy is not uncommon. The rate of progress is extremely variable, and may be so even within the same family. Thus the writer has recorded the instance of a boy of six who died within a year of the onset. A sister, who developed her first symptoms in infancy, is blind and quadriplegic, but still alive at the age of twenty-two. A brother showed primary optic atrophy, epilepsy and mental deterioration from the age of four, but his symptoms remained stationary for six years and then progressed to a fatal issue at fourteen.

CEREBELLAR ATROPHY

Degenerative changes may occur in the cerebellum in several of the diseases which have already been described, as, for instance, in arteriosclerotic softening, cerebro-macular degeneration and Schilder's disease. In these instances, however, the cerebellar lesions are associated with cerebral disease. There are also certain maladies of a degenerative character in which the cerebellum is primarily or solely affected. Of these the most clearly distinguished are the following.

Marie's Hereditary Cerebellar Ataxia. In this disease, which is usually but not always inherited, the symptoms commonly commence in early adult life and are gradually progressive. They comprise inco-ordination of the upper and lower limbs, unsteadiness of gait, nystagmus, slurred speech, and in the majority of cases optic atrophy. The disease may be distinguished from Friedreich's ataxia

by the preservation of the tendon jerks, the flexor plantar responses, the optic atrophy and late age of onset. Transitional forms between the two diseases are not infrequently seen, and it is probable that they belong to the same group.

Senile Cerebellar Atrophy. This is a disease of late middle life or old age characterised pathologically by degeneration of the cerebellar cortex. This affects particularly the middle lobe. The Purkinje cells and their axons degenerate and are absorbed, the other cortical nerve cells being less affected.

Clinically, the malady begins with unsteadiness of the gait, which is of the cerebellar type, reeling and titubant. At this stage there is often little else to be made out. As the disease gradually progresses inco-ordination of the lower limbs is demonstrable in the heel-knee test. The upper limbs are involved later and to a less extent. The speech in the later stages is slurred and explosive, but nystagmus is an uncommon feature.

The diagnosis in the early stages has to be made from hysteria. In the later stages the progressive cerebellar symptoms, together with the age of the patient, form a characteristic clinical picture.

HEPATO-LENTICULAR DEGENERATION

This is a rare disease in which progressive degenerative changes in the brain, and especially in the lenticular nuclei, are associated with multi-lobular cirrhosis of the liver. In about half the recorded cases the disease has been familial. Nothing is at present known as to its cause, but it is of interest that chronic manganese poisoning causes both cirrhosis of the liver and degenerative changes in the corpus striatum. The onset is as a rule in childhood or adolescence. The symptoms of cerebral disease take the form of tremor and rigidity of the limbs which are of the type encountered in paralysis agitans. Together with this there is slurring of the speech, and some degree of mental deterioration. In some cases, which probably belong to the same group, the motor symptoms may take a different form—that of continuous writhing movements of the limbs and trunk (torsion spasm). The symptoms of hepatic affection are inconstant, but enlargement of the liver, jaundice, or ascites may occur in the course of the nervous illness or may sometimes precede it. The disease is progressive and fatal, but its course may be acute or chronic, varying from a few months to several years. Treatment is purely symptomatic. The diagnosis has to be made from the late stage of encephalitis lethargica, a history of febrile illness with diplopia and abnormalities of the pupils or ocular movements being the main points in favour of the latter diagnosis.

PARALYSIS AGITANS

(*Shaking Palsy, Parkinson's Disease*)

This disease consists, in its fully developed form, of rhythmical contractions of the muscles of the limbs associated with weakness and rigidity.

Ætiology. It is a disease of advanced life, rarely occurring before the age of forty-five years, but, on the other hand, not often commencing after the age of sixty-five. It occurs in men twice as often as in women. It cannot be traced to any definite cause.

Pathology. Recent researches have indicated that the symptoms of paralysis agitans may be produced by lesions of certain areas of the brain, and that these lesions may be the result of various pathological processes. The exact site of the areas affected is a little uncertain. On the one hand, symptoms in many ways resembling those of paralysis agitans have been observed in association with progressive degeneration of the lenticular nuclei (*see* above), and in typical cases of juvenile paralysis agitans Ramsay Hunt claims to have found atrophy of the motor cells in the globus pallidus. Many Continental observers, however, point to changes in the substantia nigra of the mid-brain as

being the most important pathological features. The truth probably is that we are dealing with an *affection of a system of extra-pyramidal motor fibres* in which cell stations and neuronic pathways both in the corpus striatum and the mid-brain play an important part. As to the *nature* of the pathological process, there can be no doubt that the virus of encephalitis lethargica may be responsible in a certain number of cases, especially those occurring in young people (*see* p. 707). In hepato-lenticular degeneration the association with cirrhosis of the liver suggests some unknown toxic factor as the primary cause. The common form of the disease beginning in old people may possibly be due to arteriosclerotic changes in the brain, or to a system degeneration akin to that seen in progressive muscular atrophy. But of this at present we have no certain knowledge.

Symptoms. In some cases the first symptom is the tremor, after which the disease is named; in others rigidity is observed before any tremor has occurred; but ultimately they are both present.

Tremor. In the former case, it is noticed that one hand and arm are the subjects of a tremulous movement, due to rhythmical contractions of antagonistic muscles. The movement is most marked in the hand; the fingers are generally flexed, with the thumb resting against the forefinger; and the constant slight flexion and extension of the fingers and thumb produces a movement like that required for rolling pills. Similar slight movements of flexion and extension occur at the wrist and elbow joints. After the tremor has existed for some time in one arm it generally spreads to the leg of the same side, and then in succession to the arm and leg of the opposite side. The trunk may also be affected, though it is not always easy to say how much the tremor is due to the movements in the legs; and, finally, in some cases, there is a slight movement of the head. Occasionally even the muscles of the jaw and tongue, but very rarely those of the face, are affected. These movements vary in extent; in rapidity they range between 4½ and 7 to the second. As a rule the movements continue even during rest; thus, if the patient sits with the arm resting on the knee, both the leg and the hand and arm will continue to tremble. In early cases, however, support may check the tremor for a time, and in advanced cases, with the rigidity to be presently described, the tremor may only occur on movement. By voluntary efforts fixing the limb the tremor may also for a time be stopped, and it ceases during sleep.

Rigidity. This differs from that met with in spastic conditions following pyramidal lesions in that the rigidity is more evenly spread, affecting both extensor and flexor groups, and more evenly maintained in opposition to passive movements. When it is the first symptom it may be observed that the thumb and forefinger are rigid without any tremor: rigidity extends to other parts, and tremor is developed later. In a case which has begun with tremor in one limb, the rigidity may appear first in another limb, and be followed by trembling. The muscular weakness is shown by deficient power of grasp, and fatigue on exertion, so that in the early stages, for instance, a man may find difficulty in buttoning up his collar, and a woman in doing her hair. The rigidity imposes a characteristic posture, which is most marked when the patient is standing. The head and body are bent forwards; the elbows are flexed nearly to a right angle, and stand out a little from the side; the hands are in the position above described; and the legs are slightly bent at the knees. The gait in fully developed cases is very peculiar: the patient rises from his seat slowly and with apparent difficulty, and his first steps are hesitating; but soon his movements become quicker and quicker, he seems with each step to be trying to prevent a fall, and ultimately, unless stopped, he may actually fall forward to the ground. Some patients when gently pushed backwards are unable to stop themselves, and continue to walk backwards until they meet an obstacle or fall. The terms *festination* and *propulsion* have been used to describe the forward tendency; *retropulsion* and *retrogression*, the backward movement. The face has a characteristic

and fixed expression, due to the rigid condition of the facial muscles (Parkinsonian mask), and this may be a comparatively early symptom of the disease. Speech may be similarly slow at first, and afterwards rapid; it is often high-pitched or thick and feeble. Otherwise all movements tend to be slow on account of the rigidity; for instance, the patients turn with difficulty. The muscles are not hypertrophied by their excessive action, and only in late cases with long-continued rigidity do they present some atrophy. The reflexes are normal. Some subjective sensations are often experienced, such as dull aching pains, sense of fatigue, or a feeling of restlessness, and especially a sense of great heat, which is often accompanied by free perspiration; while a flush on the cheek of the patient shows vasomotor weakness.

Diagnosis. There is but little difficulty in recognising paralysis agitans when tremor is present. *Senile tremor* is distinguished from it by the constant trembling of the head. The movements also are finer, both arms are often involved together, and there is no rigidity; it comes on later in life. The tremor of disseminated sclerosis is of the intentional type, is not accompanied by rigidity and is associated with other physical signs. Especially if the symptoms are confined to the limbs of one side, there is a resemblance to a hemiplegia of pyramidal origin, but this may be excluded by the absence of alterations in the reflexes, and by the presence of the mask-like expression, which even when present in slight degree is often characteristic. Cases of slight double hemiplegia may be distinguished by the bulbar symptoms and mental changes, as well as by minor alterations in the reflexes.

Prognosis. The disease is chronic and progressive, yet its course may be very slow, two or three years perhaps elapsing between the affection of one and another limb. It is fatal only through bedsores or exhaustion in the extreme cases; intercurrent disease—*e.g.* of the lungs—terminates others.

Treatment. There is no curative treatment for the disease. The tremor may be controlled to some extent by sedatives such as bromide and luminal. The rigidity is often amenable in some degree to drugs of the belladonna group, of which the tincture of stramonium is usually the best. This should be given in a dose of 20 minims thrice daily, and this dose should be increased by 5 minims daily up to the limit of the patient's tolerance as indicated by dryness of the mouth or paralysis of visual accommodation. The patient who can take 40 to 60 minims thrice daily frequently obtains great relief. For those who cannot tolerate such doses without it, the addition of pilocarpine nitrate to the medicine in the proportion of one-tenth of a grain to 20 minims of the tincture of stramonium may be of value.

When once the optimum dosage of stramonium has been reached it should be continued, but with regular and continued use its good effect is frequently lost. This is less likely to occur if the drug is periodically omitted, *e.g.* during one week in six. Hyoscine hydrobromide by hypodermic injection in a dose of $\frac{1}{200}$ to $\frac{1}{100}$ a grain may be a useful adjuvant to the stramonium for special purposes, such as enabling the patient to fulfil some business or social engagement, or to enable him to achieve the physical relaxation necessary for going to sleep.

A great deal is to be gained if the patient can adopt a plan of living which will enable him to have assistance in dressing, undressing and the like, so that he may conserve his energies for other occupations. Fatigue has always a bad effect. Massage and passive movements have their value both in improving muscular function and in relieving the sense of stiffness which is often a source of great discomfort. In the case of a patient severely affected by the disease, stretching movements of the limbs with an alteration of the position of the body, carried out at regular intervals of half an hour by nurse or relative, may give much relief. The patient may be encouraged to take walking exercise with assistance. Travelling by car or omnibus often gives a sense of physical comfort probably due to the frequent slight changes of position which are possibly induced.

TUMOURS OF THE BRAIN

Intracranial neoplasms (including the infective granulomas) are of comparatively frequent occurrence among diseases of the brain. In the early stages of their growth they may give rise either to no symptoms at all, or to signs which require the most careful investigation by the physician before a successful diagnosis can be made. It is in these early stages, however, that surgical operation offers most chance of alleviation or cure. In the later stages the symptoms produced are as a rule easy of recognition, but the outlook from the point of view of surgical treatment is proportionately less hopeful.

Ætiology. Syphilis and tubercle account for the granulomas. In a certain number of cases of tumour there is a history of preceding head injury, but the causal connection is doubtful. Hydatid cysts and cysticercus occasionally play the part of cerebral tumours.

Morbid Anatomy. *Tuberculomas* account for a small proportion of intracranial tumours, and in Cushing's series of 2,000 verified cases amounted to less than 2 per cent. They are rarely met with except in children or adolescents, and are three times more common below than above the tentorium. They consist of globular masses in the cerebral substance, ranging from $\frac{1}{3}$ inch to 2 or 3 inches in diameter. These masses contain an inner core of yellow caseous material bounded by an outer narrow zone of a pinkish-grey colour and dense consistency. They can be easily detached from their bed. Microscopical examination reveals the presence of tubercle bacilli in sections through the wall of the granuloma, but the characteristic giant cell systems are frequently lacking. The surgical removal of a tuberculoma is almost always followed by death from tuberculous meningitis.

Circumscribed *gummas* are relatively uncommon—less than 1 per cent. of all intracranial tumours. They always grow in connection with the membranes, and are therefore commonly situated upon the surface of the brain. They may, however, be found in one of the central parts growing from a deep fold of the pia mater. They tend either to break down and become caseous in the centre, or to take the form of firm fibrous masses.

Hydatid cysts and the *cysticercus cellulosæ* are rarities which need not be described in detail. Hydatid cysts may attain to a considerable size and produce the signs of a large brain tumour. Those of the cysticercus cellulosæ are usually small and multiple, and, besides being found in the cerebral substance, may lie free in the ventricles.

Glioma. Of true intracranial neoplasms the commonest are the *gliomas*, which amount to more than 40 per cent. of the total. It has long been recognised that these tumours vary in their rate of growth, histological appearance, age incidence, and favourite situation, and several attempts have been made recently at a precise classification which will take into account all these features. The mature neuroglia contains three main types of cell derived from the ectoderm of the primitive neural tube. These are the *ependyma* cells which line the ventricles and central canal of the spinal cord, the *astrocytes* which constitute the main framework of brain and spinal cord, and the *oligodendroglia*, consisting of small round cells occurring in great numbers between the nerve fibres and around the nerve cells, which may play a part in the nutrition of myelin. In addition to these ectodermal derivatives there are the cells of the *microglia*, which are mesodermal in origin and perform the function of phagocytes. These do not give rise to tumours, but are mentioned here in order that a clear account of the neuroglial system may be presented. The ependyma cells, astrocytes, and oligodendroglia are derived in the embryo from more primitive types of cell known as *spongioblasts* and *medulloblasts*. Tumours of all these types of cell are encountered and many of intermediate character. As in the case of new growths generally those in which the type of cell is embryonic are the most rapidly growing and invasive, and those in which the cells are well differentiated are least so.

Although the gliomas are malignant tumours in the sense that they are non-encapsuled and invasive, they do not penetrate the dura mater, nor do they give rise to metastases outside the central nervous system. The *spongioblastoma* is one of the commonest varieties of glioma, and is characteristically a tumour of middle life occurring in the cerebral hemispheres or corpus callosum. These tumours appear to the naked eye as reddish, fleshy masses, with a fairly well-defined margin. They are highly vascular and frequently contain hæmorrhages, cysts and areas of necrosis. They are of rapid growth and little amenable to surgery. Microscopically they consist of relatively undifferentiated round or oval cells with no special arrangement.

The *medulloblastoma*, again composed of relatively undifferentiated cells which are round and may be arranged in rosettes, is essentially a tumour which develops in the first decade of life and is situated in the cerebellum or roof of the fourth ventricle. In Cushing's series it accounted for 10 per cent. of all verified gliomas. Like the spongioblastoma, it is vascular, of rapid growth and irremovable. Alone of the gliomas it tends to invade the pia-arachnoid and may seed itself throughout the subarachnoid space.

The *ependymoma* is a rare type of glioma, which again is seldom found except in the roof of the fourth ventricle. It is usually found in children or young adults, may be of slow growth and is capable of removal. Its situation, however, renders the operation dangerous, and Cushing's series show a 31·3 per cent. case mortality when radical extirpation is attempted.

The *astrocytoma* is a common tumour, occurring with about the same frequency as the spongioblastoma, and these two tumours together amount to 60 per cent. of all gliomas. The astrocytoma to the naked eye is a white infiltrating tumour of dense consistency. It occurs both in the cerebrum and cerebellum. In the former situation it is found in adults. In the cerebellum it is most characteristically a tumour of childhood and early adolescence, and frequently takes the form of a cyst containing a mural nodule of growth. It is a slow-growing tumour, and in the cerebellum especially lends itself to surgical removal, the case mortality for the cerebellar operation in Cushing's most recent series being 3·4 per cent.

The *oligodendroglioma* is a rare tumour of slow growth and with a marked tendency to calcification which is found in the cerebral hemisphere in adults. It has frequently been removed with success.

Meningioma or Dural Endothelioma. After the glioma the commonest tumour is the so-called *meningioma* or *dural endothelioma* (13·4 per cent. of all tumours in Cushing's series). These tumours may occur at any age, but are most commonly discovered giving rise to symptoms between the ages of thirty and forty. They are rarely met with below the tentorium. They arise apparently from arachnoid cells on the inner surface of the dura mater, and are essentially slow-growing encapsulated tumours of innocent type. They vary in size from that of a pea to a tangerine orange, are roughly spherical in shape, nodular, and of moderately firm consistency. They may have a wide connection with the dura mater or retain their attachment to it by a comparatively narrow stalk. They occur naturally upon the surface of the brain, which is compressed by the tumour, but a growth arising from the falx cerebri may so bury itself in the hemisphere from its mesial aspect as to appear as a subcortical mass beneath the lateral surface. At the point of attachment to the dura these tumours may become calcified or even ossified, or they may grow outwards, eroding the bones of the skull. They are occasionally multiple, and may be associated with multiple tumours of the nerve roots. Microscopically they consist of densely packed cells of a spindle shape, with large oval nuclei, which tend to be arranged in whorls and are supported by a connective tissue stroma. The centres of the whorls frequently undergo hyaline degeneration and calcification, and are then called psammoma bodies. Tumours of similar type may arise from the arachnoid membrane. The meningiomas obviously lend

obstruction between the source of secretion of the cerebro-spinal fluid in the lateral ventricles and the site of its absorption. The result is a *secondary internal hydrocephalus*, the distension being confined to the ventricle on the side opposite to the tumour, which is probably not occluded. There ensues a rapid further increase of intracranial pressure, wedging the pressure cone and the medulla firmly into the foramen magnum, and death follows from anæmia of the respiratory centres.

As regards their general effects, tumours situated in the posterior division of the cranial cavity—*subtentorial tumours*—may be divided into those growing from *without* the cerebellum, pons and medulla, and those growing *within* the cerebellum, pons and medulla.

Extra-cerebellar tumours are usually of slow growth, and have a certain amount of room in the lateral recess in which to expand. It is therefore only in their later stages that they cause a rise of tension in the posterior fossa. This is followed by the formation of a pressure cone from squeezing of the cerebellum into the foramen magnum, and in the manner already described secondary internal hydrocephalus is set up. In this case, however, *both* lateral ventricles are patent and become equally distended from accumulated pressure of cerebro-spinal fluid; the cerebral sulci become obliterated, the gyri flattened, and the pressure being transmitted along the optic nerves causes papillœdema.

Intra-cerebellar tumours are usually of more rapid progress, and the increase of pressure caused by them results in the early formation of a pressure cone and the rapid establishment of the conditions leading to secondary internal hydrocephalus, as described above, with general rise of intracranial tension.

Gliomas of the brain-stem will cause increased intracranial pressure early or late in proportion to the degree in which they cause obstruction to the outflow of fluid from the ventricular system. A large infiltrating tumour of the pons may be fatal without ever giving rise to internal hydrocephalus, while, on the other hand, a minute ependymoma of the iter, causing little or no local destruction, may, owing to its situation, cause a rapidly fatal increase of intracranial pressure. Tumours situated in the interpeduncular region, though compressing the structures in their immediate neighbourhood, may cause little or no increase of intracranial pressure.

General Symptoms. These are the symptoms of increased intracranial pressure, which, as has been shown in the preceding section, may develop relatively early in some cases, late in others—or may be absent to the end. They are symptoms, therefore, whose absence cannot exclude the diagnosis of cerebral tumour, though their presence may afford the first suspicion of its existence.

Headache. This is a more or less constant symptom, and though it may at first be intermittent and of slight degree, in the later stages it is often persistent and attains a severity which is rarely met with in headaches due to any other cause. It may be felt all over or localised mainly to the front, sides, or top of the head. It is often described as bursting or splitting, is frequently at its worst in the early morning, and is often associated with nausea or actual vomiting.

In the early stages the patient may be seized with paroxysmal attacks at considerable intervals, and even later on, when it becomes constant, the headache may at times become greatly intensified without apparent cause. Change of posture, such as stooping, or forcible expiratory movements, as in coughing or sneezing, often precipitate an attack or intensify pre-existing pain. Pain which is limited to the suboccipital region and radiates down into the back of the neck is strongly suggestive of a tumour in the posterior fossa. Headache which is always referred to the same spot, especially if it be accompanied by tenderness to pressure over this area, is evidence in favour of the growth being situated on the surface of the brain, or growing from the dura mater in this locality.

Vomiting is a less constant and a less frequent symptom than headache, but is present in the majority of cases. In its most characteristic form it is associated with headache and is independent of the taking of food. It is most marked in

tumours of the posterior fossa in which it may be an early symptom, sometimes preceding headache. Although the vomiting of cerebral tumour is often sudden and unassociated with nausea, this is by no means always the case. Waves of nausea may precede or may take the place of vomiting.

Papillœdema is the most characteristic of all symptoms of increased intracranial pressure from cerebral tumour. Its appearances and the mechanism of its production have already been described (*see* pp. 620, 634). Whether it appears early or late in the disease will depend upon the factors already discussed under Pathology, and it must be borne in mind that its absence at any stage does not exclude the diagnosis. The condition is nearly always bilateral, but one optic disc may be affected before the other. The side upon which the papillœdema commences or is more intense bears no relation to the situation of the tumour. A high degree of swelling is compatible with good visual acuity, though the patient may complain of transient attacks of mistiness of vision. Permanent impairment of vision only occurs with the onset of secondary optic atrophy.

Convulsive attacks are not so frequent as the symptoms already mentioned, and they are very irregular in their occurrence in the cases attended by them; thus there may be two or three in the whole course of the illness, or they may be very frequent. They may take the form of generalised epileptiform attacks, in which there is an initial stage of tonic rigidity followed by clonic spasms and a temporary condition of stupor, or they may be limited to a momentary loss of consciousness. "Focal seizures" with characteristics distinctive of their origin in definite areas of the brain will be alluded to under the heading of Local Symptoms. They may, however, occur in the late stages of increased intracranial pressure without relation to the site of the tumour, and so be misleading and of false localising value.

Vertigo is not an uncommon symptom, and is usually associated with attacks of headache and vomiting.

Slowness of the pulse when it occurs is usually a late symptom of increased intracranial pressure.

Among other general symptoms are *mental changes:* the patient may be dull, apathetic, forgetful, sleepy, careless or untidy; in later stages he becomes lethargic, and finally comatose. These, however, occurring as the result of increased pressure, are late changes. In the early stages they are more commonly due to widespread destruction of the association fibres, such as is produced by large tumours of the cerebral hemisphere, and as such will be considered under Localising Symptoms.

Localising or Focal Symptoms. It is important to realise from the first that these are of greatest value in determining the site of the tumour during the earlier stages in its growth. In the later stages the mechanical effects of increased intracranial pressure may result in damage to parts of the brain, or traction upon cranial nerves, far removed from the site of the original lesion.

Tumours involving the motor centres and pathways give rise to symptoms of irritation or paralysis of the parts affected.

Paralysis in the form of a slowly progressive hemiplegia, with increase of deep reflexes, loss of the abdominal reflexes, and an extensor plantar response on the affected side, is produced by deeply seated growths involving the pyramidal fibres. Tumours situated more superficially and at first producing a local anæmia of the cortical centres frequently give rise to attacks of *Jacksonian epilepsy* of motor type. These are localised convulsions, beginning always in one part and unaccompanied at first by loss of consciousness. In these cases, according to the severity of the temporary disturbance in the part, there may be a twitching, say of the hand alone or of the hand and arm, or of all the muscles of one side of the body; if the convulsions spread to the other side of the body, consciousness is usually lost.

In their spread from the point of commencement the movements always show

a definite sequence. If they begin in the face, they spread successively to the upper limb, beginning with the thumb and fingers, and then to the lower limb; if they begin in the leg, the arm and face are successively affected; if in the arm, the face and leg in turn. The convulsions are usually followed by some degree of temporary paralysis, especially in the part first affected, and for a short interval after the attack changes in the reflexes may be demonstrated on the affected side in the form of diminished or absent abdominals and an extensor plantar response. With progressive increase in the size of the tumour and destruction of the centres at first irritated, the fits become less frequent and less extensive, giving place to permanent paralysis. If the growth is in the left hemisphere in the case of a right-handed person, some degree of aphasia will accompany the attacks, and remain with the paralysis, especially if the arm and face centres are chiefly involved. The aphasia produced will be at first of the motor type, though later this may be obscured by mental changes.

Tumours of the post-central regions in similar fashion produce progressive hemianæsthesia if deeply situated. This is limited as a rule to loss of sense of position and astereognosis in the affected hand, but there may also be a diminution in the subjective intensity of sensations of touch, temperature and pain, which is apt to be of "glove" or "stocking" distribution. Tumours involving the cortex give rise to Jacksonian attacks of sensory character, resembling the motor seizures in the manner of their spread, but consisting of a sensation of numbness or tingling, which is often attended with extreme discomfort. An attack of this nature frequently passes into a motor seizure of the type already described.

Tumours of the occipital lobe give rise to defects in the visual fields of the opposite side, the exact area of the defect depending upon the situation of the lesion. Superficial tumours of this region may cause attacks of subjective sensations of visual disturbance, usually in the form of flashes of light or colours in the opposite visual field. An occipital growth may by downward pressure upon the tentorium give rise to compression of the cerebellum, thus leading to signs of false localising value.

Tumours involving the uncinate gyrus give rise to peculiar attacks first described by Hughlings Jackson and known as *uncinate seizures*. These are in the nature of unpleasant sensations of taste or smell, indefinitely described by the patient in various ways as being "like the smell of rotten eggs," a "bitter taste as if a gumboil had burst in my mouth," and so on. This is often preceded by a dreamy state accompanied by visual hallucinations. The attacks may be quite momentary, or may occur in the form of auræ ushering in epileptiform convulsions.

Tumours of the frontal lobes frequently give rise to no localising signs of diagnostic importance, and the symptoms are therefore confined to those of general pressure. These may, however, be accompanied or preceded by mental symptoms to a degree unusual in the case of tumours elsewhere. The changes noticed are inattention, inability to keep the mind fixed on any subject, loss of memory for recent events, and incoherence in conversation. Sometimes these patients are childish, casual and irresponsible, and show a tendency to make silly and pointless jests at unexpected moments. In the later stages apathy and stupor supervene. A high proportion of cases of brain tumour discovered *post-mortem* in mental asylums are situated in the frontal lobes. Convulsive attacks may occur either of a generalised nature or beginning with conjugate deviation of head and eyes towards the opposite side from irritation of the centre for this movement in the pre-central area, in which case they are of diagnostic significance. A tumour of the anterior end of the frontal lobe may by pressure upon the olfactory tract produce unilateral anosmia. A tumour on either side involving the posterior part of the superior frontal gyrus may produce the symptom known as forced grasping or tonic innervation, a condition in which the patient having grasped an object or closed his fingers is for the moment unable to relax his grip. Distinct from this, but often associated with it, is the grasp reflex, an involuntary closure of the fingers

in response to tactile stimulation. A tumour in the posterior part of the left frontal lobe in a right-handed person is likely to result in motor aphasia and agraphia.

Tumours of the temporal lobe, apart from those at the anterior end, involving the uncinate gyrus, and those at the posterior end on the left side, involving the speech centres, may produce no signs of localising value, the symptoms being limited to those of general pressure. Changes in the sphere of intellect and temperament may occur as described in the case of frontal tumours. A deep-seated tumour in the temporal lobe is likely to involve the optic radiation and cause a defect in the opposite visual field.

Tumours of the corpus callosum do not, as a rule, cause very definite symptoms, but may give rise early to mental changes, and are sometimes associated with motor apraxia (*see* p. 615).

Tumours of the mid-brain may give rise to localising signs in the form of weakness of upward movement of the eyeballs, defective reaction of the pupil to light, eccentricity of the pupils, paresis or paralysis of the third cranial nerves, and defective sensibility over the area supplied by the fifth nerve, due to involvement of its mesencephalic root. Additional symptoms may arise from involvement of the longitudinal tracts in this region.

Tumours of the interpeduncular space, of which the commonest are the pituitary adenoma and the hypophyseal duct tumour, cause symptoms from pressure upon the optic chiasma. If the tumour, as often, is centrally situated the temporal half of each visual field is first affected, the defect of vision beginning as a para-central scotoma. When the tumour compresses the chiasma from below it is the upper quadrants of the fields of vision that are first affected, and the lower quadrants if the compression is from above. A tumour situated to one side of the midline will cause blindness of the eye on that side with a temporal defect in the field of the other. Associated with the failure of vision there is primary optic atrophy. In addition to this a suprasellar tumour may cause papillœdema.

The intrasellar tumours (mostly adenomas) give rise to severe headache of a continuous boring character, referred most frequently to the temples, though sometimes to the vertex or occiput. The suprasellar tumours (mostly hypophyseal duct tumours) cause headaches of the type generally encountered from increased intracranial pressure.

Other structures which may be compressed are one or other third nerve, with resultant ptosis and diplopia: the crus cerebri on one side leading to unilateral weakness with an extensor plantar response: and the nuclei in the floor of the third ventricle with resultant hypersomnia, and polyuria. The pressure effects upon bone are, as a rule, evident with the X-rays. The intrasellar tumour causes expansion of the sella turcica both in an antero-posterior and a downward direction (Plate 56, A). The suprasellar tumour causes erosion and finally disappearance of the clinoid processes, the size and depth of the sella remaining normal. In the majority of hypophyseal duct tumours (80 per cent. according to Cushing) calcification can be detected (Plate 56, B). The normal sella is shown in Plate 57 A.

Occasionally an intrasellar tumour may invade the nasopharynx and cause a leakage of cerebro-spinal fluid through the nose.

The glandular symptoms produced by the suprasellar and intrasellar tumours are described in the section dealing with the pituitary gland (*see* p. 495).

In *tumours of the pons* the localising signs depend upon affection of the cranial nerves situated therein, together with symptoms of destruction of the longitudinal tracts. Symptoms of general pressure are conspicuous by their absence until the terminal stages.

Tumours of the cerebellum frequently give rise to headache, which is at first localised to the suboccipital region, with a tendency to radiate downwards into the neck. Symptoms of general pressure appear early and are prominent. In addition there are nystagmus, inco-ordination in the performance of all muscular

movements, and reeling or staggering gait. In a tumour affecting mainly one lobe of the cerebellum, the headache may be mostly referred to that side, and there may be localised tenderness to pressure.

The tendency of the eyes is to deviate towards a point somewhat to the opposite side, so that nystagmus is coarser and more easily elicited when the patient looks toward the side of the tumour. There is frequently some degree of weakness, tremor, and hypotonia on the affected side of the body, and inco-ordination may be demonstrated in the performance of the finger-nose-finger, diadochokinesis, and heel-knee tests (*see* p. 627).

Characteristic peculiarities of attitude and gait are often present. There is a tendency for the head to be tilted towards the side of the tumour, and for the whole of the body to deviate towards that side. In consequence the ipsilateral shoulder is held higher than the other, and the ipsilateral lower limb is slightly abducted and everted, the former of these being of the nature of a compensatory mechanism for the spontaneous deviation.

In walking there is a spontaneous tendency to deviate or, it may be, to fall towards the side of the lesion, which is corrected by voluntary efforts, so that the patient may appear to stumble towards the sound side. In any doubtful case, the patient may be asked to stand on either leg alternately, when the greater weakness and unsteadiness of the affected side will be apparent. The reflexes as a rule are not altered, but the knee jerk on the affected side may show a pendular character when elicited with the leg hanging free, this being due to loss of muscular tone.

Tumours of the cerebello-pontine angle. These are characterised by progressive symptoms due to pressure upon the cranial nerves, succeeded by signs of a unilateral lesion of the cerebellum when the tumour has grown large enough to compress and destroy that structure. As already mentioned, symptoms of general pressure are of late onset, and usually coincide with cerebellar involvement.

The commonest growth in this situation is the neurofibroma of the eighth nerve known as *acoustic tumour*. This proclaims its presence first by symptoms referable to the auditory nerve in the form of roaring or whistling noises (tinnitus) and progressive nerve deafness. Next, the sensory root of the fifth nerve is involved, causing first diminution or loss of the corneal reflex on that side, and subsequently numbness and anæsthesia of the trigeminal field. At this stage the vestibular reactions normally obtainable by caloric, rotatory, or galvanic stimulation of the vestibular apparatus are found to be absent on the affected side. The seventh nerve is involved, with resultant facial weakness of peripheral type; nystagmus is present, being most marked when the patient looks towards the side of the lesion; and finally there ensue the signs already described as characterising a unilateral lesion of the cerebellum, together with headache, papilloedema and the other signs of increased intracranial tension.

False Localising Signs. It has already been stated that in the later stages of the growth of a cerebral tumour the mechanical conditions arising from increased intracranial tension may result in symptoms which have a false localising value. These may be produced by traction upon the cranial nerves, by thinning of the cortex from the pressure of internal hydrocephalus, or by the obstruction of some important vessel. The cranial nerves which are most commonly affected in this way are the sixth pair. Therefore a sixth nerve palsy developing late in the course of the symptoms of intracranial tumour is of negligible value as an isolated sign. The other cranial nerves which may be affected in similar fashion are the third, fifth, seventh and eighth. Thinning of the cortex probably accounts for the occasional occurrence of motor Jacksonian attacks and signs of involvement of the upper motor neuron tracts in these late cases. Downward pressure upon the tentorium from a tumour of the occipital lobe may give rise to cerebellar symptoms.

It is also an undoubted fact that in some cases of cerebral tumour with a high

degree of intracranial pressure the tendon jerks may be lost in both upper and lower limbs. The reasons for this are somewhat obscure.

The skull should always be examined carefully in a case of suspected cerebral tumour. In children it is frequently enlarged, with separation of the sutures, especially the fronto-parietal over which percussion yields a "cracked-pot" note. A slow-growing superficial tumour may cause erosion or hyperostosis of the overlying bone, and this is especially apt to occur in the case of a meningioma. The arterial angeioma frequently gives rise to a bruit, appreciated by, and sometimes complained of, by the patient and audible by the physician on cephalic auscultation. A similar bruit may sometimes be heard over a vascular glioma.

The cerebro-spinal fluid may show an increased pressure to the manometer at a stage before other evidence of increased intracranial pressure is apparent. A pressure above 200 mm. of water is suggestive. In the later stages the pressure is often as high as 500 mm. On examination the fluid is frequently normal, but in some cases contains an excess of protein. This, as a rule, is unaccompanied by any increase in cells. Such a fluid is always suggestive of a vascular tumour from which transudation is taking place into one of the ventricles, and is also encountered with some regularity in the case of acoustic tumours. An increase of cells in the fluid may occur in the case of a growth which is necrotic and is near to the surface of the brain or of one of the ventricles.

The X-rays may reveal areas of calcification in the substance of the tumour. These are frequently seen in hypophyseal duct tumours, and less often in the chronic type of glioma (astrocytoma, oligodendroglioma) and the meningiomas. The venous angeioma is almost always visible by this means. Abnormalities in the bones of the skull to be looked for are generalised thinning of the vault, and erosion of the dorsum sellæ from hydrocephalus, best seen in children; ballooning of the sella turcica in intrasellar tumours; destruction of the clinoid processes and erosion of dorsum sellæ in suprasellar tumours; local erosion or hyperostosis, or increased vascularity of the bone in meningiomas. In the antero-posterior view displacement to one side of a normally calcified pineal body may give evidence of a tumour in the opposite hemisphere. X-ray investigation may be carried further by the injection of air into the ventricles either by means of lumbar puncture (encephalogram) or puncture of a lateral ventricle through a hole drilled in the skull (ventriculogram). The X-rays then show the outlines of the ventricular system. In the case of a sub-tentorial tumour both lateral ventricles will be symmetrically distended, and the third ventricle visible between them in the antero-posterior view. A tumour of one hemisphere will cause deformation or obliteration of the lateral ventricle on that side with distension of the other, and displacement of the septum across the mid line. A tumour of the third ventricle causes symmetrical distension of the lateral ventricles, the third ventricle itself being obliterated or deformed. Air injections may be of great value in the localisation of tumours causing increased intracranial pressure with no unequivocal localising signs, but they are not without danger and should not be resorted to except with the co-operation of a surgeon who is prepared to carry out an operation at once, should symptoms of increased compression arise.

Diagnosis. When once the signs of increased intracranial pressure are established this is comparatively easy. The presence of persistent or constantly recurring headache of paroxysmal nature together with papillœdema is in nearly all cases evidence of a tumour of the brain. A condition which may require careful differentiation is that due to a *syphilitic meningitis;* other evidence of syphilis and a positive Wassermann reaction in blood or spinal fluid may help to clear up the diagnosis, and in this connection it is to be remembered that occasionally the reaction may be positive in the fluid though negative in the blood. A further possibility to be taken into account is that a patient with syphilis may also have a cerebral tumour. In doubtful cases the effect of anti-syphilitic treatment will be decisive.

The other causes of increased intracranial pressure which may simulate tumour are *chronic cerebral abscess* and *chronic subdural hæmatoma*. In the former a history of sepsis and in the latter one of head injury should be forthcoming, and the presence of polymorphonuclear leucocytes in the spinal fluid is always suggestive of abscess. Nevertheless abscess or hæmatoma are sometimes discovered only in the course of an exploratory operation for presumed tumour.

The clinical picture of a *hypertensive crisis* occurring in the course of arterial disease, with or without renal involvement may, sometimes resemble that of a tumour, but the fundus in the case of arterial disease as a rule shows retinal hæmorrhages at a distance from the nerve head, and characteristic changes in the retinal vessels. Finally the use of the sphygmomanometer will usually settle the diagnosis.

Hydrocephalus of the kind which may follow meningococcal meningitis, otitis media, and sometimes head injury is to be distinguished by the appropriate past history in each instance.

Encephalitis lethargica or other forms of encephalitis may occasionally give rise to difficulty. The absence of increased intracranial pressure as observed clinically and by lumbar puncture is the most useful point in excluding the diagnosis of tumour in such cases.

When the characteristic picture of increased intracranial pressure is absent the diagnosis of cerebral tumour is often extremely difficult and has to be distinguished from a variety of conditions.

The cases with progressive hemiplegia, hemi-anæsthesia or visual field defect have, in elderly persons, to be distinguished from the effects of vascular disease. Here the rate of progress is the most important point for it is almost always slower in the case of tumour than can be accounted for in terms of a cerebral thrombosis. In this group of cases the possibility of chronic subdural hæmatoma also has to be taken into account.

Epileptic attacks, focal or generalised, may occur in the early stages of idiopathic epilepsy, or as the result of syphilis, or an old vascular lesion or injury of the cortex. The differential diagnosis between cerebral tumour and idiopathic epilepsy may be extremely difficult, and is sometimes to be made only with the passage of time. It is a sound rule to suspect tumour in all patients beginning to have epileptic attacks in middle life without family history of the malady or other cause, and to investigate them from this standpoint.

The mental symptoms of cerebral tumour have to be distinguished from those of the other organic dementias, in particular those caused by syphilis and arteriosclerosis, and pre-senile dementia. The optic atrophy caused by pituitary and suprasellar tumours has to be distinguished from that due to other causes—in particular, syphilis.

Tumours of the cerebellum and brain-stem may sometimes cause symptoms liable to confusion with those of disseminated sclerosis, but the scattered symptomatology in the latter disease, together with the absence of increased intracranial pressure, usually suffices for the diagnosis.

Having determined the presence of a cerebral tumour and its situation it is often possible by taking into account, in addition to the symptoms, the age of the patient, and the results of special investigations such as X-rays and lumbar puncture, to be reasonably certain of its nature. This is especially true of the pituitary adenomas, and hypophyseal duct tumours, and the acoustic tumours. A mid-cerebellar tumour in a child is nearly always either a medulloblastoma or an astrocytoma, the former tending to occur at a rather earlier age, and giving a shorter history. A rapidly growing tumour deeply situated in one cerebral hemisphere in a person of middle age or older is almost certainly a spongioblastoma. A high protein content in the cerebro-spinal fluid will strengthen this suspicion. The X-ray appearances of the bone overlying a meningioma may be characteristic of this tumour. The intricacies of pathological diagnosis will

not be laboured further. The proper correlation of the information given in the sections on Morbid Anatomy, Pathology and Symptoms should enable the student to form his own suggestions.

Prognosis. In cases which are not subjected to operation the average survival period in a series of cases verified *post-mortem* was from one to two years (Tooth). It is naturally shortest in the case of rapid growths such as the spongioblastoma, medulloblastoma, and metastatic carcinoma. The life history of the more benign tumours may be much longer. The expectation of life is perhaps longest in pituitary tumours of simple type, which by reason of their situation within the sella turcica are precluded from causing increase of intracranial pressure until a very late stage in their development.

When once the signs of increased intracranial pressure have developed, blindness is likely to supervene from secondary optic atrophy. In the later stages also mental symptoms are likely to supervene. Death, which occurs from failure of the respiratory centres, may be extremely sudden.

The prognosis for various types of tumour with surgical treatment has been indicated in the section dealing with morbid anatomy.

Treatment. The treatment of syphilitic gumma is the same as the treatment of syphilitic meningitis (*see* p. 693). A tuberculoma may call for a decompressive operation for the preservation of vision. Otherwise the treatment is that adopted for tuberculosis elsewhere—rest, sunlight, and fresh air. The treatment of other cerebral tumours is almost entirely surgical, as described in the Morbid Anatomy section. Certain types of tumour of which the medulloblastoma, spongioblastoma, and metastatic tumours are the most conspicuous examples are better left alone, though an exploratory operation may be necessary in some cases to establish the pathological diagnosis. The medulloblastomas appear in some degree to be amenable to deep X-ray therapy, as also are the pituitary adenomas.

Medicinal treatment is limited to the relief of symptoms. Complete rest, ice-bags to the head, caffein, phenacetin and aspirin in combination, and, lastly opium are the means available. Temporary relief from the symptoms of increased intracranial pressure may be obtained by means of hypertonic solutions such as 3 ounces of mag. sulph. in 6 ounces of water by the rectum, or 50 to 100 c.c. of a 50 per cent. solution of glucose intravenously.

CHRONIC HYDROCEPHALUS

By hydrocephalus is meant the accumulation of fluid within the cranial cavity. An acute effusion is mostly determined by meningitis, either tuberculous or meningococcal, and the former disease was once known as acute hydrocephalus.

A division has been made of chronic hydrocephalus into *internal* and *external* forms, according as the fluid is contained entirely in the ventricles of the brain or is formed outside between the brain and the skull, in the subarachnoid space. It is true that in old age, and from other conditions, the convolutions of the brain diminish in size, the sulci widen, and the space in the skull thus left by the disappearance of brain substance is filled up by fluid. Similarly a loss by local shrinking of the brain is replaced by fluid on the surface. But this compensatory secretion has none of the effects of true hydrocephalus. True external hydrocephalus is an extremely rare condition, the nature of which is not at present understood, but it is thought to arise as the result of chronic inflammatory changes in the meninges, and as such has also been termed serous meningitis.

Internal hydrocephalus, in which the distension is confined to the ventricles of the brain, may be divided into the congenital and the acquired types.

Congenital Internal Hydrocephalus. The condition is either noticed at birth or shortly afterwards, and must presumably depend upon some congenital abnormality in the secretion, circulation or reabsorption of the cerebro-spinal fluid.

There is no evidence in favour of the supposition that over-secretion on the part of the choroid plexus is the cause. Cases have been found in which a congenital block has been discovered in the Sylvian aqueduct or elsewhere, in the path between the fount of origin of the cerebro-spinal fluid, which is chiefly in the lateral ventricles, and the venous channels at the base of the brain into which it is reabsorbed (*see* p. 606). There remain, however, a large majority in which no such cause can be found, and the suggestion has therefore been made that the failure is on the part of the channels through which the fluid should normally be reabsorbed, and that the arachnoid villi in these cases are absent or defective.

This hypothesis remains unproven, but some support is lent to the idea by experiments showing that in animals, a small quantity of a suspension of finely divided particles of carbon (lampblack) being introduced into the subarachnoid space, these particles find their way to the arachnoid villi in the walls of the venous sinuses, and by thus blocking the channels for reabsorption of the cerebro-spinal fluid give rise to a picture of internal hydrocephalus in every way resembling that seen in man.

Morbid Anatomy. In this form of hydrocephalus, the ventricles of the brain contain an excess of fluid, sometimes amounting to a quart or more. It has the characters of cerebro-spinal fluid—that is, it has a specific gravity of 1,006–1,009, contains a small quantity of chloride of sodium, only a trace of albumin, and sometimes urea or cholesterin. The liquid may occupy all the ventricles, or all except the fourth, or the two lateral ventricles alone. By its increasing quantity the substance of the brain is enormously distended, the convolutions are flattened, sometimes reduced to a few lines in thickness, and the basal ganglia are correspondingly thinned out. The aqueductus Sylvii may be distended to the size of the finger when the fluid is in the fourth ventricle; it is often closed when the fourth ventricle is not dilated. In extreme cases the distinction between grey and white matter is lost in the parts exposed to most pressure; the ependyma is often thickened, and contains amyloid bodies, while its surface is covered with fine granulations.

Hydrocephalus is sometimes associated with other lesions of the central nervous system, *e.g.* spina bifida or syringomyelia.

Symptoms. The most obvious, and it may be for a time the only, symptom of the disease is the condition of the child's head which results from it. The pressure on the brain is transmitted to the skull, and as this expands outward the head becomes enlarged. The enlargement is often extreme. In congenital cases it may form a serious obstruction to delivery; in others it appears in the first few months of life, and the circumference may amount to 24 or even 32 inches, instead of 16 or 18 inches, which are the usual measurements up to the age of one year. The head is at the same time globular, and the skull projects over the face and neck almost uniformly all round. The face looks small and shrunken in proportion, and has a distressed, anxious, or senile expression in severe cases. The distension from within drives the orbital plates outwards, and the eyeballs are turned down so that the lower part of the iris and of the cornea is lost under the lower eyelid, and the upper part of the sclerotic is exposed. The increased size of the head is due to a separation of the cranial bones from one another, so that the fontanelles are much enlarged and the sutures widened. In these spaces fluctuation can sometimes be felt. In cases of long standing it is found that ossification has gone on at the margins of the bones, advancing into the sutures, so that ultimately, if the patient lives, by this means and by the formation, from independent centres in the membrane, of fresh plates of bone (*ossa triquetra*, Wormian bones), the deficiencies of the skull may be completely filled in. In the early stages, however, the bones are thin, wanting in diploë, and transparent. The skin of the scalp is tightly stretched, and excessively thin, and large blue veins ramify over the surface. The hair is generally scanty. In some cases,

where the fluid is not very abundant, the bones may yield sufficiently to obviate any considerable pressure upon the brain substance. The symptoms may not then go much beyond the enlargement of the head; at most there is some general weakness and loss of flesh, from which after a time the child recovers. But in most cases there are other symptoms. The muscular power is deficient; especially the large head cannot be held upright, and falls from side to side, or has to be supported by the hands when the child sits up in bed. The child cannot walk, or acquires the art in moderate cases only after a long time. Vision is often defective or lost; and in extreme instances there is atrophy of the optic nerves. The other senses may be to a certain extent impaired. The intellectual functions are often defective. The child slowly learns to talk, continues childish out of proportion to its growth, and is fretful, irritable, or vicious in temper. Nystagmus, rigidity and spasms of the weakened limbs, convulsions, and vomiting occur often in severe cases. Many of these patients die young, relapsing into a condition of apathy or semi-coma, lying in bed with eyes closed or twitching, with rigid limbs and incontinence of urine and fæces, constantly moaning or whining, and refusing food or else eating voraciously.

Finally, convulsions, or coma, or some intercurrent disease, such as bronchitis, pneumonia, or measles, may end the scene.

In some cases the fluid has escaped by rupture of the integuments or by bursting through the nose or eyes.

Prognosis. The duration is variable. Few cases survive beyond the third year. In the mildest cases recovery may take place, or rather the disease is arrested. Sir Frederick Taylor recorded a case ("Clin. Trans.," 1897) where a lad reached the age of sixteen with perfect mental development and physical capacity, and died then with rapid cerebro-spinal symptoms, the ventricles containing 30 ounces of fluid. A few cases have lived to sixty or seventy years of age.

Diagnosis. Confusion is most likely to take place between this and rickets. The rickety head is cubical in form rather than spherical, the vertex being flattened; the downward displacement of the eyeballs is absent; the limbs may be feeble, but the mental powers are not deficient; and the other evidences of rickets—beaded ribs, thickened wrists, sweating of the head, and general tenderness—are present at one time or another.

Treatment. In cases in which the Sylvian aqueduct and foramen of Magendie are not obstructed the distended ventricles may be drained by lumbar puncture. In the other cases in which there is an obstruction between the ventricles and the spinal subarachnoid space, drainage may be effected by ventricular puncture. But the effect is only temporary. Many attempts have been made to effect permanent drainage, but none so far have proved successful. Great care should be taken to prevent the development of bedsores from pressure of the tightly distended scalp upon the pillow.

Acquired Internal Hydrocephalus. This may occur either in children or in adults, but more commonly in the former. It is most commonly caused as a sequel of basal meningitis, particularly the meningococcal variety, by inflammatory adhesions which block the pathway of the cerebro-spinal fluid at its points of exit from the fourth ventricle. A similar blockage also occurs as the result of the mechanical conditions produced by tumours of the brain (*see* p. 724). It is especially likely to be caused by tumours directly blocking the Sylvian aqueduct even in their early stages. In addition there is a small group of cases to which the term otitic hydrocephalus has been given by the writer in which the symptoms develop during the course of or after otitis media, specially if this has been complicated by lateral sinus thrombosis. In some cases no satisfactory cause can be found.

Morbid Anatomy. The appearances in cases due to cerebral tumour have already been described. In the post-meningitic cases the foramina of Magendie and Luschka are obliterated by inflammatory material.

Symptoms. In the post-meningitic cases the condition of hydrocephalus closely follows the infective disease. In infants the enlargement of the head, together with the other symptoms described in the congenital form of the disease, are obvious signs of the condition. In older children and in adults the chief sign may be violent and persistent headache. The symptoms of increased pressure accompanying the condition when caused by cerebral tumour have already been described (*see* p. 725).

The rare cases for which no cause can be found when occurring in adults present symptoms of increased intracranial pressure, which can hardly be diagnosed from those of cerebral tumour. The distension of the third ventricle may give rise to optic atrophy from pressure upon the chiasma, and to paralysis of upward movement of the eyes from pressure upon the superior corpora quadrigemina.

The **Prognosis** depends upon the cause. In cases due to cerebral tumour it has already been discussed. Of the post-meningitic cases some children may eventually recover, but are often epileptics or mentally deficient; in adults the condition may continue for some months and then terminate suddenly in a fatal issue with failure of respiration. In the cases of obscure origin (primary acquired hydrocephalus), the outlook is more hopeful: there may be remissions or intermissions lasting in some cases for years.

Treatment. In the post-meningitic cases ventricular puncture and drainage have been recommended with subsequent introduction of anti-meningococcal serum. In those due to cerebral tumour the treatment has already been considered. The otitic cases can be relieved by repeated lumbar puncture with drainage of the cerebro-spinal fluid. Eventually the pressure falls to a normal level and permanent relief is obtained.

GENERAL PARALYSIS OF THE INSANE

Syphilitic Meningo-encephalitis

Pathologically this disease is characterised by widespread degenerative and inflammatory changes in the brain, caused by the spirochæte of syphilis, clinically by progressive mental deterioration together with certain physical signs, and in the last stages generalised paralysis. The title by which it is usually known dates from the time when the disease was thought to be a complication occurring in some cases of insanity, and should long ago have been abandoned in favour of a more scientific terminology. But the old name has an established usage.

The disease is much more frequent in men than in women, and occurs mostly between the ages of thirty and fifty, five to fifteen years after infection.

Cases also occur in children or young persons as the result of congenital infection.

Morbid Anatomy. The meninges as a rule are thickened with adhesions between themselves and to the surface of the brain, so that when an attempt is made to strip the pia-arachnoid the cortex is torn. The brain itself is usually smaller and lighter than is normal; the gyri, especially in the frontal lobes, appear shrunken, and the sulci by comparison wide and full of fluid. The ependymal lining of the ventricles is thickened, opaque and irregular, giving rise to a "frosted" appearance.

Microscopically there is a proliferation of the endothelial cells of the vessels with peri-vascular and diffuse infiltration of the cerebral substance with cells. Amongst these are found lymphocytes, plasma cells and various forms of neuroglial cells. Nerve cells and fibres are to be found in various stages of degeneration. There is also a marked increase in the neuroglial fibres. Areas of actual disintegration and softening may be found, but are not a characteristic feature. The spirochæte pallida, originally discovered in the brain by Noguchi and Moore,

in 1913, has subsequently been demonstrated in many other cases. It is, however, sparse in its distribution and found only if assiduously looked for. Degenerative changes consequent upon the cerebral lesions may be found in the spinal cord, and in a number of cases there is a simultaneous degeneration of the posterior columns (tabo-paresis).

Symptoms. Considerable difference is seen in the grouping of the symptoms; the nature of the mental changes in the early stages is variable, and there is no parallelism between physical and mental symptoms, nor between individual physical signs.

Most frequently the earliest symptoms appear in insidious changes in the personality. The man becomes careless or neglectful, tends to intemperance in drink, or spends more money than has been his wont without justification, or he is irritable or restless, changing in his affection towards his wife or family, or jealous without a cause. On the other hand, the early picture may be simply that of neurasthenia, with complaint of abnormal fatigue, sleeplessness and irritability. Headaches may be a prominent symptom, depending, no doubt, upon the meningeal involvement. The intellectual faculties are as a rule involved moderately early. There are defects in memory for the remote as well as the recent past, with consequent discrepancies in the dating of events in the patient's history. As a rule he possesses no insight into these defects, and will maintain that his memory is as good as ever. Disturbances of mood are frequent, the commoner type being that in which the patient is extremely elated, active and voluble, with delusions of grandeur. These concern himself alone; they express what he is, what he possesses, or what he can do. He is the Almighty, the King of England, or the Prime Minister, the most handsome or the most powerful man in the world. He has invented the most ingenious devices for making money, and is already possessed of boundless wealth. On the other hand, the dominant mood may be one of extreme depression, characterised by an extravagance of delusion which helps to differentiate it from a simple melancholia. In this condition the patient may attempt suicide. Yet another type of onset is that which shows itself in progressive apathy and deterioration of interests without any underlying disorder of mood.

Not infrequently the earliest symptom to attract attention is the occurrence of epileptic attacks. These may be of a minor or major variety, generalised or focal. They occur sooner or later in most cases of the disease.

On the physical side the facial muscles are smoothed out and expressionless, and there is commonly a tremor of the lips and cheeks in speaking. Speech is slovenly and slurred, with a tendency to miss syllables in the pronunciation of difficult phrases (such as "Methodist Episcopal"). Primary optic atrophy is sometimes present. There is a fine tremor of the protruded tongue, and there may also be atrophy from involvement of the hypoglossal nuclei. Pupils of the Argyll-Robertson type may be seen early in the illness, and are seldom absent in the terminal stages. Tremor of the outstretched hands is commonly seen, and shown also in the handwriting. The condition of the tendon reflexes in the early stages varies with the degree of involvement of pyramidal and posterior column fibres. Extensor plantar responses may be found either with exaggerated or absent knee and ankle jerks.

Occasionally apoplectiform attacks may occur with hemiplegia. This is often associated with high fever, and is characterised as a rule by a much more rapid improvement in the physical signs than is seen in cerebral hæmorrhage or thrombosis.

In the later stages there is wholesale deterioration, both mental and physical, with loss of sphincter control, and the patient dies as a rule from cystitis, pneumonia or other intercurrent infection.

Syphilitic encephalitis (Juvenile G.P. 1) is found, though rarely, in children the subjects of congenital syphilis, either manifesting itself from the first in

mental deficiency or giving rise to progressive deterioration at or after puberty. In these cases optic atrophy is common.

The Wassermann reaction in the blood is positive in 95 per cent. and in the spinal fluid in 100 per cent. of all cases. The pressure in the spinal fluid is usually raised—in the neighbourhood of 200 m.m. H_2O, there is an increase of cells which are mostly mononuclear but with an occasional polymorph or plasma cell, and the protein is increased up to 0·1 per cent. The colloidal reaction is constantly of the paretic type, precipitation being complete in the first three or four tubes of the series.

Diagnosis. The mental condition in *cerebral arteriosclerosis* may simulate that of dementia paralytica, but in the former disease the memory defect is more usually confined to recent events, and is recognised by the patient. *Alcoholism* may be mistaken for general paralysis, the tremor of the lips, tongue, and hands largely contributing to this; commencing *peripheral neuritis* might further complicate the case. But the close association of the symptoms with continued drinking, the absence of inequality of the pupils, and the improvement on prolonged abstinence, would point to alcoholism. Mental failure with definite cerebral lesions such as *tumours*, or the dementia resulting from bilateral vascular lesions (*pseudo-bulbar palsy*), may give rise to difficulties. Certain cases also of *disseminated sclerosis* with early cerebral involvement may require careful differentiation.

The positive signs of greatest value are the pupillary changes and slurring speech. A history of syphilitic infection is, of course, of the greatest importance.

The diagnosis can as a rule be made with certainty by examination of the blood and spinal fluid.

Prognosis. The course of the untreated disease is as a rule progressive to a fatal termination within five years of the time when clinical diagnosis is possible. There may, however, be remissions, and in a few cases spontaneous arrest has been reported. It is therefore difficult to gauge the effects of treatment.

Treatment. Malarial infection is now generally accepted as the best treatment for this disease. This is generally carried out by withdrawal of 5 c.c. of blood from the vein of a person with active malaria into a syringe containing a few drops of 5 per cent. sodium citrate. This is injected subcutaneously into the patient. The benign tertian parasite is that generally used and the incubation period varies from a few days to four weeks. The patient is allowed to have twelve rigors, and the infection is then cut short by the administration of quinine sulphate gr. 15 a day for three days, and gr. 10 daily on the succeeding eleven days. This is followed, as a rule, by a course of injections of novarsenobillon. The results claimed from this treatment are a high percentage of remissions—30 per cent. of the cases treated—which may last for a number of years and enable the patient in some instances to return to his work, and in other cases arrest of the disease and prolongation of life. Against this must be set a mortality rate of 15 per cent. from the treatment.

From the broader standpoint of the patient's friends and relations and the general community early diagnosis is most important, that all may be warned, and the patient if necessary be committed to a proper institution before he bring ruin upon his own fortunes and reputation, and endanger the welfare of others.

Huntington's Chorea. This is a rare disease *sui generis* to be sharply distinguished from the form of chorea already described, though in some ways it resembles it. It is a hereditary affection of middle life, of progressive nature, leading to dementia.

Ætiology. Heredity plays the most important part in the disease. It is transmitted from one generation to another, though occasionally the members of one generation may be spared. Men and women are equally affected, and the disease usually begins between the ages of thirty and forty. As the result of a genealogical research conducted in the United States of America 900 cases of

the disease were traced back to three brothers who landed in America from England early in the seventeenth century.

Pathology. In certain cases carefully examined chronic diffuse or disseminated inflammatory changes have been found in the brain and meninges.

Symptoms. The cardinal symptom is motor restlessness of a type similar to that seen in the chorea of children. There is a constant and rapid succession of purposeless inco-ordinated movements of all kinds, affecting all parts of the body. These movements show a tendency to affect the proximal groups of the limb musculature to a greater extent than occurs in the chorea of children. The limbs are consequently thrown about with considerable force, and the gait is grossly affected. The movements may be temporarily inhibited by voluntary effort.

Mental changes are constantly associated with the disease, at first in the form of irritability and restlessness, sometimes leading to suicidal depression, and finally terminating in progressive dementia of organic type, so that these patients, as a rule, end their lives in mental institutions.

The **Prognosis** is hopeless, the duration of life being from ten to thirty years.

The **Treatment** is symptomatic only.

There remain to be described certain diseases in which the signs and symptoms point to disturbances of function in the nervous system, for which, however, no structural basis can be found *post-mortem* either with the naked eye or by our present methods of microscopical examination.

EPILEPSY

(Idiopathic Epilepsy, Genuine Epilepsy)

Epilepsy has already been spoken of as a *symptom* of certain diseases of the brain, particularly those which affect the cortex (*e.g.* cerebral tumour, encephalitis, syphilis of the brain), and also of some toxic states of which uræmia is the chief example. The attacks provoked by such causes differ in no way from those presently to be described. Epilepsy in all cases probably depends upon disordered function of the brain, whether this is due to congenital defect, to local disease or injury, or to the effect of circulating toxins with a selective incidence. But in the very large majority of cases we are unable by present methods to discover any such cause. The attacks continue indefinitely without the appearance of any further signs of disease, and if an autopsy be obtained microscopic examination reveals no abnormality of the brain. It is this group of cases which, in our present ignorance of their pathology, we are obliged to group together under the symptomatic title of epilepsy.

Epilepsy, therefore, may be defined as a disease in which there are attacks of sudden loss or impairment of consciousness, with or without convulsions, or occasionally of convulsions without disturbance of consciousness, independent as far as our present knowledge goes of any demonstrable lesion of the brain, or state of toxæmia.

Ætiology. The disease is rather more common in females than in males. In about one-third of all cases there is a history of epilepsy in the family. Three-quarters of the cases begin under the age of twenty. The age of onset in the remainder is evenly spread over the remaining decades. Thus idiopathic epilepsy being on the whole a common disorder it is by no means rare to meet with cases beginning in adult life or even in old age.

In a small percentage of cases the seizures appear to be directly related to previous injury to the head with cerebral contusion (*see* p. 712). The interval between the injury and the first attack may cover several years. The clearest proofs of such relationship are cases in which the attacks commence with symptoms directly referable to the site of the injury, as in the case of a gunshot wound over the left motor cortex, and subsequent fits beginning with convulsive movements in the right side of the body. Even in these cases, however, the hereditary influence is sometimes apparent. Occasional causes for the attacks are sometimes

to be found. Chief among these are mental fatigue, excitement, or anxiety. Lack of sleep, physical fatigue, and fasting may also precipitate attacks. In some cases there is a definite relation to menstruation—the attacks occurring as a rule at the onset of the period. Some cases may possibly be allergic in origin.

Pathology. By the definition given above all cases are excluded in which a pathological cause for the epileptic attacks can be found. We are limited, therefore, to speculation. Arguing from the known causes to the unknown, we have reason to believe that epilepsy depends either (1) upon defective function of the cerebral cortex, congenital or acquired, or (2) upon the presence in the body of poisons with a selective action upon the cortical nerve cells.

Symptoms. The essential feature in most cases of epilepsy is a disturbance of consciousness, which usually, but not always, amounts to complete loss. With this in the majority of attacks there are associated convulsive movements.

It is convenient to distinguish between " major " and " minor " forms, according to the severity of the convulsive movements, but there is no absolute line of distinction.

In *Major Epilepsy* or "*Grand Mal*" there are usually to be discerned several stages: (1) aura; (2) unconsciousness and tonic contraction; (3) clonic convulsion; (4) recovery. The *aura* (or breath, from the sensation of air passing up the limb to the head, which is one form of this symptom) is any sensation or motion experienced by the patient while he is yet conscious, mostly of very short duration, and terminating abruptly in loss of consciousness and convulsion.

1. The aura is absent in about one-half of the cases. In the others it may assume a variety of forms, of which the following may be mentioned as of common occurrence: tingling and numbness in the arm, leg, face, or tongue; twitchings or spasms in the same parts; loss of vision, or visual hallucinations, such as flashes of light, or colours (generally red or blue) or definite objects or enlargement of surrounding objects (*megalopsia*); hallucinations of sound, noises, etc.; unpleasant odours or tastes; sensation of choking, nausea, vertigo, epigastric pain; flushes of heat, coldness, perspiration, palpitation of the heart; an indefinite sense of fear or anxiety; a *dreamy state*, or sense of unreality, or the feeling that what is happening has occurred before; running or jumping, or other co-ordinated movement. Auræ of sensation and motion are mostly unilateral, but may be bilateral; the arm is more often affected than the leg, and facial auræ mostly consist of spasm. Sometimes a vague sense of fear may last some time before the occurrence of the actual fit; but, as a rule, the aura is of momentary duration.

2. The fit itself commences with sudden unconsciousness; if standing or walking, the patient often falls suddenly forwards, or seems to be thrown violently to the ground, sometimes with an involuntary cry, shriek, or low tremulous groan—the epileptic cry. He is then found to be in a state of tonic convulsion, the back rigid and slightly arched, the legs extended, and the head drawn backwards or rotated to one side. The face is often pale at first; the pulse is quick, but sometimes it cannot be felt, and this has been attributed to compression of the artery by muscular contraction; the pulse has also been observed to cease at the moment of unconsciousness. The general tonic contraction fixes the chest, and respiration is stopped, so that the face becomes more and more dusky, and eventually is quite cyanosed. The tonic stage lasts from three to thirty or forty seconds, and then passes into the stage of clonic convulsions.

3. Twitchings begin in the face, the eyelids, and the side of the neck, and quickly extend to all the muscles of the body and limbs. There is a rapid succession of to-and-fro movements, of alternate flexion and extension in the limbs, of opening and shutting of the eyelids and of the jaws, lateral deviation of the eyeballs, and perhaps of the head; the tongue is pushed forward, and may be caught between the teeth; saliva is freely secreted, frothed in the mouth, and escapes from the lips mixed with blood from the bitten tongue. The face becomes

livid, or almost black, and the lips and features are swollen. Urine, fæces, and semen may escape during this stage, and the violent contraction of the muscles may even cause dislocation of the shoulder. The patient is, of course, quite insensible ; the conjunctivæ do not respond to a touch, and the pupils are dilated or oscillate.

4. The clonic stage lasts a few minutes, rarely more than five or six, and then the convulsions gradually subside—they become less frequent, and are interrupted by pauses of some seconds ; the breathing becomes easier, the frothing at the mouth ceases, and the face gradually assumes a more normal colour. Finally, the patient remains simply comatose, and the coma passes into natural sleep, or consciousness is recovered rather suddenly soon after the cessation of the convulsions. When consciousness is finally regained the patient is as a rule dazed and complains of headache.

The reflexes are mostly absent for a short time after the attack, and then for a time the deep reflexes may be increased. The plantar reflex after a temporary absence is at first extensor, then again normally flexor. The urine may contain a trace of albumin or sugar ; petechiæ may be seen under the skin from rupture of blood vessels during the stage of venous congestion ; sometimes there are vomiting, or serious mental disturbances, such as delirium, which is often of a maniacal kind.

The mechanical injuries from which the epileptic suffers will, of course, remain after the fit, and may give valuable indications in cases where the fit has not been seen—for instance, in nocturnal epilepsy. These are the bitten tongue, petechiæ on the skin, a dislocated shoulder, and, in other cases, various cuts, wounds, or bruises, from the falling of the patient upon the ground or against unyielding objects.

Minor Epilepsy or "*Petit Mal.*" This consists, in a large number of instances, of little more than a sudden unconsciousness ; in the midst of talking, perhaps, the eyes become fixed, the pupils dilated, the speech incoherent, and the patient is obviously unconscious of what is going on around him ; he may, if at meals, put his fingers in his plate or his cup, or commit some other irregularity that he would not do if conscious. The condition lasts a few seconds, and then he becomes conscious, and goes on with what he was doing, or perhaps recognises that there has been a blank, or feels giddy, or has headache, and is glad to lie down for some time. Sometimes giddiness is the most marked feature of the attack, and in other cases a sensation in one or other part of the body, or a spasmodic movement, which may be quickly followed by temporary unconsciousness, though the former will seem to the patient the chief feature of the attack. These have a close resemblance to the auræ of the major attacks, and include sensations in the epigastrium, hands, head, nose, eyeballs and cardiac region ; olfactory and visual sensations ; jerks in the limbs, head, or trunk ; sudden tremor, screaming, or dyspnœa ; mental conditions, such as a sudden state of fear, etc.

In many instances there is no complete loss of consciousness. The patient is aware of his surroundings and often of what is being said by those around him, but everything for the moment appears distant, he fails to comprehend the full significance of events and is incapable of formulating his thoughts clearly.

Jacksonian or Focal Epilepsy. Whether in a major or minor attack the symptoms may be of a generalised or focal character. An epileptic attack of focal type is frequently called Jacksonian after Hughlings Jackson, whose clinical observations upon epilepsy provide the foundation of our knowledge of this aspect of the subject. Focal attacks are those in which the symptoms may be attributed to a disturbance arising in some particular area of the cortex. Thus they may be motor or sensory, and if the latter, of a general or special type. In the motor attacks there is tonic followed by clonic spasm in the muscles of one

limb or part of a limb; this tends to spread so as to involve the whole of one side of the body. The convulsive movements may then become generalised, and if so consciousness is lost. Or they may remain localised, in which case there is sometimes no loss of consciousness. In similar fashion a disturbance of bodily sensation, smell or taste, hearing or vision may usher in a generalised attack or may itself constitute the only evidence of the epileptic episode. It is important to recognise that the nature of such attacks indicates only the situation of their origin and provides no clue to their pathology. A focal or Jacksonian attack is not necessarily of organic origin. Indeed, the commonest cause of focal attacks is idiopathic epilepsy. It may be said, however, that attacks which remain localised, that is, without going on to a generalised convulsion, and particularly focal attacks in which there is no loss of consciousness, are generally due to organic disease of the brain.

Pyknolepsy. This condition, which is considered by some clinicians to deserve a separate title, is by others regarded as a form of *petit mal.* In so far as the attack itself is concerned there is certainly no distinction. The features which distinguish the malady from other forms of epilepsy are the onset (usually abrupt) in childhood, the occurrence from the first of repeated attacks—six to fifty a day—of uniform and mild degree, absence of any mental deterioration, failure to respond to the drugs usually effective in epilepsy, and cessation of the attacks after puberty. Thus the complete diagnosis is only permissible after the attacks have ceased, but the forecast of a happy issue may sometimes be made upon the basis of the other points enumerated.

Post-epileptic Conditions. The attack is generally followed by a period of drowsiness and often by severe headache. A serious psychical disturbance is a not uncommon sequel to an epileptic fit, and follows the minor attack even more frequently than the major. It may take the form of stupor lasting some days. In another case various *automatic* actions occur of which the patient is then and afterwards entirely unconscious. Perhaps the commonest of these is the act of undressing, which in a public place may lead to a charge of indecent exposure, or the patient may put in his pocket any object which happens to be near, irrespective of its ownership. Occasionally he may be violent and aggressive, and while still in the automatic state cause bodily injury to others. These cases have great medico-legal importance, since the occurrence of epileptic fits may be quite unknown, and the criminal behaviour may be attributed to wilful and conscious action. Sometimes these attacks are maniacal in their character (*epileptic mania*), and the automatic actions are accompanied with much mental disturbance, such as terror, violent passion, delusions, and hallucinations.

Equally important, on account of the difficulty in diagnosis which they occasion, are minor psychical sequelæ. The patient recovering from an attack of true epilepsy frequently behaves in a childish, emotional manner, weeping and laughing alternately, and will sometimes pass into a hysterical "fit."

Course of the Disease. The frequency of epileptic attacks varies considerably in different cases, and at different periods in the same case. Thus there is generally an interval of one or more months between the first and second attacks, but with the progress of the disease the intervals often become shorter, and the fits may be as frequent as two or three in a week, or even several in a day. In some cases two or three fits occur in quick succession, or at short intervals, and the patient is then spared for a long time. A severe fit is much more likely than a slight one to be followed by a long interval. Probably alcoholic indulgence, injudicious feeding, and mental or physical over-exertion, increase the frequency of the fits.

Status Epilepticus. In rare instances the patient has a series of fits, extending over some hours, or one or two days, and never recovers consciousness in the intervals between them. The heart beats violently and rapidly, the respirations are quick, twitchings occur in the intervals of the convulsions, the

temperature often rises to 105° or 107°, and the patient may die collapsed, or may become delirious.

Health between the Attacks. This depends a good deal upon the frequency of the fits. Where these are not numerous, the individual may enjoy excellent health. Many epileptics are strong, hearty, and vigorous, never ailing at all except at the time of the attack. When, however, the fits are very frequent, or the disease has lasted a long time, the mind generally suffers, the patient becomes dull and irritable, the memory is deficient, and intellectual processes are slower, until eventually a condition of *dementia* is reached.

Death from epilepsy is by no means common, and, except in the case of the rare status epilepticus above described, it is mostly the result of some injury to which the patient is exposed during the fit. Thus during a fit he may be thrown from a height, or fall into water and be drowned, or be choked by food, or he may be smothered in bed by his face being buried in the pillow, or he may die later from injuries received by a fall into the fire, or from a carriage or bicycle.

Diagnosis. Epilepsy is with no great difficulty recognised when actually seen, but one is often called upon to prescribe for fits which only occur at times when the physician cannot witness them; and it is not always easy to come to a right conclusion from the descriptions of friends. The major attacks have to be distinguished from attacks of hysteria, and from simulated fits, minor epilepsy from attacks of syncope or vertigo. Hysterical attacks seldom, if ever, occur when the patient is alone or unlikely to attract an audience. The onset is seldom so dramatically sudden as in epilepsy, and the attack is usually related to an emotional stimulus. The movements in the hysterical fit never consist of simple tonic or clonic jerkings, but are of a more purposive character. Thus the patient will clutch at those around her, dash her head against the wall or floor, clench and unclench the hands, or bite at those who seek to restrain her. The convulsive movements of epilepsy are over in a few minutes. The motor phenomena of hysteria last as a rule much longer. The hysterical patient frequently talks during the attack; the epileptic never. The hysterical patient never falls so as to hurt herself severely, nor does she bite her tongue or pass water in the attack. In the hysterical fit the eyelids are often tightly closed, and attempts at opening them are resisted. The occurrence after the fit of mental disturbances and the exaggeration of deep reflexes with loss of abdominal reflex are in favour of epilepsy, while an extensor plantar response obtained after the attack is conclusive evidence of its epileptic nature.

It must not be forgotten that an attack of epilepsy may be immediately followed by one of hysteria, and that the same patient may at different times exhibit epileptic and hysterical fits.

The *malingerer*, who attempts to excite sympathy as a sufferer from epilepsy, can, with a little care, generally be detected. He is careful to fall so as not to hurt himself, whereas the epileptic is thrown down suddenly, and if in the street will probably strike his head or face, or will fall in the road, not making any effort to save himself. The malingerer is red in the face rather than pale or livid; his skin perspires from the exertion; his pupils are not dilated and are sensible to light. The fact that he has not lost consciousness may be tested in various ways: by touching the conjunctiva, when the eyelids will close, though he will probably resist attempts to raise the upper eyelid; by applying snuff to the nostrils; by producing some very painful impression, as by forcing one's thumb-nail under that of the malingerer.

Minor epilepsy, or *petit mal*, is distinguished from *cardiac syncope*, or simple fainting, by its occurrence under circumstances not conducive to fainting, by its suddenness, and by its rapid recovery, followed by mental confusion rather than physical prostration. The occurrence of spasm or of any warning sensation other than the feeling of faintness is in favour of epilepsy. Syncope comes on more slowly, and is recognised as a gradually increasing faintness by the patient. Still

this may happen as a warning sensation of *petit mal*. To distinguish other forms of *giddiness* from the vertiginous form of minor epilepsy, one must remember that ordinary vertigo is not accompanied by loss of consciousness, and that in the aural form, or Menière's syndrome, a history of tinnitus and deafness may be obtained.

When it has become certain that, in any case, the attacks are really epileptic, it has yet to be determined that they are not due to tumour of the brain or cerebral syphilis, the uræmia of Bright's disease, or other organic disease, before one can pronounce the disease to be epilepsy. In a great number of cases of idiopathic epilepsy, the long history of recurring convulsions with no associated symptoms will serve to distinguish it, whereas in *cerebal tumour* there will probably be other indications, such as headache, vomiting, papillœdema, or local paralysis. Nevertheless epileptic attacks may for many months be the only symptom of a cerebral growth. Attacks of epilepsy frequently usher in *general paralysis of the insane.* and in the absence of all other signs may be the first warning of the disease. For this reason epilepsy commencing in a man of middle age must always be suspect. The pupils and mental state must be carefully examined and the Wassermann reaction obtained if necessary in the spinal fluid as well as in the blood. In *Bright's disease* the convulsions are epileptic, but the patients, as a rule, show good evidence of their state of health in albuminuria, high tension of pulse, hypertrophy of heart, raised blood urea preceding uræmia ; the fits are often ushered in by drowsiness and muscular twitchings, are of much longer duration, and recur frequently in the same day with intervals of drowsiness or semi-coma.

Epileptic attacks may also occur as a sequel of *cerebral contusion* often after a latent interval of two or more years. The attacks may be focal or generalised. As a rule the history will be that of a major contusion (*see* p. 712).

These are perhaps the commonest causes in the way of organic disease which may cause epileptic attacks, but they may occur in the course of any malady involving structural damage to the brain, such as encephalitis, cerebral arteriosclerosis, Schilder's disease, cerebral diplegia, the infantile and juvenile forms of Tay-Sach's disease, or in certain toxæmias other than Bright's disease such as chronic alcoholism, insulin hypoglycæmia, and alkalosis.

Prognosis. Nothing is more difficult than to forecast the future of an individual who has had an epileptic attack for which there is no apparent cause. In the large majority of cases, and especially if the trouble begins in childhood, the attacks continue at irregular intervals throughout life. The intervals, however, in many cases are so long that the patient is not seriously handicapped in the pursuit of a normal existence. In some cases the attacks may cease, never to return, but the percentage in which this may occur as commonly given in statistics is almost certainly overrated. It is not uncommon to find an epileptic after fifteen or twenty 'years' complete freedom having further attacks. The *liability*, once present, probably always persists, and this must be taken into account in making plans for the lives of these patients. There is a tendency for attacks which are either diurnal or nocturnal to remain so. Mental deterioration occurs in a considerable proportion of cases, especially when the attacks are frequent and severe. There is, however, no constant rule in this. One may occasionally see a patient with relatively few fits and progressive dementia, and, on the other hand, one with many more attacks whose mental faculties are preserved. It must not be forgotten that epileptic attacks may be the first, and for a time the only, evidence of cerebral tumour. It is wise, therefore, in the early stages of the malady, especially in adults, to give a guarded prognosis.

Treatment. *General.* It should be recognised that the liability to attacks is in most cases likely to be lifelong, and is in itself a severe handicap and source of annoyance. The epileptic should therefore be subjected to as few restrictions as may be essential to his well-being and safety. Fortunately, the loss of consciousness, which is usually a feature of the major attack, renders the patient unaware

of the symptoms which are most distressing to his friends. The story of these, as obtained from a witness, should never be taken in the patient's presence. A regular life with adequate sleep, recreation and occupation is to be advised. Late nights and the excessive use of alcohol and tobacco should be forbidden. Dietetic restrictions are probably unnecessary, with the exception of the ketogenic diet to be mentioned later as an occasional resource. No epileptic should drive a motor car under any circumstances, or ride a bicycle on crowded roads. Nor should he bathe unless accompanied by someone who is aware of his liability. Apart from these restrictions he is best allowed to live an ordinary existence, and may be encouraged with the assurance that many persons who carry this liability lead happy and successful lives. That such a policy carries its risks of accident there is no doubt, but it may fairly be pointed out to the anxious parent that the alternative of complete safeguarding would render life unendurable. Advice is often sought on the question of marriage. This has no effect upon the individual. Women are, on the whole, likely to have fewer attacks during pregnancy. There is, however, a risk that the liability may be transmitted to the offspring. This, so far as the first generation is concerned, is slight, probably not more than one in twenty. But it is to be remembered that in about 30 per cent. of all epileptics a history of the complaint is obtainable somewhere in the family tree. In the case of a male the attacks may limit his earning capacity.

Medicinal. Many drugs have been used for the treatment of epilepsy, among which bromide still holds first place. The potassium salt is most generally used. It should be given at first in small doses, 10 grains night and morning for an adult, and is usually prescribed with 1 or 2 minims of liquor arsenicalis, which is said to diminish the liability to skin eruptions. If necessary, the dose may be increased up to 15 or 20 grains thrice daily. Many patients tolerate such doses without ill-effect. Others will complain of dulness or depression. The individual idiosyncrasy to the drug must be studied and the dose graduated accordingly.

Luminal is sometimes effective where bromide fails, or may be given together with bromide. The dose is up to 5 grains in the twenty-fours hours, but on this maximum most patients are drowsy and some will show other toxic symptoms, such as giddiness or an erythematous rash. If given alone, ½ grain thrice daily in tablet form is a suitable dose, to be increased if necessary. Luminal sodium being water soluble may conveniently be prescribed together with bromide, a suitable prescription for an adult being :

Potassium bromide . .	10 grains.
Luminal sodium . .	½ grain.
Liquor arsenicalis . .	℥j
Chloroform water to the ounce.	

Twice or thrice daily.

Prominal as a substitute for luminal is said to be less apt to cause unpleasant drowsiness. 1½ to 3 grains may be given twice or thrice daily.

Of other drugs, the tincture of belladonna, 10 to 15 minims, may be given thrice daily, and is sometimes effective when bromide and luminal fail. Sodium biborate in doses of 10 to 15 grains thrice daily is also sometimes of value, and having no depressing effect may be used to replace or reinforce bromide. Gelineau's Dragées, which contain picrotoxin together with bromide, occasionally seem to succeed when other remedies have failed. To be given a fair trial, any one of these drugs should be administered continuously over a period of weeks or months.

During the Attack. In cases where there is a definite aura the attack can sometimes be arrested. If the aura consists of a sensation in the hand, which gradually proceeds up the arm, the fit may possibly be checked by vigorously rubbing the part, or by tightly constricting the arm above the seat of the sensation, thus preventing, as it were, its progress to the centres. Where this is successful the patient may wear a cord looped round the upper arm, with one end conducted down his sleeve to the wrist, so that by pulling upon this end he can at once

constrict the arm. Other patients may be able to ward off fits by turning the attention forcibly to some mental or physical effort as soon as the aura is perceived, and attempts of this kind should be diligently encouraged. Occasionally the inhalation of nitrite of amyl will prevent the further development of an attack. When the fit has really begun little can be done in the way of treatment, but the patient can be protected from some of the results of the convulsions. As a rule he must lie where he falls, unless this is in itself a position of danger (a pool of water or the fire), but he can be prevented from injuring himself against surrounding objects; his collar, necktie, cuffs, and other tight bands should be at once loosened; and a piece of cork, gutta-percha, or firewood should be held between the teeth to prevent the tongue being bitten. False teeth worn by an epileptic should always be removed at night, as they may be loosened in a fit and become impacted in the pharynx.

For the *status epilepticus* prompt treatment is necessary, as the patient may die from exhaustion. Sometimes the interval between attacks is such that medicine may be given by the mouth. Chloral hydrate, 30 grains, and potassium bromide, 60 grains, may be given in this way, four-hourly, until the attacks cease. If the patient is unable to take drugs by the mouth paraldehyde, in a dose of 4 to 6 drachms in 6 ounces of water, may be given by the rectum. The proof of absorption may be found in the characteristic odour in the patient's breath. If, as not infrequently happens, the attacks are so frequent as to prevent rectal absorption hypodermics are the only resource. Luminal may now be obtained in ampoules, each containing 1 c.c. of a 20 per cent. solution for subcutaneous or intramuscular injection. One of these may be administered every two or three hours if necessary. As an alternative, hyoscine hydrobromide may be given hypodermically in a dose of $\frac{1}{100}$ grain, repeated two-hourly, but this has the disadvantage of being a respiratory depressant. Post-epileptic confusion may need to be treated with large doses of sedatives, of which paraldehyde, 2 to 4 drachms by the mouth, is the best, or failing this, any of the remedies advised for *status epilepticus*.

Dietetic. Hippocrates gives a list of the various articles of diet forbidden to epileptics by "the conjurors, purificators, mountebanks and charlatans" of his day. Successors have not been wanting. There is no evidence to show that the epileptic is better on one diet than another, with the exception of the ketogenic diet to be described. This is based upon the observation that in patients who are having frequent attacks, ten to twelve days' complete starvation will cause a considerable reduction, and often a cessation, of the seizures. The effect appears to be due to the ketosis resulting from starvation, and a similar effect may be obtained by giving a diet poor in carbohydrate and relatively rich in fat. The basal requirement of protein is calculated by allowing 1 gram of protein per kilogram of body weight. Carbohydrate is cut down to a minimum and the calorie value made up with fat. The results obtained by this method have on the whole been disappointing. Success is more likely to be obtained with children than with adults, and the treatment may be of especial value in a child presenting frequent minor attacks with mental deterioration when other remedies fail. (*See* diet tables on pp. 474 to 478.)

Infantile Convulsions. These do not differ clinically from the epileptic attacks of other persons with the exception that the disturbance of consciousness which is the main feature of minor attacks is less noticeable at this age.

Ætiology. As in adults the liability to attacks may be due to organic disease or may be of the idiopathic variety. The commonest organic causes of a limited number of attacks are meningitis, particularly tuberculous meningitis and acute encephalitis, but when the series of attacks is prolonged it is necessary to think of injury to the brain at birth, and congenital failure of cortical development. In such cases the liability may disclose itself during the first few days or weeks of life or its appearance may be delayed.

The idiopathic variety frequently discloses itself in infancy, at which age the cortical function appears to be least stable. One or two attacks may occur, perhaps precipitated by teething, prolonged screaming, an acute infection, dyspepsia, or diarrhœa, and for the rest of his lifetime the individual may be free, but in a considerable proportion of cases fits occur later in life, the commonest age of recurrence being at or before puberty. Thus in the personal history of many adult epileptics whose more serious attacks date from childhood or adolescence a history of one or more infantile convulsions is to be obtained, and in the family history of epileptics the story is often obtained of one or more members who had a convulsion or convulsions in infancy without later recurrence.

Treatment. In the past undue importance has been attached to the precipitating causes of infantile attacks. It is probably true of the infant as of the adult that the precipitating factor cannot cause an attack unless the epileptic liability is already present, and that the epileptic liability in infant and adult is of the same nature and requires similar treatment. The occurrence even of a single attack therefore indicates the need for an appropriate dose of bromide, such as 6 grains daily, or whatever is the maximal dose which is quite harmless in its effects, which should be continued regularly for a period of six to twelve months. The duration of this treatment will be guided by the circumstances in which the attack occurred. The attack which occurs without any adequate precipitating cause signifies the greater epileptic liability. In the case of a child who has had a convulsion or convulsions in infancy the possibility of recurrence later should be watched for so that if this occurs treatment may be begun at once. Epilepsy, as Gowers insisted, is a self-perpetuating disease, and the opportunity for successful treatment is greatest after the first attack. When a fit occurs it is usual to place the child at once in a warm bath. If the bowels have not been recently opened, or if there is reason to suppose the ingesta are causing irritation, a grain of calomel may be placed on the tongue. If the fits are very violent and continuous, chloroform may be cautiously administered; 5 grains of potassium bromide may be given, combined with 3 to 5 grains of chloral.

MIGRAINE

(Megrim, Sick Headache, Hemicrania)

This complaint consists of recurring attacks of headache, sometimes preceded by certain abnormal sensations, and often associated with nausea and sickness.

Ætiology. The prime cause appears to be a constitutional defect. In a large proportion of cases there is a family history of the disease. The headaches commonly begin about the age of puberty, but inquiry will often elicit a previous history of " bilious attacks " in childhood, and it appears that migraine and the so-called cyclical vomiting of children are closely related. The complaint more rarely develops in later years. Having once appeared, it usually persists throughout adult life, with a tendency for the attacks to diminish in frequency or disappear after the age of fifty. It is rather more frequent in women than in men, and the attacks are sometimes closely related to menstruation. As occasional causes of the attacks many different agencies have been held responsible. Mental strain appears the commonest, and this probably explains the relative frequency of migraine among intellectual workers and persons of an excitable disposition. In a certain number of cases eye-strain, especially that resulting from uncorrected errors of refraction or of muscle balance, may be an important factor. Constipation or dietetic indiscretions may initiate paroxysms. Allergy may perhaps be a cause in some cases. But, as in the case of epilepsy, we must confess that the majority of the attacks occur without apparent cause.

Pathology. No anatomical changes have been found to account for the disease, either in the brain or elsewhere. The nature of the attacks, especially the association of headache, vomiting, slowing of the pulse rate and visual dis-

explanation of these cases is forthcoming. The fact, however, remains that attacks of this nature may continue for twenty to thirty years without the development of any signs of serious organic disease.

Diagnosis. The periodicity of the attacks with intervals of perfect freedom, the age of onset, and the association with nausea are as a rule sufficient for a diagnosis. But in every case other causes must be excluded. The recurrent headaches of cerebral tumour are sooner or later associated with papillœdema or signs of local damage to the brain. Other causes of paroxysmal headache that must be considered are those due to infection of the nasal sinuses, syphilitic meningitis, cerebral arteriosclerosis, and toxic causes such as uræmia.

The aura may be confused with that of epilepsy. But in the latter disease the aura is of momentary duration, while in migraine it occupies about twenty minutes. Nor in migraine is there any disturbance of consciousness. Some patients may be troubled more by the nausea or vomiting than by the headache, and seek relief for these symptoms only.

Prognosis. Under treatment much improvement may be obtained both in the frequency and in the severity of the attacks, though the disease commonly continues for years. It is, however, not dangerous to life, and there is no evidence that sufferers from migraine are more liable than others to hæmorrhage, thrombosis, and other diseases of the brain. The disease often becomes less frequent or disappears altogether after the age of fifty, especially in women after the climacteric.

Treatment. *In the interval.* The patient should be placed under the most favourable hygienic conditions, including a carefully regulated diet, the avoidance of constipation, exercise without exhaustion, pure and bracing air, and exemption from excessive brain study or mental worry. Hurst maintains that many sufferers may be cured of their attacks by the correction with glasses of errors of ocular refraction or muscle balance.

Of drugs the most valuable is luminal. This may be given in tablet form or in a mixture as luminal sodium. Half a grain thrice daily is usually adequate and insufficient to cause drowsiness. It must be taken regularly for many months, and as a rule diminishes both the frequency and severity of the attacks. In some cases Gowers' mixture, containing liq. trinitrini ℥i, liq. strychninæ ℥v, tr. gelsemii ℥x, sodium bromide gr. x, dilute hydrochloric acid ℥x, taken regularly as a preventive, has a good effect.

During the attack. The sufferer usually learns from experience that the less severe attacks can be cut short. Ten or fifteen grains of aspirin and an hour's rest on a sofa in a quiet and darkened room often suffice, especially if during this period sleep can be procured. If the symptoms appear at the end of an exhausting day a good meal and a glass of wine will sometimes clear the air, provided the nausea has not set in. In the more severe attacks there is total cessation of gastric peristalsis (as shown by X-rays), and nothing can be taken by mouth except sips of water. Rest in a darkened room is then the only means of relief. If vomiting is severe and prolonged, rectal infusions of 6 per cent. glucose should be given; they help to cut short the attack and lessen the subsequent exhaustion. Cold applications to the head are usually welcomed. If the pain is unusually severe, morphia should be given hypodermically, and the dose may need to be repeated. If this should be necessary, it must be administered either by the medical attendant or by a trained nurse. The morphia should never be entrusted to the patient or her friends.

MYOCLONUS

(*Myoclonia*)

Under this title are grouped a large number of conditions, of which the essential feature is short, quick contraction of muscles, not forming part of epilepsy,

hysteria, chorea, athetosis, etc. Myoclonic movements occurring in encephalitis lethargica have already been referred to (*see* p. 706).

PARAMYOCLONUS MULTIPLEX

Friedreich described under this name the case of a man who had sudden lightning-like contractions of the large muscles of the arms, forearms, and thighs. The contractions ceased when he walked, and were worse when he was quiet in bed; if one arm was used the contractions ceased in it, but continued in the other. The contractions, though violent, produced no movement of the limb as a whole. The knee jerks were increased; the skin sensibility, muscle sense, and vasomotor and secretory phenomena were normal. The condition disappeared under treatment with galvanism, but it relapsed and persisted till the man's death. Numerous other cases have been recorded of clonic muscular contractions which differ in many points from Friedreich's case. The essential seems to be the occurrence of spontaneous rapid contractions of isolated muscles or parts of muscles in different parts of the body, in some cases the limbs, in others the face and trunk, generally bilateral, but not of necessity equally, or at the same time, on the two sides; sometimes, but not generally, causing locomotive effect in the parts involved; occurring at the rate of 60 to 100 in the minute, but quite irregularly; varying in frequency and force on different days; and often increased when the patient is under observation, or exposed to external stimuli (sound, touch). The mechanical excitability of the muscles is increased; their electrical excitability is unchanged. Some cases have been associated with epilepsy (*myoclonus epilepsy*), others have shown close resemblances to hysteria, and it has occurred in two or more members of the same family; rarely these movements have been associated with definite disease of the central nervous system. The pathology is unknown. Galvanism to the spine, hydropathic treatment, arsenic and chloral have been used to combat it, and recoveries have occurred; but the prognosis is not good.

THE TICS

(*Habit Spasms*)

A tic has been defined as a co-ordinated, systematised, purposive act, reproducing in an involuntary manner the co-ordinated movements of every-day life (Meige).

The movements usually commence in childhood, between five and twelve years of age, affecting especially the facial muscles, and being frequently repeated at irregular intervals. Such movements are blinking the eyes, twitching of the angle of the nose or mouth, shrugging the shoulders, twitching the fingers, uttering noises or words, kicking out the legs, or other simple movements. They have probably been voluntary, in the first instance, for the purpose of relieving an irritation, or in response to some local sensation, and then have been repeated reflexly, or stimulated by a thought, and finally have become automatic—a bad habit, of which indeed the child may be almost unconscious. The movements may become less under observation, and in the same child one kind of movement may be cured, and after a time another will take its place. It is a question whether certain visceral disorders should not be considered as belonging to the tics, although they are more usually referred to as symptoms of hysteria, and will therefore be described under that heading. Such are certain types of functional vomiting and aerophagy—a condition in which the individual in attempts at retching is continually taking down gulps of air into his stomach.

Movements of a reflex nature arising, in the first place, from peripheral irritation are not perpetuated as tics in persons whose mental adjustment is normal. Thus in children the disorder is frequently associated with bed-wetting, night terrors, and other signs of a neurotic constitution, and the habit probably always

originates at a psychical level as an expression of faulty adjustment of the personality as a whole. In favour of this also is the fact, ascertainable from the patient in most cases, that the movement is preceded by an imperative desire to perform it, and that if this is inhibited great mental distress is occasioned.

The distinction usually has to be made from chorea, in which the movements are, as a rule, more widespread, and are purposeless and irregular.

In the causation two sets of factors have to be considered: on the one hand, neglected sources of peripheral irritation, such as a chronic conjunctivitis or a frayed collar, and difficulties of an emotional nature, such as unhappy domestic surroundings or imperfect adaptation to school life; these are the environmental factors, and, in the phraseology of the old parable, may be called the seed. On the other hand is the neurotic personality which furnishes the soil, and it is upon this latter that the prognosis largely depends. In some cases removal of all sources of irritation, a complete change of environment, and assistance in the solution of personal difficulties may effect a cure, especially in children. In adults and in cases of long standing the disease is likely to be permanent, taking the form in some cases of a mere eccentricity of behaviour. It may be a symptom of deeply rooted mental instability. In the treatment bromides are useful for their sedative effect, together with exercises in which the patient is taught to relax the affected muscles, and to use them for other movements. These exercises may be practised daily in front of a looking-glass, and should be continued as a routine for some time after the abnormal movements have ceased. In addition, attention should be paid to the underlying psychological factors, as already indicated.

SPASMODIC TORTICOLLIS

Besides the temporary affection known as stiff neck or rheumatic torticollis (*see* p. 555), there are two more lasting conditions known by the name of torticollis: *fixed torticollis*, or congenital wryneck, and *spasmodic torticollis*. The former is due to a permanent shortening of the sterno-mastoid muscle, which is attributed in some cases to injuries during birth, is observed first during childhood, if not in early infancy, and causes asymmetry in the bones of the face.

Spasmodic torticollis, or spasmodic wryneck, is a disorder of function characterised by tonic and clonic contractions of the muscles of the neck, whereby the head is forced into an abnormal position, and it is in many ways allied to the tics.

Ætiology. The disease is rarely seen before the age of thirty; it affects both sexes, but females more often than men. The cause cannot always be ascertained; neurotic inheritance, inflammation of the cervical glands or of the muscles themselves, exposure to cold, falls and injuries, and overstrain of the muscles of the shoulder, arm, or neck in particular occupations, have been recorded as antecedents. Cases have been reported in which the symptom has occurred as a sequel of encephalitis lethargica.

Pathology. Of this little is known. No pathological lesion has been found to account for it, but it presumably depends upon disturbed function of motor centres in the brain or brain-stem.

Symptoms. It begins gradually, being first felt as a mere discomfort in the neck; then distinct jerking movements of the affected muscles are felt, by which the head is rotated or displaced. If, for instance, the right sterno-mastoid is affected, the head is constantly being jerked in the direction of the action of this muscle, the chin is thrust forwards or upwards to the opposite side, and the occiput is drawn down towards the clavicle. The contractions are sudden, irregular, and frequent; for a few moments there is a remission, during which the patient slowly and cautiously tries to bring the head straight, when the

muscle again contracts, and the face is gradually forced round to the left. The movements are for a time checked by supporting the head, and they cease during sleep, but immediately the patient awakes the movements recommence, and continue with but little rest throughout the day; they are generally increased when attention is directed to them. The muscle most frequently affected is the sterno-mastoid, and next to that the upper part of the trapezius and the splenius capitis; the complexus and trachelo-mastoid, the deep rotators of the head, and the platysma myoides are also sometimes concerned. The position of the head is of course determined by the muscles which contract. The sterno-mastoid produces the results already described; the trapezius draws the head backwards and downwards towards its own side, with slight rotation of the face towards the opposite side, while the splenius draws the head downwards with slight rotation towards its own side. Two or more of these muscles may be affected at the same time, most often the sterno-mastoid with the upper part of the trapezius of the same side, or the splenius of the opposite side. An intermediate position of the head will of course be the result. Or corresponding muscles on the two sides may act together, drawing the head backwards during their contraction. In such cases there is generally an associated contraction of the frontal muscles which normally contract when one throws back the head to look upwards. Occasionally the disease itself spreads to the muscles of the face, or to those of the shoulder or arm, especially at the height of the paroxysm; and in rare cases the lumbar or spinal muscles may be affected so that the body is drawn down to one side by the frequent contractions. In slighter cases, or in early stages, there may be no pain, but in severer forms there is neuralgic pain in the contracting muscles. From their excessive action the muscles often hypertrophy; they at least retain their natural bulk. The electrical irritability is normal or increased.

Diagnosis. The constant movements distinguish this disease from congenital wryneck, with its early history and facial asymmetry; from the temporary disorder "stiff neck"; and from spasm of the muscles in caries of the cervical vertebræ.

The **Prognosis** is unfavourable; the spasms may subside after a few months, but far more often persist in a more or less severe form for the rest of life.

Treatment. The disease is most intractable, and numbers of drugs have been tried with but a small amount of success. Those which have been most useful are the bromides, luminal, zinc valerianate, belladonna, and hyoscine hydrobromide by subcutaneous injection. Opiates and chloroform inhalation check the spasm for a time, but it returns in a few hours unless the dose is repeated. In some cases exercises are of value as described in the treatment of tics, and especially education in the relaxation of the affected muscles.

Many operations have been devised for the treatment of the disease but without much success. In the early stages, if the sterno-mastoid alone is involved, section of the spinal accessory nerve may give relief, and occasionally this may be permanent, but as a rule the spasm appears in other muscles. Foerster, of Breslau, claims success from section of the upper three or four cervical nerve roots, both anterior and posterior, but the operation has so far not met with general acceptance. The disease seems to depend upon a disorder of the higher nerve centres whose tendency to impose spasm will usually find means to assert itself despite obstruction at the periphery.

The symptoms are invariably worse under the influence of mental fatigue and anxiety, and may therefore be improved by means of rest and psychotherapy.

WRITERS' CRAMP AND ALLIED NEUROSES

Those persons whose occupations necessitate complicated movements for long periods of time, such as clerks, pianists, violinists telegraph operators, cigar-

makers, and others, may be subject, when engaged at work, to spasmodic and irregular contraction of the muscles concerned, so that the movement is badly performed and ultimately cannot be effected at all. The exciting cause may be some depressing mental condition, mental anxiety, or business worry ; an injury, or local disease of the hand or fingers ; but more than all an excessive use of the hand in the occupation concerned.

The disease is most common in those who have a great deal of writing as their daily occupation, such as lawyers' clerks, secretaries, etc. It is hence called *writers' cramp* and *scriveners' palsy ; graphospasm* and *mogigraphia* have been used as technical terms. This form is naturally more frequent in men than in women, and occurs mostly between the ages of twenty and forty. Gowers pointed out that in the act of writing the pen may be moved across the paper in four different ways: (1) The little finger is fixed on the paper, and the fingers carrying the pen work upon the little finger as a pivot ; (2) the wrist is fixed and acts as the pivot ; (3) the pivot is at the centre of the forearm, resting perhaps on the edge of the table or desk ; (4) all the movements take place from the shoulder. In the first method the movements of the fingers are most complicated and strained, and in the last there may be no finger movements at all. He stated that writers' cramp scarcely ever affects those who employ the last two methods of writing.

Pathology. The cause of this affection is quite obscure. A probable explanation is that it is due to a defect in the centres associated for the act of writing by a morbid lowering of resistance in the commissural connections between the centres, so that there is a radiation of impulses, and so over-action of muscles not necessarily engaged in the act.

Symptoms. The affection generally comes on gradually ; it may be felt at first as some degree of aching or strain, which is relieved by ceasing to write. After a time the act of writing is accompanied by a spasmodic tonic contraction of the finger or thumb holding the pen ; the finger is pressed firmly on the pen, or it is flexed so as to move up the pen, or it slips off the pen so that the latter is grasped between the fore and middle fingers. The thumb may be similarly affected, or the fingers may be extended or lifted from the paper, or the pen may be driven into the paper, or the hand stops its movements entirely. The attempt to continue writing under these conditions produces a cramped, irregular, angular writing, with thick down-strokes ; and after a time the spasm becomes so pronounced as to render the act impossible. This is the *spasmodic* or *spastic* form of Benedikt, which is by far the most common ; but sometimes there is tremor of the fingers—*tremulous* form ; and a *paralytic* form with fatigue alone has been described, but is quite rare. The spastic form often leads, by the frequent contraction of the muscles, to pains in the hands and wrist, which may after a time become distinctly neuralgic in character ; and there is often some tingling or sense of numbness. The spasm may be limited entirely to the act of writing, and other movements, even of a delicate nature, can be performed without difficulty. Sometimes writers' cramp is associated in the same person with spasm on playing the piano or violin, and not infrequently in severe cases some other operation may be at the same time imperfectly performed.

The muscular power is well preserved. There is no wasting, sensory loss or disturbance of reflexes.

The course of the disease is variable. In slight cases treated at once by perfect rest from writing the patient may recover completely ; but if he has persevered, forcing himself to write by steadying his hand with the other, or by mechanical contrivances, and has ignored all treatment, the disease is often quite obstinate, and may never be thoroughly cured.

The **Diagnosis** is not generally difficult ; writers' cramp at least is not likely to be mistaken for anything else, but it must be remembered that some nervous diseases, such as chorea, hemiplegia, and other paralyses involving power in the

hand, may be first detected in the attempt to write, and may be regarded wrongly as writers' cramp. Nervous people, too, who have obtained some acquaintance with the disease, may easily fancy that a little fatigue is the commencement of it.

Treatment. The first essential is complete rest from writing. In mild cases this is sometimes sufficient to effect a cure in one or two months. Gowers insisted that, on again beginning to write, the patient should learn to write from the shoulder entirely. In more severe cases a much longer rest is required, and if writing is necessary to the patient, he may learn to write with the left hand or use a typewriter. Occasionally, but by no means always, the newly educated left hand also becomes affected. Various devices have been invented, or are improvised by the patients themselves, to save the strain on the muscles of the fingers, such as running the pen through a cork, which gives a larger grasp; or holding a wooden ball in the hand, upon which the pen is fixed at the required angle. Nussbaum's "bracelet" carries the pen, and surrounds the fingers, so that they hold it by muscles (abductors) different from those commonly employed in writing. But, as a rule, these instruments only postpone the time at which complete rest must be taken. A return to the normal action of nerve and muscle may be sought in the use of general tonics, such as iron, quinine, arsenic, and strychnia, and in local treatment, gymnastic exercises, passive manipulations, and massage.

The treatment of the other occupation neuroses must be the same in principle as that already described for writers' cramp.

NEURALGIA

This term is sometimes used for pain, felt in the course of a particular nerve and its branches, for which no organic cause can be found. It therefore describes a symptom rather than a disease. Pain of such distribution may be due (1) to disease of some part of the body supplied by the nerve in question, the pain being, as it were, reflected throughout the whole distribution of the nerve; (2) to disease affecting the nerve fibres either in the peripheral nerves, the posterior nerve roots, or occasionally the grey matter of the spinal cord; (3) to disease of some internal organ whose sensory nerve supply comes from that segment of the spinal cord which corresponds with the superficial distribution of the pain.

As examples of the first cause may be mentioned pain of trigeminal distribution caused by an inflamed tooth; of the second, pain of intercostal distribution due to pressure upon a posterior nerve root from tuberculous caries of the spine; and of the third, the pain along the ulnar border of the left arm experienced in angina.

A common cause of neuralgic pains is a local neuritis the result of trauma, intoxication or infection. In these cases there may be no positive indication, such as muscular wasting or numbness, of actual disease of the nerve concerned. There is, however, usually tenderness to pressure over points where the nerve lies against bone, and the occurrence in some cases of definite signs, such as the loss of ankle jerk in sciatica, makes it highly probable that the others are also due to a localised neuritis. They have already been described. There is, however, one form of neuralgia which, on account of its distinctive features, merits separate description.

TRIGEMINAL NEURALGIA

(Trifacial Neuralgia, Tic Douloureux)

In this affection there are recurrent attacks of paroxysmal pain, referred to the distribution of one or more branches of the fifth nerve. The attacks begin most frequently in the area supplied by the second division, less often in that of the third; the first, or ophthalmic, division is rarely involved, and then only when there is neuralgia of the second division also. In a few cases all three

divisions of the nerve may be affected at the same time. The disease may occur at any period of adult life, but is most common at about the age of fifty. Women are attacked more frequently than men. The ætiology and pathology of true trigeminal neuralgia are at present obscure. It cannot be traced directly to dental sepsis, and may occur in persons who have been edentulous for years. No constant changes are found in the branches of the fifth nerve or in the Gasserian ganglion. Nevertheless the frequency with which the second and third divisions are primarily involved suggests that the disease may be due to the action of bacterial toxins originating from septic foci in the teeth or air sinuses, and reaching the Gasserian ganglion by way of the perineural lymphatics.

As a rule the initial paroxysm is sudden in its onset, and there may be an interval of weeks or months before the next. The intervals, however, gradually become shorter, and the paroxysms more intense, until the patient's life is made intolerable by attacks occurring every few minutes of the day. The pain is extremely severe, and may completely incapacitate the patient while it lasts ; it is described as burning, darting or quivering, or as a sensation of red-hot needles being thrust into the cheek. It is often accompanied by a flow of saliva or tears, and there may be flushing of the cheek. The paroxysm is as a rule of brief duration, lasting only a few minutes. During the attack the skin and mucous membranes of the affected area are extremely sensitive, and a breath of cold air upon the cheek, the contact of food with the buccal mucous membrane, or even the movement of talking may suffice to initiate a further paroxysm. In the quiescent intervals, however, and even in the brief remissions between a succession of paroxysms, there is a complete absence of pain or tenderness.

Apart from the paroxysms of pain there are no signs of impairment of the functions of the fifth nerve. The corneal reflex is normal ; cutaneous sensibility is preserved ; there is no weakness or wasting of the muscles of mastication. By these facts true trigeminal neuralgia may be distinguished from cases of gross organic disease (syphilis or tumour) involving the Gasserian ganglion or its branches.

Treatment. Drugs are of little or no avail; tincture of gelsemium in large doses, combined with bromide, may be tried. The patient will usually discover for herself the advantage of protecting the affected side of the face from cold by means of a shawl or other covering, and may ward off paroxysms by employing writing instead of speech, and taking nourishment through a straw inserted into the opposite corner of the mouth. In skilled hands injection of the nerve roots with alcohol has given good results. The second and third divisions may both be dealt with in this fashion, and relief may often be obtained for as much as a year before the injection has to be repeated. In time, however, this method may fail to give relief, and some more drastic procedure is necessary. The most satisfactory is division of the sensory root of the fifth nerve between the Gasserian ganglion and the pons ; this involves a surgical operation of some magnitude, but is more certain than the alternative, which is to inject the Gasserian ganglion with alcohol through the foramen ovale. The disadvantage of either of these procedures is the risk of trophic changes occurring in the eye with subsequent blindness, which is considerable. Most patients, however, will cheerfully take the risk rather than continue to endure the pain.

DISEASES OF MUSCLES

Fibrositis has been described among the chronic rheumatic diseases.

MUSCULAR ATROPHY

Amyotrophy

Atrophy of muscular tissue takes place under a variety of conditions, and has been divided into *simple atrophy* and *degenerative atrophy*. In the former the

muscular fibrillæ diminish in size, while in the latter they diminish in number as well. The two conditions are not entirely distinct in their origin—that is, the same cause may in one case produce the first, and, operating for a longer time or more acutely, may bring about the second, severer form.

Simple atrophy is seen especially after acute or long illnesses, as a result of starvation, some kinds of intoxication, and locally from disuse, and from paralysis in cerebral lesions.

The different forms of arthritis, acute and chronic rheumatism, and gonococcal synovitis, are frequently accompanied by atrophy of the associated muscles; and this may be simple or degenerative. In the slightest degrees only one muscle is affected in the case of each joint; and these are the deltoid for the shoulder joint, the triceps for the elbow, the gluteus maximus for the hip, the extensor cruris for the knee, the pectoralis major for the sterno-clavicular joint, and the flexor brevis for the metacarpo-phalangeal joint of the thumb. In a higher degree of amyotrophy all the muscles connected with the joint are wasted; and in the most severe forms muscles remote from the joint may be involved, as, for instance, those of the whole arm and shoulder in arthritis of the wrist. The cause of arthritic amyotrophy is still obscure, but there are some grounds for thinking that lesions of the anterior grey cornua are determined by the arthritis, and that these cause the muscular wasting (Klippel and Weil). It would thus fall into the myelopathic group.

The degenerative variety is seen in the most pronounced form in the several lesions of the spinal cord and nerves which involve the lower neuron in one or other part, and hence bring about Wallerian degeneration in the periphery. These *myelopathic* and *neuropathic* forms have already been described (*see* Multiple Neuritis, Progressive Muscular Atrophy, Acute Poliomyelitis, etc.).

PROGRESSIVE MUSCULAR DYSTROPHY

(*Myopathy*)

This is a condition in which there is progressive weakness and wasting of the skeletal muscles in the absence of any local or constitutional cause, and without clinical or pathological evidence of disease of the nervous system.

Ætiology. The cause is unknown, but the disease probably depends upon some congenital abnormality of the muscular fibres. It commonly occurs in several members of the same family, and may be transmitted from one generation to another, usually through the females. Except in the case of the pseudo-hypertrophic form, which is commoner among males, it affects both sexes equally. The first symptoms are developed as a rule during childhood, and are nearly always manifested before the completion of adolescence.

Pathology. The changes are confined to the striated muscles, in which the earliest change appears to be hypertrophy of the fibres with subsequent degeneration, a great increase in the number of sarcolemma nuclei and the deposit of fat in the interstitial tissues. The motor nerves and end plates are intact.

Symptoms. Several clinical varieties of the disease exist, and will presently be described. The features common to all types are the early age of onset and progressive weakness of certain muscle groups. With this may be associated atrophy or pseudo-hypertrophy, but the weakness precedes obvious changes of this kind, and the attention of the parents is usually attracted by clumsiness shown by the child in the performance of certain movements, such as walking or climbing upstairs, by a tendency to fall about, and by difficulty in regaining the erect posture after a fall. The child learns to compensate for the weakness by the acquisition of new methods of muscular co-ordination, and this may result in certain peculiarities of gait and posture, which are somewhat characteristic. The patient has a waddling gait, the feet are widely separated, and the body is thrown from side to side with each step; the gait is further modified by the

produce improvement. Carefully planned gymnastic exercises have done good, and rubbing, massage, and passive movements may be of some use. When the gastrocnemii are so shortened as to prevent the patient standing, the tendons should be divided.

THOMSEN'S DISEASE

(*Congenital Myotonia*)

This disease consists of a peculiar rigidity of the muscles, which comes on whenever they are called into contraction by voluntary impulses after a period of rest. Thus, if the patient wishes to walk and tries to rise from his seat, his muscles become rigid, and he is unable to move; the rigidity lasts a few seconds, and then relaxes so that he can at length get up. His first few steps are attended with the same difficulty, but soon the contractions become more natural, and shortly the trouble ceases altogether, so that he walks with complete freedom and ease. If, however, he should stop for a minute, the muscles become rigid on his beginning to walk again. Quick movements are thus impossible immediately after rest, and sometimes accidents occur, as, for instance, when the patient is descending from a train, and having placed one foot on the ground, he is unable to bring the other out quickly after it, and falls in consequence. Involvement of the muscles of the arms may give rise to a considerable degree of disability in manual workers. After grasping an object firmly, especially if this action is prolonged, the patient is unable to relax his grip sometimes for several minutes. The tendency to rigidity seems to be increased by cold and emotional stress. On inspection there is as a rule no abnormality of the muscles affected, nor is their power diminished. Their excitability to direct mechanical stimulation, however, is altered. When the belly of the muscle is struck with a percussion hammer the resultant contraction, instead of disappearing at once, persists for several seconds. This so-called "myotonic reaction" cannot always be obtained in all the muscles involved, and the ease with which it can be elicited varies from time to time. The closure contraction to strong galvanic currents is much prolonged beyond the time of application, and with continued application of the current a series of contractions has been seen to pass in a wave-like manner from the kathode to the anode. The reactions to faradism are often normal, but may be exaggerated in force and duration. The disease often lasts a very long time, but it may subside.

Ætiology. It happens often early in life, may affect more than one member of a family, and is commonly regarded as being congenital.

Pathology. In a case reported by Dejerine and Sottas, the patient died of nephritis. The muscles were large, protruding, tending to be more globular in shape, of a duller red colour, and less elastic than normally. The number and size of the muscle nuclei were found to be increased; the fibres varied much in size, some being very large indeed, as if swollen. Sometimes the sarcous elements were separated, and the sheath was filled with granules; or the muscle substance was degenerated and vacuolated. The connective tissue was not hypertrophied or fatty, as in pseudo-hypertrophic paralysis. These results agree closely with what had been seen in portions of muscle excised during life. The muscle nerves, nerve trunks, spinal cord, and bulb were healthy.

Treatment. Nothing has been found of use. Thomsen, who suffered from it himself, advised a life of continued activity.

MYOTONIA ATROPHICA

In this disorder stiffness of the muscles similar to that of Thomsen's disease is associated with muscular atrophy. The stiffness, or myotonia, is especially noticed in the inability to relax the flexor muscles after grasping strongly with the hand. The muscles affected by atrophy are the orbicularis oris and orbicularis

palpebrarum (so that there is some resemblance to the Landouzy-Dejerine type of muscular dystrophy), the masseters, temporals, sterno-mastoids (severely), the muscles of the forearm and hands, the vasti femoris, and the anterior tibial and peroneal muscles.

The tendon jerks are frequently absent, although the muscular atrophy is insufficient to account for this symptom.

Outside the nervous system there are other symptoms of a degenerative nature, the most striking being premature baldness, general wasting and loss of weight, and in males atrophy of the testicles with impaired sexual desire. The disease generally begins in middle life and is slowly progressive. It occurs frequently in several members of the same family, as a rule affecting only one generation. It is often associated with cataract, and with a history of cataract in the forebears. Pathologically no constant changes have been found in the nervous system. The muscles show degenerative changes.

AMYOTONIA CONGENITA

(*Myatonia Congenita*)

In this disease the muscles are extremely flaccid and wanting in tone, and the child lies about in any position and cannot sit up. The condition is noticed at or shortly after birth and may be familial. Later the child is unable to walk; all its actions are feeble, and passive movements at the joints are unusually free. The response of the muscles to faradic excitation is diminished, and the deep reflexes are absent. In many cases there is slow and progressive amelioration, but the majority die of intercurrent affections during childhood. The disease is differentiated from the myopathies by the age of onset, which is, as a rule, earlier, and by the tendency to improvement. The pathology is obscure, but there is some evidence in favour of a congenital arrest of development of the lower motor neurones. Massage, faradism and exercises assist improvement.

FAMILY PERIODIC PARALYSIS

In this curious complaint, the patient suffers from attacks of gradually developing paralysis of the muscles of the trunk and limbs, which lasts on each occasion several hours and then completely passes off.

Ætiology. This disease has also been observed in several members of a family, and is transmitted to the descendants of the sufferers. It affects the two sexes equally, and the first attack has generally occurred between the ages of six and twenty-four.

Symptoms. The paralysis often begins at night. The muscles of the legs, then of the arms, and lastly those of the trunk and neck, gradually lose power, so that in the course of four or five hours the patient is quite unable to move his limbs. The weakness affects first the proximal parts of the limbs, and the distal parts later. The intercostal muscles are weakened, so that the breathing is shallow and feeble; and probably also the diaphragm is involved. The muscles supplied by cranial nerves are generally spared, and the sphincters remain unaffected. The heart may become dilated and the pulse rapid and irregular. The reflexes are gradually lost; and the reactions to both faradic and galvanic currents, which get less and less as the weakness increases, are entirely lost with complete paralysis. Sensation and the mental state are unimpaired. After a few hours improvement begins; the muscles regain power in the reverse order of their loss of it, and after another six to twelve hours power is completely restored as well as the reflexes and electrical reactions.

The attacks at first occur at intervals of months, but they become more frequent until they may occur weekly or oftener; as middle age is reached they again become less frequent.

The **Pathology** is at present obscure. The probability seems to be that some toxin is operating upon the muscular fibres; and some interesting observations on the relations of the urine and of creatinin excretion to the attacks have been made.

Treatment. Diuresis should be encouraged by salines and mineral waters in order to get rid of toxins.

MYASTHENIA GRAVIS

This is another disease profoundly affecting the action of the muscles; and in the absence of any constant change in the nerve centres or nerves, while lesions are frequently found in the muscles, it must be regarded for the present as a primary disorder of those structures, probably toxic in origin.

Ætiology. It is slightly more frequent in women than men (142 to 108, Starr) and begins most often between the ages of twenty and thirty, but no age is exempt.

Morbid Anatomy. Several cases have now been examined *post-mortem*. In more than a quarter the thymus has been persistent or enlarged, or the subject of lymphosarcoma; but in others it has been absent in accordance with normal conditions. In nearly all cases there are found collections of lymphocytes (lymphorrhages) in the muscles, and in some organs such as the thymus, liver, pancreas, kidney and adrenals; the blood and lymph glands are healthy.

Symptoms. The characteristic feature of the disease is weakness of the voluntary muscles, which are very rapidly exhausted by exertion, but recover their power after rest. In severe cases the weakness persists, and death often results either suddenly or with dyspnœa from respiratory paralysis. The muscles most frequently and generally first involved are those of the eyes, head, and neck, so that the patient has ptosis, diplopia, immobility of the face, difficulty in mastication or in swallowing, defective articulation, nasal quality of the voice with weakness increasing up to aphonia, and inability to support the head upright. But nearly all the muscles in the body may be affected, and in 12 per cent. of the cases it has commenced in the muscles of the limbs; the patient may be unable to sit up, can only walk a few yards without stopping, or his respiration is impeded, and he has dangerous attacks of dyspnœa. In the limbs the proximal muscles are attacked more often than the distal; women find their arms tire when doing their hair. The condition is very variable in its intensity, and is aggravated by emotion, by cold, and by the menstrual function in women. The knee jerk is generally active, but may be exhausted by repeated stimulation, sensory symptoms are seldom present, and the sphincters are not affected.

It has recently been shown that the sugar tolerance is low in cases of this disease (**5**). The affected muscles mostly, but not in every case, react in a special manner to electrical currents—the *myasthenic reaction*. If the faradic current is applied to the muscles, they contract normally, but if it is continued, they soon become exhausted and fail to contract any further. If then the electrodes are removed, the muscle recovers, and then contracts well to the current, again becoming soon exhausted. Contraction to the galvanic current is persistent, and is scarcely at all affected by the length of application.

Temporary improvement may take place, and long remissions have been recorded with relative freedom from the symptoms, but a fatal result generally ensues from respiratory failure or from choking. Forty-five per cent. of the cases collected by Starr died within six months, but many have lived for ten years or more.

Diagnosis. It is likely to be mistaken for hysteria, diphtheritic paralysis, and bulbar paralysis. From the latter it may be distinguished by the absence of atrophy in the muscles, by the myasthenic reaction and the varying degrees of weakness.

Treatment. In 1934 it was discovered by Dr. M. B. Walker that physo-

stigmine given by injection produced an immediate and striking amelioration of symptoms in a case of myasthenia gravis. The observation has now many times been repeated. The most effective drug is prostigmin, which is prepared in a solution containing 0·5 mg. in 1 c.c. From 3 to 5 c.c. of this solution is given by hypodermic injection, together with $\frac{1}{100}$ gr. of atropin sulphate to counteract the slowing of heart action and increased peristalsis otherwise caused by the prostigmin. The effect lasts for a few hours only, so that at present this method of treatment is chiefly of value as a temporary measure to enable the patient to perform a task or eat a meal in comfort, and it is likely to prove of vital importance when the respiratory muscles are in danger from fatigue as the result of intercurrent bronchitis.

Ephedrine hydrochloride, gr. $\frac{1}{2}$, taken thrice daily, appears to give some patients a subjective sense of improvement.

Strychnine appears to improve power and prolong life in some cases (**6**). Large doses must be given. Hypodermic injections should commence at gr. $\frac{1}{32}$ of strych. sulph., and may be increased to gr. $\frac{1}{4}$ twice daily. If this has a good effect, it may be continued indefinitely, or equivalent amounts may be given by the mouth.

Respiratory embarrassment should be a signal for absolute rest. A temporary fatigue paralysis of the respiratory muscles may sometimes be overcome by artificial respiration. When the muscles of swallowing are severely involved tube feeding may be necessary.

SOME OTHER DISORDERS OF MUSCLE

In addition to the spasm and paralysis, which are the result of central and peripheral nervous disorders, and which have been described previously, some disorders may be mentioned of which it is perhaps difficult to say whether they are due primarily to failure of nerve or of muscle, or whether they are due sometimes to one and sometimes to the other.

Muscular Exhaustion or Fatigue. The gradually lessening capacity of a muscle to contract as the result of excessive use is generally regarded as being due to the saturation of the muscle with the chemical products of its work, such as sarcolactic acid, extractives, and possibly a special toxin, though it has been also stated that fatigue in the ordinary way is much more largely due to the effect of the poisons upon the nervous centres than to their influence upon the muscles themselves. The actual consumption of the muscular fibre itself in the process cannot be entirely disregarded.

The loss of muscular power after exhausting illnesses and febrile attacks and in advancing years is probably referable to the nervous system as much as to the muscular apparatus.

Fibrillary Contractions (*Fibrillary Tremors*). These have been mentioned among the symptoms of nervous diseases (*see* p. 626). But they occur in conditions of practically normal health. The most common form is a twitching of the orbicularis palpebrarum muscle, causing a slight flickering movement of the eyelid, which is felt by the patient, though it may escape the notice of a bystander. It is sufficiently common to have received the name "live blood" from the public. The same fibrillary contractions occur sometimes in other muscles, such as the deltoid or the biceps. They may be troublesome for an hour or two, or for a few days, and then pass away entirely. Their occurrence is not readily explained, whether they happen in apparent health or in connection with muscular atrophy.

In the latter they are common in the atrophies due to degeneration of anterior horn cells, such as progressive muscular atrophy, and may occur in disease of the peripheral nerves. Of course they cannot take place when the wasting is complete, but only while the degeneration is progressing. If they are dependent directly upon the changes in the anterior cornua of the cord, it must be supposed

that the degenerating cell body sends erratic stimuli to the separate muscular fibrils. Such stimuli are attributed to hyperexcitability, though it is not clear why a degenerating cell should be over-excitable. When occurring in the healthy person, the explanation is even less satisfactory, the little trouble passes away entirely, and nothing remains to show a permanent change in nerve or muscle. There appears to be nothing to show whether it is caused by a temporary or functional change in the nerve-cell or by a primary functional disorder of the muscular fibril.

Fidgets. This appears to be a small matter, but it is of interest in connection with this subject. The condition of physical restlessness, to which the name is popularly given, is often brought on by excessive exertion and consists of a sense of discomfort in the limbs, mostly the lower extremities, which is followed by a contraction of a whole muscle, sudden and sometimes briefly clonic, by which a temporary relief of the discomfort is obtained. The contraction is involuntary and very difficult or impossible to control, and it has the effect of moving the limb to a small extent. The sensation appears to be in the muscle ; at any rate, it is deep-seated, and it is not a pain, only the sense of a desire to move. If the contraction is reflex, as it probably is, it may still be that the sensory fibres in the muscle are poisoned by the chemical products of muscular action.

When the " fidgets " occur in these circumstances—but they are not limited to them—they can be generally efficiently treated by massage of the lower extremities, by which it may be supposed the removal of the poison products will be facilitated. A change of position, as, for instance, from recumbent to sitting, will sometimes suffice.

Cramp. This is apparently an involuntary, slow, forcible, prolonged and painful contraction of a muscle, not preceded by any sensation whatever, and only slowly giving way to complete relaxation. It may be repeated at once, or at an interval of some minutes ; it may occur only rarely and at long intervals.

This is also a frequent result of over-exertion, and occurs often in bed after a long day's walk, or other continuous effort. Though often spontaneous, it may be induced by a voluntary effort in the muscle affected.

Its exact causation is as difficult to state as is that of the previously described muscular disorders. In the fatigue cramps the influence of muscle poisons is naturally suggested ; and this is supported by the well-known occurrence of cramps in certain diseases, such as cholera, choleraic diarrhœa from food-poisoning, and some other exhausting diseases. Poisons are certainly concerned in the cramps of tetanus, of strychnia, of tetany, and of alcoholic or other forms of toxic neuritis. In the first two of these the muscles apparently receive their stimuli from the poisoned spinal cord ; in tetany the existence of Chvostek's sign shows that irritation of the peripheral nerves will produce the spasms ; but in multiple neuritis it is perhaps not so obvious that the muscles are not set in action by the poison circulating in their own substances as by the change in the nerve trunks. The same may be said for gout and Bright's disease, in which cramps are not infrequent. The spasms of hysteria and the so-called professional cramps (*see* p. 752) are, on the other hand, more clearly central in origin.

The treatment of cramps is not very satisfactory. Where a toxic action can be recognised, the removal or neutralisation of the toxin is obviously the object to be aimed at. When after fatigue or otherwise a single muscle is the subject of cramp, the antagonistic muscle should be at once put into action, so as to stretch the affected muscle, when the spasms will generally give way promptly. For frequently repeated cramps massage may be usefully employed.

MENTAL DISEASES

We have now to consider the illnesses whose symptoms are due to disturbances at the highest level of bodily integration, that is in the mental processes of the individual. In order to understand the manner in which these disturbances arise it is necessary to know something of the laws governing the mental activities under normal conditions.

PSYCHOLOGICAL PRINCIPLES

Adaptation. Our working hypotheses depend on a conception of living process as an adaptive one ; we assume that each living organism is involved in an unceasing attempt to adapt itself to the external environment and to maintain equilibrium among its own internal arrangements. For the purposes of this adaptation, intricate processes develop in the organism, the most intricate of them being carried out by the nervous system.

If we consider the adaptive process of the organism to be carried out at a series of levels of increasing complexity, then we can regard the purely automatic nervous processes involved in the digestive function, for example, as being at the simplest " vegetative level." The next higher in this series, the sensori-motor or spinal level of adaptive activity, involves the muscles and the co-ordination of their movements by the nerve centres and their connections in the spinal cord ; while in the brain are conducted still more intricate and varying processes of adjustment—the cerebral level. " Above " this again are the most complicated processes of all, namely, those which we call mental. The latter are concerned especially with the adaptation of the whole organism to its whole environment and especially its social environment.

Physiology has not yet succeeded in expressing activity at this level in its own terms, and therefore the language of psychology is the only one available and must be learned if we are to describe the functions of the individual organism at the mental level.

" Levels " of Integration. If in this way we think of an organism as built up in a series of levels of increasing complexity, we get an impression of continuity, mental processes appearing as the most complicated in a series of adaptive processes. In this way we can avoid being perplexed about the particular mode of relation that exists between mental and brain processes ; and we can understand how disorder can arise primarily at any level, so that it is not necessary to presuppose brain disease to explain mental illness. But it is equally clear from this scheme that disorder at one level may upset function at another, so that disorder of brain function may produce disorder of mental function and *vice versâ*.

Emotional Reactions. This is a fruitful idea for the understanding of many physical symptoms which patients present for medical examination and which are not found to have any discoverable physical basis. They are the result of an event at the mental level producing a disturbance at the underlying cerebro-spinal and vegetative levels. For example, the perception of a lion in one's path would normally result in the quickening of the heartbeat, a sensation of discomfort in the epigastrium and perhaps some trembling. Mental happenings associated with these effects are called emotions. For example, those just given are associated with the emotion of fear. It has been much argued whether fear

or any other emotion can exist apart from such physical perturbation. What is certain is that such bodily disturbance may exist apart from any conscious emotion and that, nevertheless, it may be dependent on events at the mental level of complexity. The patient having perceived no lion and being aware of no fear comes to his doctor and asks why he feels ill. One of the discoveries of modern psychology is that something mental may exist without the subject being aware of it, that is, a process at the mental level is not necessarily accompanied by consciousness, or, as is usually said, the process is unconscious, at least for the time being. There are many grounds for this conclusion, but a single example will suffice here. A workman may have injured his back at work and shown no sign of injury afterwards, and yet suffer from general weakness no physical basis for which is discoverable. An exploration of his mind may show that he is *afraid* of returning to his work, perhaps on account of increasing disability for it on account of his age, although he may deny this fear even to himself; that is to say, the fear is not in the realm of consciousness but it is responsible for the feeling of weakness nevertheless.

The effects of emotion on the bodily systems are various and can be conveniently classified as follows :—

Circulatory System. A sudden and severe emotional stimulus may cause temporary cessation of the heart-beat through vagal inhibition. This results in loss of consciousness, and is responsible for the common faint or swoon of emotional origin. Less severe stimulation causes acceleration of the pulse with forcible thumping action of the heart and throbbing of the large vessels. The peripheral arterioles and capillaries, under the influence of severe emotion, may contract, with resultant pallor, but more commonly dilate, the phenomenon of blushing being due to this cause. Except in the cases of severe emotion with vagal inhibition, the blood pressure is raised.

Alimentary System. The secretion of saliva is diminished. There may be spasm of the pharynx and œsophagus. The movements and tone of the stomach and intestines are diminished, there is spasm of the pyloric and ileocolic sphincters. In acute emotion vomiting may occur. Gastric secretion is abolished or reduced. The pelvic colon contracts, and the anal sphincter is relaxed, leading sometimes to evacuation of the bowels.

Respiratory System. The respiratory movements are increased in depth and frequency, and with this there may be a sensation of "suffocation."

Genito-urinary System. The secretion of urine is increased, and the bladder contracts. This leads to a call to micturition, or in extreme cases there may be involuntary relaxation of the sphincter with incontinence of urine. In males prostatic secretion and emission may occur.

Endocrine Glands and Metabolism. The output of adrenalin is increased, and this in turn may cause further stimulation of the organs innervated by the sympathetic system. The blood sugar is raised, and glycosuria may occur. Metabolism generally is increased.

Nervous System. Besides the mental condition of anxiety, which fills the mind to the exclusion of purposeful thought and of sleep, there may be tremor of the limbs and sensations of numbness. Discomfort or pains in the head are commonly experienced, and are probably due to changes in the cerebral circulation. The pupils are dilated, and the eyes may be protruded.

Skin. The erectors of the hair follicles may be excited, producing the phenomenon commonly described as "goose flesh." Profuse sweating may occur.

The emotional reaction, if it persists for any length of time, is accompanied by an unusual sense of mental and physical fatigue.

The Conditioned Reflex. Pavlow has shown in animals by means of experiment that a previously indifferent stimulus may become so closely associated with an effective one as itself to become effective. The experiment in which the sound of a bell was in this way converted into a stimulus to the salivary reflex

is familiar to students of physiology. In the same way an indifferent stimulus may through association become capable of producing the emotional reaction.

The association may be produced either by frequent repetition or by the coincidence of particular circumstances with an especially severe emotional reaction. Many examples might be quoted of such an association leading to a conditioned emotional reaction. During the recent war men who had been exposed for long periods to occasional shell-fire would afterwards exhibit tremor and palpitation at any loud and unexpected noise. A woman who was summoned to the telephone to hear that her husband had been killed suffered for several months afterwards from a sensation of extreme anxiety and palpitation whenever she was called to the instrument.

Similar emotional disturbances may be experienced by a man who has met with an accident while driving a motor car when next he takes the wheel, even though he is an experienced driver and the road is clear. Such associations are usually lost with further experience in the same way as the simpler conditioned reflexes established in animals can be broken down by lack of " reinforcement."

Mental Integration. Hughlings Jackson's concept of levels in the nervous system is one that can be extended, by analogy, to the internal arrangements of the mental level. And here also, as in the nervous system, the " layering " is largely of historical origin. The uppermost layer of the mental level is, in Hughlings Jackson's phrase, the last acquired, the most complex and the least organised. The lowest levels are those of infantile experience. Between, as it were, is all that has been experienced in the course of life. But it is necessary to postulate also for the organism a phylogenetic endowment with instincts, which underlie even the infantile experiences.

Release. This analogy enables us to think in terms of another of Hughlings Jackson's concepts—that of " release phenomena." The abrogation by the higher levels of their function will allow, earlier, more primitive reactions to occur. This is perhaps most easily seen in alcoholic intoxication, which sometimes has the effect of uncovering unexpected trends. A similar release can also occur from the operation of purely psychological factors.

Consciousness is the quality that appertains to that mental function which is for the moment the one most concerned with adaptation.

Unconscious " Mental " Events. The other mental experiences exist in a form which can sometimes be revived in consciousness with effort. But the constitutional endowment, that is the instincts, since they are not individual experience but only the forces behind it, remain outside of consciousness or " unconscious." We shall see that there are other reasons than never-having-been-conscious for mental experiences remaining away from consciousness. It has to be remembered also that the so-called instincts are not entities so much as abstract concepts to cover a great many phenomena which are not explicable as the result of acquired experience. These phenomena are mainly divisible into classes, those associated with self-assertion or self-preservation, and those associated with reproduction or the preservation of the race.

It has to be noted that adaptation has two aspects : it has to face two ways. There is adaptation to circumstances without and adaptation to instinctual urges from within. We therefore have a concept of the adaptive function in the individual operating as it were between two forces, the environmental stimuli and the stimuli from within (the tendencies initiated by instinctive forces), and it has to preserve a balance between them. This adaptive function must clearly be intimately connected with what is called the self, or, in technical terms, the ego.

The environmental stimuli include all experience ; what makes them important for adaptation at the highest or mental level is their personal quality. That type of adaptation, failure of which leads to the appearance of symptoms of a mental order, is always a matter of personal relationships. One does not get a nervous illness merely because one has seen or heard something, but only if it

has some particular meaning for oneself in relation to the other persons in the environment. The important persons are especially other people in the family or those who might be regarded as their substitutes, such as nurses, etc., companions, lovers, teachers and the like. These might all be classed as environmental stimuli, while the inner stimuli are the instinctual urges principally concerned either with self-assertion, *e.g.* social ambition, or with sexual satisfaction (in the full sense and not in the sense of merely physical satisfaction).

Conflict. An important consequence of this complication of arrangements is the possibility of conflict, especially between the environmental demands, the instinctual urges on the one hand, and what are conceived to be the wishes of other persons on the other. Conflict of this sort may result either (*a*) in complete repression of one side or other of the contending forces, in which case there are no symptoms, or (*b*) both forces may continue to contend for dominance, with the result that symptoms are produced in the form of signs of disturbance at one or all levels. There may then be partial repression with the result that at the conscious level there appear evidences, usually distorted and disguised, of the conflict that has been repressed. These evidences constitute symptoms ; for example, depression and anxiety, phobias delusions, and the like.

Repression therefore means, if successful, a complete blotting out of the repressed tendencies from consciousness. If repression is only partially successful these tendencies appear in consciousness in a disguised form. The simplest example of disguise is the repression of a desire (forbidden by conscience, *q.v.*) and its substituted appearance in consciousness as a fear. Sometimes repression has the curious effect of making both sides of the conflict unconscious, with the result that that part of the individual's mental experience is no longer accessible to his consciousness and he develops an amnesia which may cover anything from a small period up to the individual's entire life.

So we see that there are items of a mental order which are unconscious because repressed, in addition to those that have never been conscious at all (instincts) and, in addition, to those which can be recalled at will.

What does the repressing ? An analogy from the lower levels of the nervous system, *i.e.* a physiological analogy, will help to make clear one type of repression—for clearly where there are two parties to a conflict and one of them is repressed, the other holding the conscious field, you get something analogous to inhibition. One of the contending parties is nearly always the ego or self, which will often wilfully repress some unpalatable fact, that is, unpalatable to the ideal that the ego has shaped for itself. Another closely allied contending element is the " conscience," which is a kind of mental precipitate of the injunctions and prohibitions conceived by the ego to be laid down by the environment, especially the parents. This kind of conscience therefore is a mental structure deeply rooted in the individual history, and for that reason alone functions largely automatically and unconsciously. It often is responsible for the feelings of inferiority and guilt which are so common in neurotic personalities.

This tendency for a man to remain unconscious of his own emotions if they are of a repellent nature is of great importance in causation. Thus, for instance, in the recent war a man whose training had taught him to regard the emotion of fear as tantamount to cowardice would sometimes remain oblivious to the presence of this emotion within himself. The emotional reaction would then be present without cognisance of the emotion, and the individual would be driven to explain the phenomena of palpitation, sweating and so on as evidence of bodily disease.

Furthermore, he might be led by his fear to evade his duty without being conscious of the motive which impelled him. Physical disease under such circumstances offered a way of escape, and in this state of mind a man would, in the face of all reasonable considerations, accept the least suggestion of bodily disability.

A blow on the arm with temporary numbness would suggest the idea of paralysis of the limb. This idea, exerting by means of the unconscious motive a strong positive influence, would keep attention fixed upon it; all evidence to the contrary would for a similar reason be excluded from conscious attention, so that in a short while the paralysis of the arm became a fixed belief.

Many of the phenomena of daily life depend upon the influence of unconscious motives in directing attention towards certain aspects of self and environment and away from others. Men are notoriously blind to their own faults. They tend to remember their virtues and successes, to forget their failures and peccadilloes. Many acts of forgetting depend upon such a cause.

The man who is being influenced in his actions or his judgments by an unconscious motive is usually ready to defend his position upon logical grounds. His arguments, however plausible, prove on analysis to be fallacious. They are in fact further products of the hidden motive, and to distinguish them from processes of true reasoning they are called by psychologists " rationalisations " (**4**).

With these principles of adaptation, integration of levels, emotional reactions, unconscious mental events, repression, and conflict we are in a position to understand the main phenomena of psychological illness.

CLASSIFICATION

Psychiatric classification is particularly difficult and particularly misleading. Every " case " is an individual and not a disease. The disease *is* the individual. The essential thing is to understand the patient and not to classify him. His mental condition can only be understood by taking account of the patient's history and situation in all practicable ways. To place him in a class is only permissible for the purpose of making certain rapid conclusions of a safeguarding, therapeutic and prognostic kind. The following classifications may be used, but there is no hard and fast line between many of the groups: (1) Psychoneuroses; (2) affective reaction-types; (3) schizophrenic reaction types (dementia præcox); (4) paranoic and paranoid reaction types; (5) organic reaction types; (6) epilepsy; (7) psychopathic reaction types; (8) mental deficiency. Groups 2, 3, 4, 5, 6 and 7 constitute what are known as the " psychoses," to distinguish them from the mental deficiency (Group 8) and the psychoneuroses (Group 1). Mentally defective persons may, of course, develop a psychosis or a psychoneurosis (**5**).

Broadly speaking, mental disorders can be divided into those which are dependent upon detectable organic disease of the brain (blastophoric, degenerative, inflammatory, neoplastic or toxic) and those which are not. In the former class the defects found are principally, but not entirely, in the sensorial field (*i.e.* in perception, comprehension and memory); in the latter the positive findings are mainly, but not always or entirely, in the fields of behaviour, affect (or emotion) and thought content.

Brief clinical definitions of these principal types of mental disorder are given here in a preliminary form:

(1) **Psychoneuroses.** The psychoneuroses involve as a rule much less disturbance of the personality than the other groups. It is much more usual for a patient suffering from a psychoneurosis to go about his daily business than it is for a person with a psychosis; a psychoneurosis usually betrays to the casual bystander no sign of its presence; a psychosis commonly does so. There is no misconstruction of reality by the psychoneurotic. The psychotic, on the other hand, commonly suffers from delusions or hallucinations, or at least from a feeling that the outside world has changed. The commonest psychoneurotic disorders are complaints of fatigue, headache, pains and paræsthesiæ of all kinds, morbid fears, paralysis, tremors and tics, disturbances of memory

(usually patchy) and disturbances of consciousness such as somnambulism and fugues.

(2) **The Affective Reaction Types.** The chief clinical characteristic is the *disorder of mood or affect*, with which the other symptoms more or less conform. Thus in the manic condition there is excessive happiness (*elation*) with much *restlessness* (often of a playful kind) and a *flight of ideas*, with punning and rhyming. In the depressed condition there is *sadness*, with slowing of speech and action ("*retardation*"), and often also gloomy delusions of personal unworthiness and guilt and of the ruin of family and affairs.

Involutional melancholia is a type of depression occurring chiefly, but not exclusively, at the involutional period of life, and characterised by sadness, but with restlessness rather than retardation, much apprehension, and nihilistic and hypochondriacal ideas.

(3) **The Schizophrenic Reaction Types.** The characteristic features of these are the more or less pronounced *lack of contact with the environment* and the *internal inconsistencies* in the clinical picture. The patient is seclusive and apathetic, living in a world of his own, while his speech is more or less incoherent and his mood and his thought often do not harmonise. There are erratic and impulsive or fantastic conduct, absurd delusions, hallucinations, chiefly auditory, and feelings of influence.

The differentiation of sub-types within this syndrome is artificial, as most cases show features belonging to several of the sub-types. The most distinct of these subdivisions is the catatonic, in which there is stupor and resistiveness alternating with wild impulsive excitement.

(4) **Paranoia and Paranoid States.** In these conditions more or less systematised *delusions of persecution* or, more rarely, of grandeur are the prominent symptoms. There is no apparent affective or intellectual disorder, the delusions being fairly consistent within themselves, so that if certain premises were granted the delusions would more or less reasonably follow.

Paraphrenia is artificially distinguished from paranoia by the presence of *hallucinations* in the former. On the whole, it has become customary to designate as paraphrenic those cases in which the delusions are not well systematised, in which hallucinations are prominent, and the general personality undergoes more deterioration than in paranoia. Paraphrenia therefore stands nosologically between paranoia and paranoid schizophrenia.

(5) **Organic Reaction Types** are the result of toxins, infections and nerve-degenerative processes; they are especially characterised by *impairment of the intellectual functions*, especially memory and comprehension, leading to defects of orientation and of attention. The severity of the condition is apt to fluctuate —the so-called *mental tension defect*. In the acute form of organic reaction—delirium—there are in addition usually hallucinations. Mood disorders also occur, *e.g.* fear in delirium, and based on the latter and on the intellectual disorder, changes in conduct take place, so that the whole personality is impaired, at least in the chronic forms.

(6) **Epilepsy.** The most important clinical feature is the occurrence of fits, major or minor, but there is also in some cases an epileptic change in character which exists in the interparoxysmal period and may at times or continually constitute a more or less severe disorder in itself. The epileptic character is typically selfish, childish and religiose, with no real depth of feeling, and with, in many cases, *intellectual* defects of attention, comprehension and memory. There are also episodic disturbances in the form of *depression, irritability, excitement* and *ecstasy*, and in the period immediately after the fit *automatic actions*, which sometimes take the form of physical violence or other anti-social acts such as blatant thieving and indecent exposure. The general account of epilepsy has already been given.

(7) **Psychopathic Reaction Types.** In these conditions the prominent

feature is a nearly lifelong emotional instability, which leads to erratic, anti-social, or impulsive conduct at times. Mental disorders of the other types appear readily in these patients, and as readily disappear.

(8) **Mental Deficiency.** This group comprises all individuals who from birth or from an early age have suffered from intellectual deficiency, as defined in the Mental Deficiency Acts of 1913 and 1927.

METHODS OF PSYCHIATRIC EXAMINATION

Since mental disorder in the full sense of the term is a defect of social adaptation, and since a medical examination is but one of the numerous social situations to which the patient has to try to adapt himself, it follows that the examining physician may have the opportunity of seeing only a portion of the patient's symptoms; therefore he must take careful account of all the information that may be obtainable from other sources and from observers in other circumstances (home, school, companions and the like). In this there is a difference of degree from what occurs in general medicine, where symptoms and signs are elicitable either at the time of examination or by direct questioning of the patient. With psychiatric patients it not infrequently happens that very little that is clearly abnormal is to be detected at an interview. The patient's abnormal behaviour may be reserved for special circumstances, as in the naughty child who is a tyrant at home and an angel at school. On the other hand, the signs of mental disorder are often as definite as the signs of physical disease, if one knows how to elicit them. The following scheme provides an orderly system of examination; the results when applied to any patient can be tabulated at the end and deductions made from them.

Perhaps the most important function of the examination is to get the patient to talk. Specific questions are to be regarded either as short cuts (not to be resorted to except when the patient's spontaneous talk may cease to be helpful) or as organised methods of getting the patient to speak along the lines known by experience to be the most fruitful for reaching conclusions.

The following outline is intended to cover almost any type of mental case. It is more uniformly detailed than is necessary in the individual instance; only experience will teach what facts to lay stress on in a given instance.

HISTORY OF THE CASE

Complaints. It is necessary to start by getting a list of the patient's complaints from the patient himself or, in the case of an unco-operative patient, from the relatives or friends. The latter should always be carefully interviewed: their account may be very different from that of the patient, and the discrepancies are themselves illuminating. It is necessary not to be prejudiced beforehand by the notion that the relatives' account must necessarily be more reliable than that of the patient. Particular topics that should be inquired into when there is any reason to suspect such abnormalities are suicidal attempts, exhibition of temper or violence, alcoholism, idleness, tendency to lie long in bed and the like. These usually are more readily acquired from the relatives than from the patient.

History of Present Illness. The history of the present illness should be obtained in careful chronological order from the patient himself if possible. It is a good rule in psychological medicine to distrust the ostensible beginning of the illness and to seek for incidents further back. Very frequently a condition that is said to have begun suddenly has had prodromal symptoms of long standing. In particular the setting of the onset of the present illness is extremely important. The possibilities of precipitating factors actually in the home, at business, in the

financial circumstances and in personal relationships, have to be borne carefully in mind.

Personal History. For these and other reasons, an adequate account of the personal history is very necessary. Inquiries may be made systematically under the following heads :

(A) *Pre-natal conditions* include the health, habits and social circumstances of the family at the time of conception and gestation (alcohol, drugs, syphilis, tuberculosis, and chronic diseases generally of the parent).

(B) *Conditions at birth* are such as the character of the labour (prolonged, instrumental, complicated, premature), the occurrence of an unusual amount of asphyxia or of actual injury to the skull. (A) and (B) are more apt to give relevant information in cases of primary mental defect.

(C) *Native endowment and post-natal development.*

(I.) Physical. Inquiry should be made as to the general health, whether healthy or sickly in childhood, and later what specific diseases the patient has had, and what amount of attention the patient paid to his physical condition (including unusual maternal concern about illness, dietetic and other fads). Inquiry should also be directed to the general development—the time of teething, walking, talking, control of the sphincters (bed-wetting), age of puberty and habit and amount of sleep ; and to the general habits of action—whether the patient was lively or placid, active or sluggish, energetic or lazy. Nervous phenomena should be searched for in detail—convulsions, local spasms, tics (head-rolling or nodding, nose-picking, nail-biting), excessive crying or screaming, sleep-walking, sleeplessness and fears of the dark.

(II.) Intellectual. This should include the school record, giving the class and age at leaving, and the general attainment and any proficiency or deficiency in special subjects. The after-school education should be noted, especially in relation to opportunity and desire for it. Adult intelligence is displayed principally in foresight, planning, ability to concentrate, and in the kinds of interest (literary, scientific, artistic, etc.). Where there is any suspicion of backwardness, an intelligence rating should be done. (The Terman modification of the Binet-Simon scale, adapted for British children, is the most convenient. The necessary forms are published by G. Harrap & Sons, but the method gives reliable results only in the hands of those accustomed to use it.)

(III.) Emotional. Emotional reactions, which the patient may have shown conspicuously in childhood and later, are best inquired for specifically. Was he timid, anxious, happy or serious, moody or placid, or given to worry ? Did he have temper outbursts ? Was he easily depressed or easily elated ? Did he have any unusually intense interests, *e.g.* in religion ? Was he suggestible ? These are subjects which naturally have to be approached very carefully and are usually best inquired for piecemeal in the course of increasing acquaintance with the patient.

(IV.) Psychosexual. Where the case seems to demand it, some of the following inquiries should be made, but with the utmost tact. The source and nature of sex information as first acquired and later should be ascertained, as well as early evidences of sexual curiosity, the time during which masturbation was indulged in, whether the patient was frank or prudish, the presence of any perversions, the attitude to the same and the opposite sex, as shown by attachments, love affairs and their outcome, attitude to marriage and reasons for celibacy.

(V.) Economic. The degree of economic independence achieved by the patient is important. The jobs held, the reasons for changing from one to another, the general efficiency in them, and the remuneration, give a useful objective basis for estimating the degree of success obtained in general social adaptation.

(VI.) Social. The family environment is of great importance. The disposition of both parents should be ascertained as nearly as possible, and that of

brothers and sisters with whom the patient was closely associated. Preferences for one or another on the patient's part are to be inquired for. The type of school and the patient's ability to get on with others—teachers, employers, companions—are important topics.

Personality. From the data thus obtained of the patient's history previous to his illness an opinion may be formed of his development as an individual and as a member of society. We learn what his handicaps were, and with what success he met them, as well as what disadvantages he possessed and what use he made of them. There emerges not only the history of the patient, but a conception of his " personality " as well. " Personality " is an important notion in psychiatry. It denotes not the mere additive product of an individual's traits of character and temperament, but their integration into a working whole. It has been found that there is often a specific relationship between an individual's personality and the type of mental illness he develops. The most frequent and clear-cut types of personality are the syntonic or cyclothymic, the schizoid, the paranoid, the hysteric or mythomanic, and (of disputed significance) the epileptic. Moreover, it has been observed that the progress of most cases of mental illness depends to a considerable extent on the personality that the patient possessed before the outbreak of symptoms : the better psychical stuff the patient is made of, the more likely is he to make a good recovery, just as in diseases of the body the constitutional resistance matters a great deal. Hence it is very important to know how the patient dealt with the various problems that life presented to him before his illness—whether he met his difficulties in a straightforward, determined way, or was shirking, timid, shy, or sensitive, or was readily depressed and worried ; whether he tended to blame others rather than himself when things went wrong, or resorted overmuch to day-dreaming instead of working ; and whether he (or she) made the most of his aches and pains, or was given to exaggerated self-display in other directions. These are only a few of the numerous lines of inquiry that will furnish clues not only for understanding the patient as a human being, but for grasping the significance of many of the symptoms. Such inquiries are naturally much more important in the preponderatingly " endogenous " variety of psychosis (developing more from within the personality), *e.g.* paranoia, than in those resulting from the incidence of traumata from without (as in infections, *e.g.* syphilis producing general paralysis).

MENTAL EXAMINATION

(I.) **General Demeanour.** This is to be obtained from direct observation of the patient. The following points should be noted : (1) *Facial expression*, manifesting or lacking expression, as sad, uneasy, anxious or afraid, or happy, elated, beatific or ecstatic, or dull, unresponsive, immobile or mask-like. (2) *Dress.* Some patients are careless and untidy ; others are over-elaborate or fantastic in their dress. (3) *General activity.* Some patients are under-active and may, in addition, show slowness in movement (retardation). Others are over-active (psychomotor excitement), which is usually an expression of the prevailing mood, *e.g.* wringing of hands in apprehension. Many patients show bizarre or peculiar activity, such as stereotyped movements and attitudes, echopraxia (automatic imitation of what he sees others do), mannerisms, *flexibilitas cerea* (waxy flexibility, the patient's limbs remaining indefinitely in any position in which they are placed by the examiner). Local disorders of activity, as tic or tremor, rigidity, paralysis or abnormal gait, should also be noted. (4) *Speech* (including stream of talk and disorders of articulation (dysarthria) and aphasic disorders). It is important to take verbatim samples, especially of the spontaneous utterances. (*a*) In his talk the patient may pass rapidly from one topic to another by apparently superficial association (" flight of ideas "), or there may be mere pressure of talk (much talk but no rapid change of topic), circumstantiality (too much detail, like Mrs. Nickleby), retardation (slowing) or blocking

(sudden interruption from within), and all degrees of disconnection up to "a word-salad," or "verbigation"—a superficially meaningless concatenation of words, usually substantives. (*b*) Mutism (absence of both articulate and whispered speech), with or without ability to write, occurs in some patients, especially as part of a stupor (failure to respond to any stimuli whatsoever). (*c*) Articulation disorder occurs as mannered intonation in, *e.g.* fantastic paranoics, or as slurring and syllable-stumbling in general paralysis. (*d*) Aphasic disorders, if present, require special investigation by the methods described in the neurological section. (*e*) Writing. A sample of this should always be taken as part of the neurological examination, but in the absence of spoken speech it is sometimes possible to obtain information in writing, which then becomes of the highest importance. Inability to write may be associated with absence or defect of speech (*i.*) without organic lesion as *mutism*, depending on the patient's belief that he ought not to or cannot speak, or *aphonia*, depending on a functional paralysis of the vocal cords; (*ii.*) with organic lesion, when the writing difficulty is part of an aphasic or dysarthric disorder.

(II.) **Extent of co-operation** with the environment (*rapport*). The degree of co-operation is most important from the aspects of medical examination, treatment and general handling, and prognosis. Some patients refuse to eat, others to take medicine; some will not see a doctor, others refuse to go to hospital. Mental patients differ from most others in that many of them will not admit that they are ill in any sense.

(III.) **The patient's own story** of the events leading up to his present condition is of the utmost importance. The patient should be encouraged to give his own account. This may be done spontaneously (when verbatim samples will already have been secured) and require only occasional interpolation of a question, or it may be given only in answer to questions, beginning with the simplest (and making verbatim notes), *e.g.* "What is your name? your occupation?" The patient's attention may be obtained only on reiteration of the same question (in preoccupation and in some organic conditions). The relevance of the answers should be observed.

(IV.) **Activity,** subjectively described (the objective data being obtained from Section (I.)). "Can you do things as well as formerly?" (feeling of insufficiency). "Have you difficulty in beginning to do things?" (initial retardation). "Have you felt able for your work?" The questions must be varied to suit the case. The above might only succeed in irritating an over-active elated patient, who may be asked if his work comes very easily to him, etc.

(V.) **Affective status (mood)** is gauged in the following ways:—

(a) From observation of the *facies* and *behaviour*.

(b) *Spontaneous account* of, *e.g.* happiness, fear, depression (often expressed directly as "downhearted," "miserable," or indirectly as "lack of interest," etc.). It is usually necessary, however, to resort to direct inquiry. The language of the emotions is sadly wanting, and few patients have the gift of describing their affective condition, even when descriptive words are supplied to them.

(c) *Direct Inquiry.* It is best to begin with general questions, as "How do you feel?" "What mood are you in?" "How are your spirits?" If these do not elicit a satisfactory statement it is useful to enumerate a variety of words descriptive of mood to enable the patient to choose the appropriate one. Thus: "Are you sad, or happy, or afraid, or anxious?" The degree of the patient's insight into (realisation of) the abnormality of his affective condition is important. "Why are you depressed" (anxious), "etc.?" "Is your depression justified?" Depressive moods in particular are accompanied by inability to have emotional response to or to enter into the feelings of others. This may distress the patient, and may be his chief complaint. A *feeling of unreality* may result when the patient *knows* that things are real, but on account of his own lack of emotional response cannot *feel* that they are.

(d) *Affective or Mood Fluctuations.* There are often exacerbations of a given affective condition from time to time. Depressed patients usually feel worse in the mornings. Anxiety often occurs in attacks. Variation in the depth of depression may be so great that there may be periods of a few hours, especially in the evenings, when the patient feels and looks almost normal. This variation can be very deceptive unless one is constantly on one's guard.

Laughing or weeping may occur with undue readiness, and may be appropriate to the prevailing affect, as in manic excitement, or a depression, although often the depressed patient, for example, complains that he cannot weep; or may take place inappropriately, *i.e.* without corresponding affect or in the presence of a situation calling for a different type of emotional response. This may be accompanied by insight, as in certain organic (especially arteriosclerotic) conditions. In other cases (psychogenic dissociation, as in schizophrenia) there is no apparent realisation of the discrepancy.

Specific reactive tendencies arising from the affective condition are of great practical import from the points of view of care and treatment.

Suicidal wishes or actual attempts, usually in a setting of depression, aggressive acts (homicidal) or tendencies in panics of fear or in morbid anger or in persecuted states, should be very carefully inquired for both from the patient and from his friends. It is much better that a depressed patient should ventilate his suicidal ideas than that the physician, from a false notion that he may suggest them, should not inquire and consequently remain in greater uncertainty than is necessary.

The congruity or otherwise of thought-content and mood must be estimated from a consideration of this section and Section (VI.). Apparent incongruity suggests a serious type of disorder (schizophrenia). For example, a patient may have the most disturbing kind of thoughts, the most vilely threatening hallucinations, and yet appear unmoved; or may hear sad news, as of the death of a relative, and either display indifference or giggle immoderately.

(VI.) **Thought** includes the subjective experience of thinking and the *form* of thinking, which must be distinguished from its *content:* the latter is what the patient says; the former is how he says it.

(a) *Subjective Experience.* "Is thinking easier or more difficult, faster or slower, than formerly? Can you concentrate?" Inability to concentrate may result from an attention defect (*v. infra*), as in the organic type of mental reaction. A simple and useful test of the capacity to sustain a train of thought is the patient's ability to subtract 7 successively from 100 till there is no remainder. Lack of concentration is more commonly the result of absorption of attention in personal concerns—worry, etc.

(b) *Form.* Change in the form of thought is deduced from the talk of the patient. All degrees of disconnection may exist up to incoherence. Also the patient may attach symbolic meanings of his own to ordinary words, or he may invent new words (neologisms).

(c) *Content.* General inquiries include such questions as "Do you worry about anything?" "About what?" "Have you had any unusual experiences?" "Have you felt as if people were watching you or talking about you?" (ideas of reference). Persecutory (delusional) trends should be inquired for, at first in an indirect way. "Does any one treat you badly?" "Is there a concerted plan in this?" "What makes you think so?" A grandiose trend, if present, usually appears readily in the course of conversation. If it does not, and is suspected, it may be sought with such special questions as one's knowledge of the individual case may suggest. Delusions of unworthiness or of sin usually appear spontaneously, but if not, and they are suspected, they can be brought out in appropriate cases by asking the patient whether he feels he has done wrong, and in what way. Hypochondriacal delusions are revealed in the investigation of the physical state, in which the patient should always be questioned regarding the functions of his

bodily systems. Anxiety about physical illness, or the possibility of it, should be carefully distinguished from the more or less settled (and usually unfounded) conviction of disease in hypochondriasis. This has to be done from the manner of statement, the amount of reassurance possible, and the affective setting.

Feelings of influence or passivity may find expression in curious acts or bodily attitudes, or may be revealed only in questioning. "Do you do anything queer or strange?" "Why do you do so?" "Why do you do this?" (naming some unexplained act). "Do thoughts come into your head that do not belong to you?" (autochthonous ideas). "Have you ever had the feeling of being hypnotised or of mind-reading, of hearing your own thoughts or those of others?" Hallucinatory experiences may be betrayed by such acts of the patient as his assumption of a listening attitude, mumbling, gesticulating, sudden or maintained silence and impulsive episodes. More often they have to be inquired for in a general way, as "Have you any peculiar thoughts?" "Do you hear voices?" The presence of auditory hallucinations leads to the questions "Are they noises or voices which you hear?" "Real voices or only your thoughts?" (pseudo-hallucinations). "What do they say?" Visual hallucinations: "What do you see?" "Are they real or only a vision?" "Are they small" (Lilliputian) "or coloured?" "Are they to one side or another?" (hemianopic hallucinations). Hallucinations of taste, smell and hearing should also be inquired for. It is important to know whether any of the sense-deceptions are illusions and whether they depend on local disease (of the sense-organ involved) or, as is sometimes the case, on disease elsewhere affecting the sense-organ reflexly. Organic misinterpretations are more probably of illusory than hallucinatory nature, although some experiences, such as that of "a voice coming from the stomach," are difficult to interpret as based on disordered organic sensation.

(VII.) **Orientation** as to person, place and time.—"What is your name?" "What is my name? my occupation?" "What place is this?" "What is to-day's date?" and if the latter elicits an indefinite reply, "What month is it? what year?"

(VIII.) **Memory** should be tested for inconsistencies or actual blanks.

(a) *Personal Events* (i.). Remote. "When born? and where?" "How old does that make you?" Age of beginning and leaving school, dates of changing jobs, of marriage, births of children, etc., should be asked for where the power of memory is under suspicion. Some or all of these will have been answered in the personal history given by the patient. (ii.) Recent. The patient's account of the chronological development of his illness will have furnished hints under this head. The dates can be checked from the story of the patient's friends. "Since when has there been a change in you?" "How did you come here? With whom?" "What meals have you had to-day?" "Where were you yesterday?"

(b) *Formal Tests of very Recent Memory.* (i.) Ask the patient to remember three things: an address, *e.g.* 315, Bond Street; a part of the body, *e.g.* a finger; and a vegetable, *e.g.* a carrot. Read them over to him once and have him repeat them. Tell him you will ask for them again in five minutes. (These five minutes may be occupied with other questions and this fact noted.) If at the end of that time he is unable to reproduce them on demand, another similar test should be given and the results noted. (ii.) The span of immediate memory may be tested by the number of disconnected digits, letters or words the patient can retain. The lower limits of normal retention are six digits, six letters, and five words. For example, six digits should be read to him at the rate of one per second, *e.g.* 485736. If he succeeds more should be tried; if he fails, fewer.

(c) *Rote Memory.* Ask him to repeat the alphabet, the months of the year, the Lord's Prayer, and to count from 1 up to 20.

(IX.) **Attention.** (*a*) This may be gauged from general observation during examination. Any tendency to spontaneous fluctuation should be noted.

(*b*) Special tests may be used where there is a doubt as to the continuity of attention, *e.g.* in certain organic conditions if sufficient co-operation can be obtained.

(X.) **Apperception.** The patient is asked to read aloud a test story, such as the following, which is given to him in ordinary type:

"A cowboy from Arizona went to San Francisco with his dog, which he left at a dealer's while he purchased a new suit of clothes. Dressed finely, he went to the dog, whistled to him, called him by name and patted him. But the dog would have nothing to do with him in his new hat and coat, but gave a mournful howl. Coaxing was of no effect, so the cowboy went away and donned his old garments, whereupon the dog immediately showed his wild joy on seeing his master as he thought he ought to be."

Any mistakes in reading are noted. If his eyes are not in sufficiently good condition for reading, the story may be slowly read to him. He is then asked to reproduce it in his own words. The result throws some light on attention (IX.), interest, recent memory (VIII.), tendency to invention where details are forgotten (confabulation), emotional responses, and the ability to see the point.

(XI.) **General knowledge of past and recent events.** The grasp of the former is dependent chiefly on education and memory, of the latter (especially those since the onset of illness) largely on the amount of interest which has recently been devoted to ordinary affairs. The patient should be asked to name, for example, the capitals of some of the chief countries of Europe, the dates of the recent war. Knowledge of more recent events is to be estimated from questions based on recent newspaper information.

(XII.) **General Intelligence.** The "average adult" tests of the Binet-Simon scale may be a ppliedin whole or in part, *e.g.* the differences between laziness and idleness, evolution and revolution, poverty and misery, character and reputation, and ability to repeat six digits reversed. Where intellectual defect is suspected, the Binet-Simon series of tests, or a selection from them, should be applied sufficiently to determine the mental age (= total score in Binet-Simon test).

(XIII.) **Insight.** The degree of the patient's appreciation of the fact that he is ill and of ability to regard his symptoms of illness as such is of the greatest importance for prognosis and treatment. The questions already posed under "Mood" and "Thought," and the patient's spontaneous statements, will already have thrown some light on this. In addition, special inquiries should be made, as, for example, "What do you think of your present condition?" "Do you consider your present condition in any way abnormal?" "Is it an illness?" Special incidents should be elucidated, *e.g.* impulsive or peculiar actions, suicidal or homicidal attempts, moral lapses, and anything betraying lack of judgment (*e.g.* monetary extravagance).

Finally, the results of the above investigations should be summarised, the positive findings being tabulated in what appears to be their approximate order of importance for the symptom-picture.

A perusal of the above account of a moderately complete mental examination, together with its application in as many cases as the student can find, will give him some grasp of the spirit and general principles of a psychiatric examination. With this preliminary training, the following brief scheme may be used as a framework for the more rapid clinical examination that the exigencies of time and practice may compel.

ROUTINE EXAMINATION OF MENTAL STATE

(1) *General Behaviour.*

(2) *Stream of Talk.* Note special characteristics, such as slowing, flight of ideas, incoherence. Give brief verbatim sample.

(3) *Mood.*—"How do you feel?" If necessary make the question more specific, *e.g.* "Sad?" "Afraid?" "Happy?" etc.

(4) *Special Preoccupations* ."Any trouble recently?" "Peculiar experiences?" "Have you had any imaginations?" "Been fairly treated?" "Persecuted?" "Under any special influence, *e.g.* hypnotism, electricity, etc.?" *Hallucinations.*—"Do you hear voices?" "Do you see things?" "What, where and when?" *Obsessions* and *Compulsions.*—"Any troublesome thoughts?" "Have to do certain things in a certain way?"

(5) *Sensorium* and *Intellectual Resources. Orientation* (as to place and date and persons). *Memory* (specially important in organic psychoses). (*a*) Remote past (life with dates) controlled in taking history. (*b*) Recent past (some account of past few days). (*c*) Immediate retention (number, name, objects shown, digits). *Attention*, steady or fluctuating; distractibility. *Grasp of General Information* (kings? premier? wars? etc.). *Calculation:* 100-7 (errors? Time in seconds). *Judgment.*—Ability to make reasonable plans. *Speech* and *Writing Tests.*

(6) *Insight into Illness.* Any admission of being sick or nervous? Realisation of the nature of the disorder (complete or incomplete).

(7) *Sleep* and *Dreams.*

(8) Make a special note of topics to be further investigated in subsequent interviews.

THE PSYCHONEUROSES

ANXIETY PSYCHONEUROSIS

This psychoneurosis is a state of mental distress or anxiety, usually accompanied by physical symptoms, which is out of proportion to the apparent facts of the situation in which it arises.

Ætiology. 1. Heredity may play an important part. Some individuals appear to be constitutionally sensitive and therefore prone to emotional overreaction.

2. Acquired habits of mind as a rule are the chief cause of the illness. These frequently originate in childhood as conditioned reflexes. The emotional reactions of the child depend largely upon those of the adults who surround him. The child whose mother shows signs of terror at a thunderstorm will himself develop an excessive emotional reaction to this stimulus. So with other and more commonplace happenings. If the mother displays anxiety over the child's health, he himself is likely to grow up with an exaggerated fear of illness. Particular emotional experiences also may have a lasting effect in this way. A girl who has been the victim of an indecent assault may develop a morbid fear of the male sex, and so with other kinds of emotional trauma. In adult life the common fault is that of ignorance. In response to some adequate stimulus, an emotional reaction occurs with its train of physical accompaniments. There is, for instance, a feeling of faintness and palpitation of the heart. The subject takes this to be evidence of cardiac disease, and develops anxiety over his symptoms. This in its turn leads to further emotional reaction and palpitation. So a vicious circle is frequently set up which in time becomes a veritable habit. It is doubtful, however, whether anxiety ever develops in this way in a subject not predisposed by temperament, training, or present conflicts.

The original emotional reaction may simply have been misunderstood. Often, however, the emotion itself may have been unconscious, and this for reasons such as have already been discussed. A man may, for instance, be seized with symptoms of excessive anxiety at having to give an account of his work to his superiors. The associated emotion is one of shame and therefore fails to come within the field of consciousness. The emotional reaction, with its consequent palpitation, anorexia, gastric discomfort or other physical symptoms, then

appears as an isolated phenomenon, and actually becomes a source of further anxiety. Unfortunately much harm may result in such cases from erroneous or uncertain medical diagnosis. If the physician accepts the symptoms as having a basis of physical disease, the patient's anxiety is likely to become greater, and the symptoms to be aggravated.

3. Physical disease and disorder may contribute to the development of an anxiety neurosis in two different ways. They may, in the first place, form the starting point for a vicious circle, as has been described, if the patient is already predisposed by past experience to over-anxiety about his health, or if his physician takes an exaggerated view of the gravity of his illness. In the second place, fatigue and toxic illness may by their direct influence upon the mental processes impair judgment and give rise to false perspective, so that molehills in the path of life are regarded with the anxiety due to mountains.

4. The definition given does not exclude environmental stress from the ætiology of anxiety psychoneurosis, but emphasises the apparent lack of circumstantial justification for the patient's reaction. This is because the circumstances mean more to the patient than is consciously apparent either to him or to an observer.

Symptoms. MENTAL. At the root of all the symptoms lies morbid anxiety. This, however, is by no means the most frequent complaint. The anxiety itself may be latent, and the secondary symptoms first lead to a medical consultation. Common complaints are of inability to concentrate, loss of memory, indecision and a general sense of inadequacy. Such are the natural results of continuous anxiety, which fills the mind to the exclusion of other subjects. They are, however, often misinterpreted by the patient, who regards them as signs of approaching insanity. *Insomnia* is frequently an important symptom. Two varieties are met with. In the first, which is associated with manifest anxiety, the patient's mind is so full of his cares as to prevent the onset of sleep. The other is met with where repression has occurred, when the patient is to a great extent unconscious of the emotional origins of his illness. In these cases it often happens at bedtime that the mind becomes over full of a stream of thoughts upon neutral subjects, to the exclusion of any view of the hidden worry, and also of sleep. When sleep has eventually been won in such a case it is often broken by terrifying dreams or nightmares, from which the subject wakes with all the sensations of extreme terror. Anxiety about the sleeplessness and its possible effects aggravates the condition.

The anxiety when manifest may be of a general or of a particular nature. General anxiety reveals itself in a tendency to exaggerate difficulties, and exhibit an excessive emotional reaction to all stimuli. Particular anxieties (sometimes called phobias) are numerous and variable.

Fears of Disease. The patient becomes convinced as the result of some abnormal sensation that he is suffering from a serious disease. The common fears are of cancer, syphilis and pulmonary tuberculosis. Although examination and reassurance may for a time dissipate the fear, it usually recurs until the underlying neurosis has been properly treated. Fears of cardiac, renal and gastro-intestinal disease are also of common occurrence.

Fear of insanity has already been alluded to. It is of common occurrence, and is based by the patient upon the difficulty in mental concentration, and sense of emotional tension from which he suffers.

Fears of certain Situations. These are innumerable. Some of the commonest are fear of open places, of crowds, of closed spaces, of travelling in trains. They may be paralysing in their intensity and seriously interfere with the patient's life.

Fears in relation to Sexual Matters. The commonest of these concerns masturbation. The patient has perhaps practised this habit in the past or continues to practise it at intervals with much emotional conflict. He feels that he has thereby ruined his mental and physical health, and that his illness is due to this cause and

is a punishment for his sins. Any chance encounter with sexual topics gives rise to an emotional over-reaction. The subject being one of which he is ashamed, the origin of his anxiety is frequently, at least for the moment, unconscious. Similar fears may have their origin in anxiety concerning sexual thoughts of which the subject is ashamed. In certain phases of life, and especially in certain persons, these may be of a homosexual nature.

The occurrence of seminal emissions is sometimes the centre of anxiety. Since anxiety itself may result in seminal emission, this is apt to set up a vicious circle.

Impotence in the male is a not uncommon complaint. The symptom may consist of premature ejaculation or of inability to obtain a sustained erection. This is commonly associated with fears concerning past masturbation or seminal emissions.

NERVOUS. *Extreme liability to fatigue* (mental and physical) is a common symptom. The patient complains that he is incapacitated for his work, is unable to sustain his part in conversation, and becomes exhausted after walking up a flight of stairs. Careful inquiry will usually discover that this fatigue is differential in its action, varying with the extent to which the patient is interested in his surroundings. Thus a man may be unable to concentrate upon work of a monotonous character for more than half an hour, yet give his undivided attention to a play for two or three hours at a stretch. Despite his inability to meet the obligations of social small talk, he will discuss at great length and with the utmost keenness the symptoms of his illness, and although he may feel unequal to visiting his doctor, will walk a mile to see a football match without undue fatigue.

Headache is another common symptom. Sometimes it is described as a pain, which is then as a rule intermittent, coinciding with moments of intense anxiety. More frequently it is referred to in terms of discomfort and is continuously present, as a feeling of pressure upon the top or back of the head, a leaden feeling, or a sensation of tightness, fulness or heat.

Giddiness is a frequent complaint. It may be continuous or take the form of attacks which last from a few minutes to several hours. There is no sensation of whirling (as in the vertigo of organic disease), but a subjective feeling of unsteadiness with fear of falling. This fear may be so vivid that the patient dare not move and will cling to others for support. When the symptom is continuous he will sometimes complain that he cannot walk abroad without the arm of a friend to steady him.

Tremor of the limbs is an occasional symptom in association with paroxysm of fear.

ALIMENTARY SYSTEM. Dysphagia is not uncommon. It may be in part due to lack of saliva, but the complaint is usually that the food sticks in the throat and will not go down. It is often associated with fear of cancer. Gastric discomfort and flatulence are common complaints. The feeling is one of fulness which bears no constant relation to the taking of food, but commonly occurs during or immediately after the meal. The patient seeks to relieve this sensation by belching, and in consequence swallows air, which may produce actual distension of the stomach. A characteristic feature of this form of dyspepsia as a rule is its selective nature. The patient will assure us, for instance, that he invariably has indigestion after eating beef but not after mutton; tea is fatal to his stomach, but coffee innocuous; he cannot tolerate green vegetables, but can eat raw apples with impunity.

Constipation is a common complaint. The patient having for some trivial cause been unable to obtain an evacuation and having had recourse to a purge, becomes anxious upon the next occasion whether his bowels will open without the aid of a drug. The anxiety itself interferes with the reflex process of defæcation, and this in turn leads to a habit of mind in which the consciousness of an aperient taken beforehand is necessary to success.

Diarrhœa is sometimes complained of, but on analysis proves a misnomer, the fact being that the patient feels need to open his bowels under particular circumstances, especially when no convenience is available.

CARDIOVASCULAR SYSTEM. Præcordial discomfort and palpitation are the prominent complaints under this head. Extreme liability to blushing may be the focus of anxiety.

RESPIRATORY SYSTEM. Subjective sensations of choking and dyspnœa may occur with paroxyms of panic and fear of impending death.

SKIN. There may be profuse sweating, commonly associated with fears of consumption. Numbness and tingling is an occasional complaint.

Many so-called "neurasthenias" are really anxiety neuroses in which complaints of fatigue are specially prominent.

Diagnosis. This must depend partly upon the exclusion of organic disease as a direct cause of the symptoms, partly upon the recognition of morbid anxiety as their source. As a rule this is not difficult. It must be remembered, however, that certain chronic intoxications, of which phthisis is the chief example, may be important contributory factors.

When the illness has been recognised as a mental disorder it still has to be distinguished from others, such as dementia præcox and manic-depressive insanity.

In some cases of dementia præcox morbid anxieties and fears may occur as early symptoms. These, however, differ from those of the anxiety neurosis in being not only unreasonable, but inexplicable, except in terms of the patients' fantasies if these can be elicited. The patient may, for instance, be anxious about the state of her digestion, but behind this will lie the fixed belief that the lining of her stomach has been corroded away by poisons introduced into her food.

The symptoms of a mild case of manic depressive insanity may resemble in many respects those of an anxiety psychoneurosis. In the former illness, however, depression is usually a more prominent feature, and is largely independent of circumstances. The patient cannot so easily be roused to take an interest in his surroundings; his symptoms show little variation with changes in his environment. He gains little or no comfort from the physician's reassurance, whereas the neurotic almost always shows a marked, if temporary, improvement after such an interview. The manic-depressive is more consistently apt to blame *himself* for his troubles, and will often in giving his story interpose remarks to this effect. His depression also is apt to show a daily rhythm, being at its worst in the early morning. He is less likely to be troubled with difficulty in getting off to sleep than by waking in the small hours of the morning with a feeling of profound melancholy. The differential diagnosis may require in some cases a period of observation. It is important in a doubtful case that it should be settled, for the treatment of the two conditions is dissimilar. There is, moreover, a serious risk in the manic-depressive of suicide.

Prognosis. So far as serious sequelæ are concerned the prognosis is good. These patients do not become insane; but if untreated they may be incapacitated for work and social intercourse for long periods of time, during which they are miserable themselves and a burden to others. With proper treatment the outlook is good except in those cases in which the hereditary factor is prominent.

Treatment. This consists of analysis of symptoms, explanation and reassurance, the procedure being termed psychotherapy. Rest and drugs are also needed in certain cases. Isolation from friends is often desirable at the beginning, and it may be wise to forbid correspondence.

The taking of the history and the physical examination are all-important in the treatment as well as the diagnosis of the condition (**11**).

The patient should be encouraged to describe his main symptoms in detail, and further questions should then be directed towards the various bodily systems.

Notes should be taken. The patient should then be systematically examined. If analysis of the history and physical examination are sufficient to exclude organic disease, the patient should be told this. If any further investigation is necessary, he should be informed of this, and arrangements should be made as soon as possible for carrying it out. If there are any definite signs of physical disease, this knowledge should not be withheld from the patient, who must be led to feel that he is being treated with absolute frankness. He should further be given some idea of what the signs are and what is their significance. He may thus be led to understand that such organic defects as may be present are insufficient in themselves to explain his symptoms.

The taking of the history and physical examination should occupy at least one hour. Often this is insufficient, and a further interview must be arranged. It is essential that the patient should feel confident that his whole story has been appreciated, and that no possibility of physical disease has been neglected, for these preliminaries form the basis for further treatment.

Having assured the patient that his symptoms are not due to organic disease, the physician should proceed to explain that they are of course real, not imaginary, symptoms, and are such as may have their origin in emotional disturbance. An outline should be given in suitable language of the psychological principles described above (*see* p. 778). It may be pointed out, for instance, that a cat when frightened by a dog shows many disturbances of its bodily organs, including chemical alterations in the blood, acceleration of pulse rate, and rise of blood pressure, which may be measured, and alterations in the gastric movements, which may be observed with the X-rays, yet these changes do not indicate any disease either of the organs affected or of the nerves controlling them.

Further interviews should then be arranged for analysis of the patient's symptoms in the light of these principles.

The symptom is first traced to the date of its origin, and the patient is cross-examined as to any emotional difficulties which may have existed at the time. Often at first he may fail to call to mind any such troubles. The existence of unconscious mental processes should then be explained, and examples given of the way in which an emotional disturbance outside the field of consciousness may nevertheless give rise to symptoms of an emotional reaction.

In this way it is usually possible to discover adequate causes for the various symptoms, and as these are gradually explained they tend to disappear. An attempt should also be made to discover and explain to the patient the underlying habits of mind which have led up to his illness. In some cases these will be plain to his view ; in others a great deal of skill and experience may be necessary to unravel the emotional tangle.

Special methods of mental analysis may be necessary in some cases in order to bring to the light unconscious mental processes of importance. For these the works of Freud and his followers upon psychoanalysis should be consulted. The great majority of cases can be successfully treated by less complicated methods. As the patient begins to realise that he is being treated with sympathy and understanding, and that the treatment offers a real hope of recovery, his desire to co-operate gives strength to turn the light of attention towards aspects of his mind which have before been concealed by motives of shame or dread. Thus he gradually reveals himself to the physician, who is able by collecting the scattered threads of the story to discover the causes of his neurosis. In the presentation of these causes the physician needs to be sympathetic, for it will involve asking the patient to face faults and weaknesses in himself to which he has been blind. There is, however, nothing which these people appreciate more than the quiet assurance that others have passed through similar experiences, and that many of their friends (with whom they are apt to compare themselves unfavourably) have almost certainly suffered, perhaps in secret, from the same miseries and fears.

Since the treatment is chiefly concerned with the elicitation and evaluation of symptoms, those which have been described may be considered again under this heading.

An anxiety neurosis, if sufficiently severe and prolonged, is likely to lead to true exhaustion. It is wise therefore whenever symptoms of undue mental or physical fatigability are prominent to commence treatment with a period of rest. Insomnia should always be an indication for rest in bed as a preliminary to further treatment. It is important that the reasons for this procedure should be explained to the patient, who should not be allowed to conclude that rest alone will bring about recovery.

A week in bed, with subsequent return to normal activities in a further two or three weeks, will usually suffice. Psychotherapy should proceed simultaneously. If possible, the patient should be in a nursing home for this part of the treatment.

Mental Symptoms. *Inability to concentrate* is so often interpreted as a symptom of incipient insanity that inquiry should always be made in this direction. The fear is often concealed by the patient from others, if not from himself. This is especially likely if there is any family history of mental disease—a fact sometimes omitted or denied at the first interview. Complete assurance should be given upon this point. It should be made clear to the patient that, although his illness is a mental disorder, it belongs to a class of minor disorders or psychoneuroses which is distinct from the major mental disorders or psychoses, and that patients rarely pass from one illness into the other. The lack of concentrating power should then be explained as being due to anxiety. A man who has some unsettled worry at the back of his mind cannot give his full attention to his work. The origin of the anxiety and the causes of its perpetuation should then be dealt with in the manner already indicated.

Insomnia. In so far as this is directly dependent upon anxiety, it may be expected to improve with treatment of the cause. The patient often develops undue anxiety over this particular symptom, and will then need to be assured that many persons are in the habit of doing good work with fewer hours of sleep than he himself is getting, and that without any untoward symptoms. It should further be explained that anxiety is a *natural* cause of insomnia, and that as the treatment proceeds he will find himself improving in this respect. The power of hidden anxiety to cause terrifying dreams should also be discussed.

If the insomnia is of recent origin, such simple measures are often sufficient. Sleep, however, is a *reflex* process which depends largely upon habit, and this unfortunately holds good also for insomnia. Therefore, if this symptom has persisted for more than a few days, the physician should not hesitate to treat it by means additional to psychotherapy. The patient, as always, should be given an explanation of these means and their rationale.

The additional means available are (1) drugs, (2) habit formation, and (3) muscular relaxation.

1. If the insomnia is of comparatively recent duration, and is an object of much anxiety, the following plan is suitable. The patient is instructed the first night to take a sufficient dose of a reliable hypnotic to induce sleep (medinal grs. x, paraldehyde drs. ii, or chloral hydrate grs. xx, with pot. brom. grs. xl). On the following night he is told to have the medicine ready by his bedside and to take it without hesitation if he finds himself unable to sleep without it. A supply of the hypnotic is prescribed sufficient for a week. The patient should be assured that there is no danger of this procedure leading to a "drug habit." After a few nights it will usually be found that he will fall asleep naturally with the drug untasted by his bed, and will then have regained confidence in his ability to sleep unaided. When the insomnia is of longer duration it may be necessary to give sufficient doses of hypnotics to procure sleep over a longer period, the dose being gradually reduced as psychotherapy and other methods of treat-

ment become more effective. Treatment with drugs should always be combined with the other methods referred to.

2. Most persons have some kind of a ritual which, under normal circumstances, precedes and favours sleep. The hour, the room, the order of undressing, the book read in bed, all play a part as conditions facilitating the sleep reflex. This also is true of insomnia. The patient who is being trained to regain the habit of sleep will therefore benefit from a change of surroundings and of bedtime habits. A change of bedroom is often in itself useful.

3. Muscular relaxation is the most important physical condition for the onset of sleep. Patients suffering from anxiety are frequently in a state of excessive muscular tension, which places them at once at a disadvantage. This symptom, of course, depends upon the underlying neurosis, and improves with treatment of its cause. Nevertheless as a cause of insomnia it may be controlled to some extent by training the patient to relax his limbs. The physician should ask the patient to allow one limb to lie absolutely passive, and test its passivity by raising and handling it. It will usually be found that the patient, so far from letting the limb follow the directions of gravity, is constantly exercising it by his will. With daily practice and concentration, most persons can be taught to relax in turn, and finally simultaneously, all the muscles of neck, trunk and limbs, and this becomes a valuable preliminary to sleep.

Fears of Disease. The preliminary examination must be sufficiently thorough to provide an impregnable position from which the physician can give an assurance that the symptoms are not due to organic disease. This assurance, although it may give temporary relief, is not in itself sufficient treatment. The intelligent patient as a rule will proceed to state that the symptoms exist and must have some cause. The physician then proceeds to explain the manner in which bodily symptoms, often simulating those of organic disease, may result from emotional disturbance. The fear is traced back to the date of its origin, and analysis and explanation are continued. Fears of disease are often associated with primitive ideas of illness as a visitation for past sins, and thus not infrequently have their origin in remorse over sexual misdemeanours.

Fears of special situations should be analysed by giving the patient a preliminary explanation in simple terms of the conditioned reflex and unconscious mental processes. When he has been taught that behind his unreasonable terror there may be an intelligible cause he is urged to carry his thoughts back to the time when the trouble began, and to talk freely of his life at that time, especially of any secret hopes, fears, or disappointments. If the physician himself is sufficiently assured that a cause is to be found, the facts will as a rule gradually disclose themselves. The patient is led to face the truth, and encouraged not to avoid the situations which provoke his fears, but to train himself to meet them in the light of the common-sense explanation which he has received.

Fears in relation to Sexual Matters. The commcnest of these concern masturbation. Upon this subject the physician, whatever his own prejudices, must be ready to give unbiassed and impersonal advice.

The patient often feels that in practising this habit he has not only fallen from his own ideals, but has proved himself morally degenerate and unworthy to associate with his fellows. He may be honestly assured that among healthy males there are few, if any, who at one time or another have not practised masturbation, and that the friends and acquaintances with whom he compares himself so unfavourably have certainly had experiences similar to his own.

Additional fears are concerned with the ill effects which masturbation has been supposed to have upon the health. Such notions as that the habit leads to insanity and consumption are occasionally inculcated by ignorant parents or schoolmasters, and are sedulously fostered by quacks for their own mercenary ends.

Actually there is no evidence to show that the act of masturbation *per se* has

any more harmful effects than natural sexual intercourse. The sequels, such as headache and depression, of which the patient complains, are the results, not of the act itself, but of the mental distress with which it is associated, and this is to a large extent proportionate to the patient's fears of its consequences. The patient will often maintain that the seminal loss is in itself weakening. It may be pointed out that it is no greater than in normal sexual intercourse which occurs regularly in the lives of thousands who are in no way the worse for it. As to the remorse occasioned by falling from the standards which he has set himself, it may be pointed out to the patient that possession of such standards is itself a point in his favour, and that it is in the nature of ideals that a man's reach should exceed his grasp.

Fears concerning frequent seminal emissions should be dealt with in similar fashion. Such " losses " cannot cause the symptoms which the patient attributes to them, and are in themselves harmless. Anxiety, on the other hand, may be the cause of seminal emissions.

Frank discussion of these subjects will, as a rule, reduce them to their proper place in the mental perspective and leave the way clear to further inquiry into the origin of the neurosis. The patient who suffers from anxieties of this nature is often shy of confessing to them, but will always respond to inquiries if these are made in the proper way. He should be told that all normal persons suffer to some extent from sex difficulties, and he should be questioned directly about his own experiences in regard to seminal emissions and masturbation.

Difficulties of this nature are less frequently encountered among women, and when present are less easy to disclose. Nevertheless worries over masturbation are not uncommon, and must be discussed with similar frankness if there is reason to suspect their existence.

Sexual impotence in the male is commonly associated with worries over past masturbation. Such a man on his marriage proceeds to intercourse in a state of anxiety lest his past misdemeanours may have rendered him incapable of the sexual act. The anxiety is itself sufficient to cause impotence. When it has been explained to the patient that masturbation is a universal habit he will regain confidence. Or a man who has previously been normal in this respect may attempt intercourse at a time when he is suffering from real exhaustion, and having once failed, may develop anxiety which renders him impotent on future occasions. Here again frank discussion and explanation will often suffice to cure the condition. It is sometimes necessary to see the wife separately and clear her mind upon the subject of sex hygiene. There is no more potent factor in causing impotence than a wife who exhibits doubt or anxiety as to her husband's sexual ability.

Physical Symptoms. After the negative physical examination the patient's symptoms should be examined in detail, and explained as being due to emotional reaction. Such an explanation is often new to the patient, and he may need time to comprehend it. Any attempt at forcing it upon him is likely to arouse opposition. Arguments have to be repeated and illustrations given from other cases or from daily life. Every one knows, for instance, that worry may cause a headache. That a man who stands up to address a large audience may experience a sensation of giddiness or unsteadiness on his feet in association with his anxiety to create a good impression is a matter of common experience. Tremor of the limbs is a frequent accompaniment of fear.

Dyspepsia is a well-known symptom of anxiety. A man whose digestive functions are disturbed by a hidden worry is apt to ascribe his discomfort to some particular article of his food. Having once conceived this idea, whenever he partakes of this foodstuff it is with the fear that it will produce symptoms. The fear itself is sufficient to interfere with normal digestion. A vicious circle is thus set up which is at the bottom of the " selective dyspepsia " which is so common a symptom of the anxiety neurosis. Flatulence is due to misinterpretation of

the sensation of fulness. In his efforts to belch the patient swallows air, and may produce an actual distension of the stomach. If the patient is simply instructed to restrain the impulse to eructate, he may prove for himself the truth of this explanation.

Præcordial discomfort and palpitation are again well-known accompaniments of anxiety, as also are sensations of respiratory embarrassment and perspiration. When the patient is satisfied that his particular symptoms have no organic basis, and are such as *may* be caused by emotion, he is led along the lines already described to call to memory the origin of his symptom and its emotional contexts. Thus the inner history of the illness may in time be disclosed.

The aim of treatment is to give the patient such insight into the origin of his symptoms as will rob these of the appearance of illness. Even when this is accomplished his troubles are not necessarily at an end, for he may still be obliged to meet the emotional difficulties which formed the basis of that illness. Often the illness itself will have provided some excuse for avoiding these difficulties. Recovery may bring with it the necessity to return to distasteful surroundings. Hence at this point there is a tendency to relapse. The patient begins again to doubt his mental or physical fitness for ordinary life. This tendency must be met by analysis and explanation of the unconscious motive which is responsible—the desire to find in illness an excuse for evading unpleasant duties. Often the situation may be made easier for the patient by an interview with relatives or friends, whose sympathy may be enlisted on his behalf.

HYSTERIA

The term hysteria is used to describe a particular variety of mental disorder which finds expression in the form of bodily symptoms, or gives rise to abnormal behaviour of a characteristic type (somnambulism, fugues). Some obviously mental symptoms, however, such as islands of amnesia, or hallucinations, may appear as the total or partial manifestations of a hysterical mental disorder.

Ætiology. Symptoms of hysteria may appear at any age after infancy. They are more commonly met with in the female sex, but under exceptional conditions, such as those met with in the Great War, may be of frequent occurrence amongst adult males. In the majority of cases heredity plays a relatively unimportant part in the ætiology. Of far greater importance are the habits of mind developed by precept and example during childhood and adolescence. In many instances slight physical illnesses or accidents are exaggerated by the parents, who comfort the child with toys or sweetmeats, or the symptoms form an excuse from the performance of some unpleasant duty, or they may secure for the child the desired position of being the centre of attention. In this way too often are laid the foundations of a habit of mind which tends to make the individual unconsciously rely upon physical symptoms as a refuge from the various difficulties of everyday life. On the other hand, the person who is trained in the exercise of his critical faculties, and is able to take a more or less logical view of his life problems, even if he is unable to solve them, is unlikely to develop hysterical symptoms, unless his criticism is disarmed by peculiarly appropriate suggestion. The responsibility of education as an ætiological factor was clearly demonstrated during the Great War, when, although functional nervous disorders were probably equally common among officers and private soldiers, hysterical symptoms were relatively of far more frequent occurrence among the latter.

According to the modern conception of hysteria, the essential point in the ætiology of a particular hysterical manifestation is the presence of an *unconscious motive* for its existence. This has already been illustrated in the instance quoted above of the soldier developing a hysterical paralysis under stress of warfare when the unconscious motive was the desire to escape from danger. In other cases, the motive may be much more difficult to understand, but it is probable that in all cases it exists. Thus fits of a hysterical nature

occurring in a young woman may be shown to result from a repressed wish to attract to her side an inattentive lover, a paralysis or tremor of the right hand may occur under circumstances which demand the writing of an unpleasant letter, or the symptoms may have as their motive in a shy individual the desire to assert himself and to become the centre of attention.

An additional cause for the symptoms is usually to be found in the shape of a *suggestion*. This may come from within. For instance, a woman has a twinge of pain in the back; she remembers a friend who had the same symptom and afterwards developed paralysis of the legs, and is convinced that she is suffering from a similar disease. Or the suggestion may come from without, from the chance remarks of friends or the erroneous opinion of a medical man.

Whatever the suggestion of disease, it is accepted without logical grounds by reason of the unconscious motive in the background. There is no more satisfactory excuse for evading emotional problems than the assumption of illness. This, of course, is well recognised by the malingerer. But there is a real difference between the malingerer and the patient who is suffering from hysterical symptoms. The business of the former is to deceive others; the patient with hysteria deceives himself, and to provide a satisfactory solution of his difficulties this self-deception must be complete. The malingerer can, and will, discard his symptoms whenever it may be convenient; the hysterical disability, however inconvenient it may be in some ways, remains constantly present until the patient's belief in its reality is removed.

The **Symptoms** of hysteria may be of the most diverse nature, and may closely simulate many forms of organic disease, from which they are to be distinguished only by careful examination. By certain writers in the past a good deal of stress has been laid upon the value of certain physical signs said to be pathognomonic of the condition and therefore known as the *stigmata* of hysteria. More recently, however, it has been shown that these signs have probably in all cases been due to suggestions made by the physician in the course of physical examination. It is to be remembered that the hysterical patient is lacking in the critical faculty, and therefore his judgments upon the nature of his own bodily sensations are likely to be influenced by the least suggestion made by another, especially if this falls in with his own fixed idea of serious physical illness and is made by a person in whose knowledge of disease he has implicit belief. Therefore, for instance, in the course of our examination of cutaneous sensibility, the tone in which an inquiry is addressed to the patient may suffice to determine his answer, even if this be at variance with all considerations of common sense. Thus may be developed areas of cutaneous analgesia in which the patient states that he is unable to feel the pricking of a pin, even if this is pressed in deeply enough to draw blood. Or in the examination of the visual fields abnormalities may be discovered which vary with, and depend upon, the method of examination (Hurst).

It is important to remember that in a large number of cases of hysteria there are to be found signs of underlying organic disease either of the nervous or other bodily systems, which has formed the starting point for the development of a neurosis. The physician must, therefore, be prepared on occasions to find signs of hysteria and of organic disease in the same patient, and must, in summing up the case, decide what proportion of the symptoms is functional and is, therefore, amenable to cure by psychotherapy. For instance, a patient may be seen complaining of paralysis of the whole arm from the shoulder downwards starting from an injury received at work; examination reveals the scar of the injury to be below the elbow; the signs of division of the ulnar nerve at this level are present in the form of the appropriate wasting of the small muscles of the hand; sensory examination, however, shows the anæsthesia to extend up to the level of the axilla, and there is total loss of power of the muscles without any wasting or alteration in the tendon jerks. In such a case the greater part of the symptoms

may be removed by the methods of psychotherapy to be described later, leaving a small organic residue which needs surgical treatment. Or a woman may be seen who has for some months been bedridden with total paralysis of the legs. Examination of the nervous system reveals definite signs of organic disease in the form of extensor plantar responses and absent abdominal reflexes, and a careful analysis of the history is sufficient for the diagnosis of disseminated sclerosis. Yet the defects of nervous function in the shape of paralysis, loss of sensibility, spasticity, or inco-ordination, are insufficient to account for the inability to walk. In such a case psychotherapeutic measures, though, of course, without any effect upon the underlying organic disease, may serve to restore to the patient the power of walking. Some of the commoner manifestations of hysteria will now be described under the headings Mental, Nervous and Visceral.

Mental Condition in Hysteria. It has already been stated in the definition of hysteria that the disorder is primarily one of the mental processes, and although the outward manifestations of this disorder usually take the form of physical symptoms, the mental condition may sometimes be recognised in the general behaviour of the individual. The essential feature in the mental state of hysteria is the process of dissociation whereby a group, or complex, of ideas and feelings belonging to the personality is shut out from the field of consciousness. In certain cases there may occur temporarily a complete reversal of this state, so that the whole field of consciousness is filled for the time being by the ideas and feelings previously excluded, while those which formerly constituted the conscious mental activities of the individual are, in their turn, shut off. Thus arise the cases of dual personality in which a person may for a period of minutes, hours, or even days, speak and behave in a manner wholly foreign to her usual demeanour, and on returning to her usual self have no memory whatever of what has occurred. In its simplest form such dissociated behaviour takes the shape of sleep walking, of which the classical example in literature is that of Lady Macbeth in Shakespeare's play. Waking episodes of a similar but usually more complex nature are called "hysterical fugues." The same mental process of dissociation is responsible for the condition of so-called hysterical amnesia, in which the individual loses all memory of some phase of his life which is associated with painful and unpleasant experiences.

The patient with physical symptoms of hysterical origin does not, as a rule, show signs of emotional stress, and is, therefore, not commonly "hysterical" in the lay sense of the term. On the other hand, it is frequently to be observed that these patients, in spite of a superficial anxiety to be relieved of their symptoms, show no real depth of feeling in this respect, and are, in fact, abnormally content with their condition. This is easily understood if it be admitted that the symptom itself is providing satisfaction for certain underlying wishes in the patient's mind of which he himself is not clearly aware.

Nervous Symptoms. *The Hysterical Fit.* The attacks known as hysterical convulsions and "fits of hysteria" are commonly caused by emotional disturbance. They occur as a rule in the presence of others, or in circumstances where they are likely to attract attention. The patient may complain of sensations of choking, giddiness, or faintness, and burst into a fit of crying or uncontrollable laughter. In other cases the patient falls to the ground, as a rule gently, or on to a chair or sofa, and at once passes into a state of convulsive movements. These, if they are witnessed by the physician, are as a rule easily discerned to be of a purposeful nature. There may be phases of tonic contraction in which body and limbs are held stiffly with hands clenched, but these never involve the respiratory muscles to such a degree as to produce cyanosis. The eyelids are generally closed, and resist attempts to open them; if they are opened, the eyeballs are rolled upwards under the upper lid. There are no true clonic twitchings. The patient may tear at her clothes, beat her head with her hands, or clutch at bystanders. She may gnash her teeth, and saliva may issue from the mouth, but the tongue

is not bitten. There is no loss of sphincter control. Often the attack is punctuated by shrieks, groans or articulate cries. There is no true loss of consciousness. Though the patient does not reply to questions, she is influenced by what is said or done in her presence. The greater the alarm evinced by those around her, the more violent is the display of excitement. The attack may continue in this way for two or three hours. If the patient be ignored, the symptoms may at first increase in severity, but if treated quietly, rapidly diminish. Neither during nor after the attack is there any disturbance of the reflexes. At its conclusion recovery is as a rule rapid, and the patient is in a few moments again in possession of all her faculties. All knowledge of the episode may be denied. This is often a pretence, but may be due to a hysterical amnesia, in which case the patient becomes able as the result of treatment to recall the incidents of the attack.

Disorders of the Special Senses. Hysterical blindness is by no means common; but many cases have been recorded arising out of the Great War. In most instances they occurred in the case of a man exposed to irritating gas and for the time being unable to see on account of acute conjunctivitis, photophobia and blepharospasm. Some of these patients remained blind for years before their symptoms were removed by psychotherapy. In such cases, of course, there are no abnormalities to be found on ophthalmoscopic examination. *Hysterical deafness* is not infrequent, and was another symptom commonly observed during the war in a man who had been temporarily deafened by the explosion of a shell. It is usually unilateral, but may affect both sides. Hysterical deafness may be diagnosed by the absence of any history or signs pointing to chronic inflammation of the middle ear, and by the performance of the tests for vestibular function. If under such circumstances the reactions to these tests are normal, the deafness is almost certainly of hysterical origin.

The Cranial Nerves. Hysterical spasm of the orbicularis palpebrarum, or blepharospasm, is of quite common occurrence, and usually accompanies hysterical blindness. It commonly follows irritation of the conjunctivæ, as in chronic conjunctivitis, the usual cause in the war being irritant gas. The face and tongue also are sometimes affected by spasm. In this way a hysterical patient may simulate facial paralysis by contraction of one side of the face, the other side appearing weak by contrast while at rest.

Hysterical mutism is a not uncommon symptom, and has already been referred to. It may appear after a severe emotional shock, as, for instance, in the war cases, in which it may be imagined that the individual was for the moment struck *dumb with terror*. The patient is unable to make any sound whatever on attempting to speak, yet in some cases he may be able to cough quite audibly. In the condition of *hysterical aphonia* the patient is able to speak only in a whisper. This most commonly arises after an attack of catarrhal laryngitis, and may be regarded as a perpetuation of a symptom which was originally organic. On laryngoscopic examination the adductors of the vocal cords can be seen to be immobile. It is noteworthy that in a number of these cases the patient speaks in a high-pitched whisper without any hoarseness, which is in itself a point of diagnostic value. (*See* Paralysis of Laryngeal Muscles.)

Sensory Symptoms. Complaints of pain or tenderness not infrequently occur as accompaniments of local symptoms of a hysterical nature. Thus there may be complaint of headache or backache and tenderness over the top of the head or the vertebral spines, or in association with hysterical contractures of the limbs there may be complaint of great pain on attempted movement. Hysterical anæsthesia has already been referred to, when it was stated that this symptom is usually produced as the result of neurological examination. It is often present also as an accompaniment of hysterical paralysis. It may usually be distinguished by the nature of its distribution, which does not follow any anatomical laws, but depends on the patient's own idea of anatomy. Thus,

accompanying a paralysis of hand or foot, it is usually of a "glove" or "stocking" distribution.

Motor Symptoms. These may be divided into paralyses and contractures and involuntary movements.

Motor paralysis is one of the commonest of all hysterical symptoms. It may take the form of a monoplegia, a hemiplegia, paraplegia of the legs, or paralysis of all four limbs. The paralysis is usually complete and may be flaccid, or accompanied by contracture of the muscles, the latter form being the commoner. As a rule, it is of sudden onset, commonly following physical or emotional trauma, or it may often appear in the form of a perpetuation of a weakness of organic origin, as, for instance, after a fracture for which the limb has been splinted for a considerable time. In both the flaccid form and that associated with contracture, the paralysis usually affects all groups of muscles equally without regard to cortical, segmental or peripheral nerve distribution. When the patient is requested to put the paralysed limb into action, in spite of much exhibition of effort, there is little or no movement. It is to be noted that, although there may be some atrophy of the muscles from disuse, this is never so marked as in the case of a lower motor neuron lesion, and that in the cases with contracture the rigidity does not conform either in type or muscular distribution to the clinical picture of spasticity from a lesion of the upper motor neuron. Moreover, the anæsthesia which is frequently present follows no anatomical laws in its distribution, nor is there any abnormality of the tendon jerks. One phenomenon of positive value in the diagnosis of hysterical paralysis is the simultaneous or rapidly alternating contraction of the prime movers and their antagonists in attempting to perform any particular movement. Thus, if the patient with a hysterically paralysed arm be asked to perform the movement of flexion at the elbow, the observer by simultaneous palpation of both biceps and triceps can feel these muscles contracting simultaneously, or in rapid succession, so that, in spite of much expenditure of muscular effort, either no movement at all or else a succession of jerks occurs. This phenomenon does not occur in any condition due to organic disease. In some cases a hysterical contracture may closely simulate an organic condition, but may usually be differentiated by careful neurological examination. In contrast with the rigidity of organic nervous disease, it will be found in hysteria that the force opposed to passive movement varies directly with that applied by the observer. A form of paralysis of quite frequent occurrence in hysteria has been described as astasia-abasia. In this condition the patient is able to perform all voluntary movements of the lower limbs with normal power and accuracy so long as she is lying in bed, but is unable to walk when set upon her legs. The involuntary movements of hysteria may assume the most diverse forms, of which various types of tremor may sometimes with difficulty be distinguished from those of organic disease. The signs, however, which are usually associated with the organic tremors of Graves' disease, disseminated sclerosis, paralysis agitans and other diseases are absent.

The reflexes in hysteria do not as a rule show any abnormalities, though it has been stated (Hurst) that in cases of hysterical anæsthesia of the abdomen the abdominal reflexes may be absent, to return with the disappearance of the anæsthesia.

The functions of micturition and defæcation are sometimes affected, the commonest symptoms being retention of urine on the one hand and dyschezia on the other. In such cases, great care must be taken to exclude the possibility of organic disease.

Abnormalities of the posture and gait in hysteria are as a rule easily distinguished from those which depend upon organic lesions. Disorders of gait in some instances take the form of mannerisms, such as hopping or prancing, or even of walking sideways crab fashion. Among the postural abnormalities may be

mentioned that of the bent back simulating that seen in some advanced cases of osteoarthritis of the spine.

Trophic changes do not occur as isolated symptoms in hysteria. Although blueness of the skin and brittleness of the nails may be seen in long-standing paralysis of hand or foot, these are but the concomitants of disuse. In some cases of contracture of prolonged duration, excoriation of the skin may occur in the neighbourhood of the joints.

Hysterical dysphagia is not uncommon, and may be associated with the sensation of *globus hystericus*. There is no reason for supposing that this particular sensation is different in its physiology from the "globus" sensation which normal people experience from time to time, and which is produced in the œsophagus (*see* p. 333).

So-called *hysterical vomiting* and *aerophagy* have been mentioned under the Tics and are described on pp. 338 and 341.

Hysterical polypnœa is a condition in which there is extreme rapidity of respiration unassociated with any pulmonary disease. Although the rate may amount to sixty or seventy respirations a minute, the individual breaths are very shallow.

Diagnosis. This depends, in the first place, upon the exclusion of signs of organic disease sufficient to account for the symptoms observed. There are, however, some symptoms which are in themselves of positive value in making the diagnosis, such as aphonia with isolated paralysis of the adductors of the vocal cords, and the simultaneous movement of prime movers and antagonists in a paralysed limb or muscle.

The association of paralyses which could not be accounted for on the basis of a single lesion is also a suspicious circumstance, such, for instance, as an inability to open one eye together with an apparent paralysis of the same side of the face. The failure of a muscle to function in one movement, together with good power in the performance of another, may also be a valuable point in evidence. The circumstances under which the illness has arisen and the previous history of the patient, with special reference to her reaction to emotional difficulties, may also be useful; but the mere fact of the symptoms having immediately followed an emotional shock is not to be taken as evidence of their hysterical nature, since a cerebral hæmorrhage or an attack of genuine epilepsy may be precipitated by such conditions.

Of organic nervous diseases, that most likely to be confused with hysteria is disseminated sclerosis, but the mistake made is usually that of diagnosing the organic condition as functional.

In difficult cases, especially those in which a hysterical disability is superimposed upon an organic affection, it may be necessary to resort to psychotherapy as the final criterion. Symptoms which are removed by these methods must be of mental origin.

Diagnosis of a Hysterical Fit. The features described above (p. 788) serve to distinguish this from an epileptic fit if the physician is able to witness an attack. Often, however, the diagnosis has to be made upon the history alone. Here points which are definitely in favour of epilepsy are the occurrence of attacks when the patient is alone, especially if he falls and hurts himself, true disturbance of consciousness, cyanosis, biting of the tongue, incontinence of urine, and a period following the attack in which the patient is dazed or behaves in an automatic manner. The epileptic often gives a groan at the commencement of the fit, but is thereafter silent; the hysteric frequently continues to cry out during the whole attack. The duration of the movements in an epileptic attack is brief—as a rule not more than ten minutes; in the hysterical fit they are commonly of longer duration. The circumstances of onset have also to be considered. It must be borne in mind that an epileptic may also have hysterical fits, and that after an attack of minor epilepsy the patient may sometimes pass into a hysterical condition.

The **Prognosis** in hysteria is on the whole good as far as individual symp-

toms are concerned, although this depends to some extent upon early diagnosis and proper treatment. A person with hysterical paraplegia, if the condition be pronounced a grave one by the physician, may remain bedridden for years, yet even so she may recover spontaneously, the symptoms disappearing suddenly and being attributed in most cases to emotional shock. Of such a nature are the many "miraculous cures" effected by quacks. On the whole, it may be said that the longer a symptom has persisted the more difficult it is to remove; when the symptoms are of short duration they are easily caused to disappear. The underlying disorder of the mental processes, however, is by no means so easily remedied, and it is a notorious fact, therefore, that the hysterical patient is liable to relapses in which the original symptoms may be reproduced or new varieties may be displayed. In estimating the prognosis, due weight must be given to considerations of the patient's power of intellectual grasp and the environmental circumstances against which she has to contend.

Treatment. Hysteria is a disorder of the mental processes, and treatment must therefore be directed towards the mind, the general title given to the methods employed being *psychotherapy*. The forms in which psychotherapy may be used in the treatment of hysteria are classified as *suggestion*, *persuasion* and *analysis*.

An outline will be given of these three methods, together with some indications for the use of each, but it will first be of value briefly to restate the theory already enunciated of the causation of hysteria.

The condition, then, is one in which the patient is led by motives of which he is unconscious to accept the suggestion that he is suffering from bodily illness. The relative importance of these two causes, unconscious motive and suggestion, varies in different cases. When the unconscious motive is powerful, as in the case of a workman seeking compensation, the suggestion may be of trivial importance. On the other hand, a definite diagnosis of organic disease made by a medical man of standing may need no more support than a natural tendency to surrender to illness in order to produce a hysterical symptom.

Whatever the chain of mental processes which has led up to the hysterical condition, the penultimate link is the patient's conviction that his symptoms exist and are dependent upon physical causes over which he has no control. It is the aim of psychotherapy to remove this conviction, and this may be accomplished by any one of the methods already mentioned or by the use of all three in combination.

The object of all three methods is to replace the patient's conviction as to his symptoms by another and opposite belief.

The method of *suggestion* aims at achieving this end by making use of emotional or instinctive trends in the patient's mind, of which the most important are his implicit belief in the knowledge and power of the physician and his readiness to expect miraculous cures from treatment which is novel, spectacular, or mysterious. The success of this method clearly depends to a large extent upon the personality and reputation of the physician, as also upon the readiness of the patient to abandon the exercise of his critical faculties.

The technique of the method may be illustrated as follows: The physician is asked to see a woman with a paralysis of the arm. Having discovered that the paralysis is functional, he will remark to the patient that the condition is a nervous one, which is readily curable by means of a new form of electrical treatment; he will mention the fact calmly with the air of one accustomed to such cases and their cure, and may proceed to relate one or two instances which have occurred in his practice in which long-standing paralysis of this type has been completely removed by a single application of the new treatment. Having led the patient's friends and relations also to expect an immediate and certain cure, he will return later with a faradic battery and wire brush, and after further preparation of the patient's mind will apply the current to stimulate the muscle groups of the affected limb, at the same time insisting that she has recovered her powers of

voluntary movement. Similar methods may be applied to the treatment of other hysterical symptoms. The actual instrument used is of no importance, provided that the method is new to the patient. If, for instance, faradism has previously been tried and has failed, some new means must be devised. The essential fact in successful treatment is the establishment of implicit confidence of patient in physician. It will be noticed that when this method is employed the conviction of cure by which the conviction of illness in the patient's mind is replaced rests not upon any reasoned chain of belief, but upon instinctive feeling.

Hypnosis may be regarded as a form of suggestion, which has been now largely abandoned in favour of more direct methods in the treatment of hysteria.

The object of *persuasion* is to induce the patient to replace the false conviction as to his illness by a reasoned belief. To take the instance of functional paralysis of the arm again, the physician will explain to the patient that there are no signs of disease of the muscles of the limb, or of the nerves controlling it; that a muscle which can be used for one movement must be equally available for another, and therefore that if she first relaxes the muscles of the affected limb, and then sets out with the single aim of performing a definite movement, she will be able to accomplish it. The advantage of this method over suggestion is that it leaves the patient with a conviction of cure which is more stable in that it depends upon a chain of reasoned arguments which she can reproduce for herself in time of need. The disadvantages are that it makes a certain demand upon the intellectual, and especially the critical, faculties of the patient, and that it takes longer, and is perhaps for this reason less certain in its immediate effects.

In practice these two methods of suggestion and persuasion are usually combined, for it is clear that the success of the latter method must depend upon the implicit confidence of the patient in her physician as well as upon processes of cold reasoning.

The method of treatment by *analysis* has a much deeper purpose, namely, to discover the whole chain of mental processes leading up to the production of the hysterical symptoms, and to remove these by helping the patient to readjust his mental attitude in the light of the analysis. If the patient can be led to an insight into his own condition, and is enabled by the methods of analysis to recall to consciousness the dissociated ideas which are the basis of the hysterical symptoms, the latter tend to disappear as the ideas and the feelings associated with them are assimilated. Such a procedure involves more or less complete self-understanding on the patient's part, and protects him much more effectively against relapse than the other methods.

Analysis of this kind may be a comparatively simple matter, or it may call for much patience and skill on the part of the physician, and the use of certain technical methods (*see* p. 781). To take as a hypothetical instance again the case of a young woman with functional paralysis of the arm, the physician may discover that, having hitherto lived at home, she has lately for the first time in her life been away in domestic service, that she has found her new duties trying, has been feeling very homesick, and has not obtained the sympathy she desired either from her co-workers or her parents; further analysis of the patient's inner thoughts and feelings, as well as of her behaviour and utterances, leads to the conclusion that the unconscious motive for her illness has been the desire to escape from her unpleasant duties and to gain sympathy from those around her, the precipitating factor having been a trivial injury sustained at work. The patient is given this explanation of her malady and is encouraged to meet her emotional difficulties frankly, being told that when she does so her symptoms will disappear. It is clear that he who employs this method is at the same time availing himself of both suggestion and persuasion, which probably play a considerable part in the procedure, since appeal is made both to the patient's implicit belief in the physician and to her powers of reasoning about her own mental processes.

In the practical treatment of hysteria these three methods of suggestion, persuasion and analysis are generally used in combination, due consideration being given in every instance to the intellectual grasp of the individual, and to the time available for treatment, in deciding which shall be chiefly relied upon. There are some patients of low educational level for whom crude methods of suggestion alone are the best available. In all other cases it is advisable as a preliminary step to give the patient some kind of explanation of his illness in terms which will help him to understand the nature of the disorder and the rationale of the treatment to be adopted. After this it is well to begin with the removal or alleviation of the symptoms by means of suggestion and persuasion, which may be followed up by analysis in selected cases. Whenever possible the patient should be led to realise that his illness results from a disturbance of the mental processes—processes which he can, if he will, examine and control. Since the perpetuation of hysterical symptoms frequently depends upon the patient's emotional reactions to factors in his environment, it is of value in many cases to have him removed to a nursing home or hospital before treatment is commenced, and to forbid him receiving letters or visitors until the cure is complete.

In conjunction with mental treatment carried out on these lines, the physical condition of the patient should be carefully considered, and every effort made to eliminate physical causes of bodily inefficiency, whether in the nature of septic foci or faulty habits of life.

AFFECTIVE REACTION TYPES

THE MANIC-DEPRESSIVE PSYCHOSES

The characteristic feature is the predominance of affective (emotional) abnormality in the direction of excess of happiness (elation) or of excessive sadness (depression). This is accompanied by a corresponding disturbance of thought and action, and the correspondence is characteristically a harmonious one, the elated patient being also over-active (psychomotor over-activity) both in the more physical sense of incessant busy-ness and in the domains of thinking and speech, as shown by the continuous talkativeness ; while the depressed patient, on the other hand, shows a corresponding reduction of activity, sitting doing nothing for hours at a time. Besides being reduced in quantity, his activity both of thought and action is slowed (psychomotor retardation). These are the leading characteristics of the typical forms of the manic-depressive psychosis ; but there are intermediate and atypical forms, which will be described below (8).

Incidence. Patients suffering from this form of psychosis constitute 16 per cent. of the admissions to mental hospitals ; but many more with a mild degree of the condition do not become resident in hospital.

Ætiology. There are some facts and many theories. Inheritance is undoubtedly a frequent factor. Eighty per cent. of patients show a morbid taint of some kind in recent ancestors or collaterals, but this figure covers such a heterogeneous diversity of conditions as organic brain disease and vagrancy. More important is the evidence that a direct similar inheritance from parent to child is relatively common. If one parent has had a psychosis of this type, it is said that one-third of the children will also have it, while others will exhibit a cyclothymic personality.

Constitution, mental or physical, is a predisposing factor. The temperament more prone than others to develop a manic-depressive psychosis has been variously called " syntonic," " cycloid " or " cyclothymic." The characteristics are persistent cheerfulness or quiet sadness, with a tendency to fluctuate from one to the other, and an open, frank, sociable attitude. The depressive type of cyclothymic personality was found in 64 per cent. of a series. The principal depressive traits in the series were worry, periods of gloom and lack of confi-

dence. The elated or hypomanic type of cycloid personality is always very active and cheerful, full of affairs and sociable to a high degree. A manic-depressive psychosis is held to be more commonly found than other types of psychosis among persons of " pyknic " constitution, although its occurrence is not by any means confined to persons of this physical make-up. The " pyknic " physique is of middle height, muscular, given to *embonpoint*, with a short neck and rounded head and face.

Women are more commonly affected than men (70 : 30), and Jews relatively more frequently than Gentiles. Fifty per cent. of all first attacks occur before the age of thirty. A case has been recorded as early as five years of age ; but the period fifteen to thirty years of age is the one of greatest susceptibility. A change in type occurs as age progresses, depressions, which are always the more common form, becoming even more frequent in proportion to instances of manic excitement.

Precipitating Causes. Stress, mental or physical, can usually be found preceding the first attack ; any physical illness may precipitate an attack in a predisposed person. This has to be distinguished from the liability of manic-depressive patients to develop intercurrent infections as the result of their carelessness of themselves. Mental stresses are more frequently found than serious physical ones. Bereavement, financial loss, domestic difficulty, disappointment of any kind, frustrated love-affairs, and the like, are all frequent precipitants of first attacks. Subsequent attacks occur with much less, or even no, apparent external provocation.

Theories. (*a*) Physical. A disordered metabolism, an organic basis of, *e.g.* structural brain-disease, and a toxic origin have all been invoked, on insufficient evidence so far. (*b*) Psychological. A special, often inherited, affective constitution has been suggested to account for the persistent emotional disturbance so characteristic of manic-depressive psychoses, this constitutional tendency being released in the circumstances noted. Psychoanalysis has postulated, in addition to a constitutional factor, an arrest (or *fixation*) of the development of the libido at the anal or sadistic level.

Psychopathology. Manic elation can be regarded as the emotional accompaniment of a phantasy, which pleases the patient and in which he becomes exclusively interested at the expense of reality. Depression, on the other hand, may be simply the exaggeration, perhaps on a constitutional basis, of the downheartedness that normally accompanies disappointment ; or it may be the conscious accompaniment of a feeling of guilt and wrong-doing, the origin of which remains repressed and unconscious. When the basis of elation or depression remains unconscious in this way the emotional disturbance naturally appears inexplicable both to the patient and the observer (9).

Mental Symptoms. These are usually described in triads, of elation, motor activity, and flight of ideas, on the one hand (manic phase) ; and depression, diminution of activity, and slowness of thought (retardation), constituting the depressive phase, on the other. In addition, there are mixed conditions in which symptoms are combined in various ways, *e.g.* elation plus immobility plus poverty of ideas constitutes " manic stupor."

Manic Phase. Three degrees of intensity are described : hypomania, acute mania, and acute delirious mania, in that order of increasing severity. The onset in all is usually sudden.

(1) The hypomanic patient is always busy, sleeps little, rises early, drives his car at breakneck speed, talks much and loudly, writes numerous letters (psychomotor excitement), begins many things and finishes none (distractibility). He is very happy (elation), laughs, jokes, and puns. His talk shows a rapid change from one topic to another, the change occurring often on the basis of superficial associations (flight of ideas). " Clang " associations, depending on the similar sounds of words, are a common type. The mood shows sometimes a rapid but

temporary change to irritability. Inhibition is diminished—the patient says things not heard in polite society, is rudely outspoken, and may drink to excess or indulge in venery. The intellectual and sensorial functions (memory, etc.) are well preserved. Insight is lacking.

(2) Acute Mania is a further development of the above condition. The classical triad of symptoms is again present; but the over-activity has reached a pitch of incessant restlessness, of an increasingly aimless character. Sleep is reduced to a minimum, food is neglected, and talk is incessant. The change of conversational topic may be so rapid as to produce the impression of incoherence. Attention is so distractible (the patient commenting on any chance noise or incident in the midst of his activity) that recent memory and orientation are interfered with—he notices nothing long enough to remember it. The patient's gaiety is infectious, but changes readily to irascibility, which may, in combination with the over-activity, lead to acts of violence. Destructiveness in the form of tearing up bedclothes and destroying articles of furniture is common. Clothing is divested, so that often a special indestructible one-piece suit is necessary to keep the patient from exposing himself to cold. Delusions are frequent, ordinarily grandiose, sometimes persecutory, but usually transient and loosely organised.

(3) Acute Delirious Mania. Clouding of consciousness is the prominent feature of this stage. Complete disorientation in all spheres accompanies the extreme restlessness. Attention is very fleeting, and misidentifications and hallucinations are prominent. The patient sees visions and hears voices, all in a transitory disconnected way. The mood, typically elated, changes rapidly to ecstasy or despair, and back again. The activity includes dancing wildly, shouting and screaming, throwing things about, smearing the walls and furniture, tearing up clothes, etc. Talk is incessant and consists of prayer, abuse, entreaty, punning, rhyming, and the like. The patient seems tireless, but in reality is wearing himself out and succumbs readily to infections. It is in fact probable that most, if not all, cases of acute mania of delirious intensity are associated with infection, which has much to do with the intensity of the symptoms.

Depression. (1) Simple retardation consists of sadness with reduction of activity both in speech and action (psychomotor inhibition). There is a slowing (retardation) as well as reduction. The slowing is both initial (slowness in beginning an action) and executive (slowness in carrying it out). In thinking and speech the retardation is more marked in relation to special topics ("Painful thoughts are slow"). The patient complains of difficulty in thinking. The mood is one of hopelessness, and there is a lack of emotional resonance; nothing has any joy or interest in it. The content of thought exhibits ideas of unworthiness, of actual sinfulness and of failure. Obsessive fears, especially of harming those dearest to the patient, and obsessive thoughts of a sacrilegious nature, are common. A desire for death and suicidal intentions are universal at one stage or another, although the retardation fortunately puts an obstacle in the way of their execution. The world and the patient himself seem to him strange and altered (feeling of unreality). Intellectual and sensorial functions are intact, except that mental operations, as a whole, are slower. The patient looks distressed or anxious, and sometimes complains that he cannot weep. He sits almost immobile for hours at a time, head bowed, and hands on knees.

(2) Acute Depression. This is a further stage, with even more obvious inhibition and retardation. The patient says nothing spontaneously and moves little. Questions are answered monosyllabically. The facies and posture make a picture of gloom. Delusions of economic, bodily and spiritual ruin persist, in spite of all persuasion to the contrary. The patient believes he has ruined himself by masturbation or other misdeeds; that he is faced with financial disaster and that he has ruined his family (delusion of poverty). Hypochondriacal delusions reach a considerable pitch of exaggeration: the bowels are stopped up, the brain

is disintegrating, and the entrails are rotten. These may be based partly on alteration of physiological functions (*v. infra*). Food is refused, usually because the patient believes he is unworthy. Much more rarely he believes the food is poisoned, but delusions of persecution of this kind are not typical. Sensorial and intellectual functions are intact, but there is no insight.

(3) In Depressive Stupor the patient is so completely absorbed in his hypochondriacal and self-accusatory delusions that he takes no interest in his environment whatsoever. No question is answered. He has to be tube-fed ; he does not attend to the calls of nature, and retention of urine and fæces results. It is impossible to test the intellectual and sensorial functions, but, naturally, knowledge of current events is interfered with on account of the lack of interest.

" *Mixed* " *States.* These are principally as follows : Agitated depression—depression of mood plus bodily over-activity (restlessness, wringing of hands, bemoaning of fate), but still with retardation in thinking. Manic stupor—elation plus complete inactivity and indifference to environment. The patient is preoccupied with fantastic delusions of his happiness and importance. These are the only two " mixed " states met with at all commonly. Manic stupor is probably always a transition stage between depression and mania or the reverse. Unproductive mania (elation with poverty of thought), depression with flight of ideas ; akinetic mania (elation with flight of ideas but lack of motor activity) ; anxious mania (anxiety, psychomotor activity and flight of ideas), are all very uncommon. The importance of recognising mixed states lies chiefly in the more prolonged course of the illness in which they occur.

Physical Symptoms. Sleep is much reduced and difficult to control with remedial measures. Loss of appetite and refusal of food lead to emaciation in depressed patients ; over-activity and carelessness about food lead to the same result in manic patients except in hypomanic cases, who may slightly increase in weight. There is a diminution in all secretions in the depressive phase, with which constipation is correlated. The skin becomes dry and harsh and the growth of the nails irregular. The opposite conditions obtain in manic excitement. Metabolism, as measured by gas-exchange, urinary secretion, blood-pressure, and the like, show no characteristic alteration. Menstruation, as in all mental illnesses, is frequently disturbed. Not infrequently an improvement in these physical symptoms precedes the beginning of a recovery from the psychosis. Fragmentary indications of hyperthyroidism appear in some manic patients. Some depressed patients show a delayed fall in the sugar tolerance curve.

Course and Prognosis. Recovery from the individual attacks, and recurrence are the principal features. A second attack occurs in at least half the cases. Some patients have a recurrence nearly every year. Nearly 50 per cent. of cases show depressive attacks only, and 16 per cent. manic attacks only ; the remainder show both at some time or another. Manic and depressive attacks may succeed one another immediately (circular insanity) or after an interval (alternating insanity). Depressive attacks may succeed each other, and so may manic attacks (recurrent depression, recurrent mania). The duration of an attack ranges from four or five days to many years. Recovery can occur even after fourteen years. The interval between attacks has been as long as forty-four years. With recurrence the free intervals tend to become shorter and the individual attacks longer, until sometimes the illness becomes continuous. When attacks have been often repeated, a terminal state of mental enfeeblement is apt to occur—a state of mild depression with little interest and little activity. A few patients remain in a state of chronic mania, especially those past middle age. These patients are over-active busybodies, apt to be quarrelsome, mischievous, and irritable if thwarted. They talk a great deal in a boastful way, and are not so much happy as exalted and silly. They show a loss of finer feelings, making coarse jokes and eating ravenously, and having no realisation of their condition. They often adorn themselves fantastically and hoard rubbish.

Age and severe hereditary taint are supposed to be factors in the causation of chronic mania.

Treatment. The principal aims are to protect the patient from himself, from suicide in depression, and from exhaustion or the injuries resulting from impulsive violence in manic excitement, to secure sufficient sleep and nourishment, and to promote elimination. For the prevention of suicide, incessant supervision by trained nurses is essential; knives, cords, and all sources and instruments of harm must be excluded. Unless elaborate provision can be made at home, removal to a special hospital is necessary. Exhaustion may be forestalled by hydrotherapy (continuous tub and packs), nursing in the open air, confinement to bed, and the procuring of rest. Sleep, if not sufficient by these methods, may be increased by medinal, paraldehyde, chloral and bromide, and, if necessary, hyoscine. Feeding requires personal supervision from the nurse; tube feeding should be resorted to wherever refusal of food extends for forty-eight hours.

A study of the manic patient's utterances will often give clues to the stresses that have precipitated the illness, and will serve a useful purpose in the after-treatment when recovery has occurred and it is desired to give the patient a clear understanding of the cause, with an idea to preventing a recurrence. Reassurance will not appear to help a depressed patient at the time, but is, nevertheless, often a useful means of support. It has been claimed that psychotherapy of a more intricate kind may cure the attack; but it is usually wise to confine intensive psychotherapy to the intervals as a prophylactic measure.

The patient should be carefully supervised for some time after apparent recovery, in view of the chances of supervention of another phase.

INVOLUTIONAL MELANCHOLIA

This occurs, as the name denotes, in the involutional period of life, in the fourth or fifth decade, but cases with a similar symptomatology sometimes occur earlier. It is characterised by depression, with anxiety and apprehension, and delusions of a hypochondriacal, persecutory and nihilistic kind. There has been much discussion whether involutional melancholia is simply a manic-depressive psychosis occurring at the involutional period, and coloured by the changed outlook of later life. It has been asserted that there is frequently a history of previous mild attacks of a manic-depressive type, and that involutional melancholia exhibits all the principal symptoms of the manic-depressive psychosis. Moreover, the condition is recoverable in one-third of the cases. But involutional melancholia is worth considering separately, as the symptomatology and general course are sufficiently characteristic. An agitated type of depression is particularly common. The course is apt to be prolonged upwards of a year, and often over a number of years, but the prognosis is only indirectly vitiated by the degenerative physical changes of the period—arteriosclerosis and early senile changes, and the like.

Ætiology. The relation to external stress is specially clear in this group. A person who has succeeded in keeping stable hitherto breaks down at last in face of financial embarrassment, the discouragement of physical illness, the death of relations or a difficult domestic situation. Failure of potency, nominally discovered after a marriage late in life, is also in the male patients a not infrequent precipitating circumstance. The type of personality is also a feature, quiet seclusive people developing an involutional melancholic illness with disproportionate frequency. This throws light on the nature of some of the symptoms, especially the delusions of persecution, the negativism, the stereotypy, and the hallucinations that sometimes occur. Persons of a worrying and pessimistic description, who have always taken things seriously and have habitually "fought their battles over again," are also prone to develop an involutional depression.

The most characteristic symptoms however—delusions of poverty, of impending death and of bodily disease—are the result of the changing outlook of increasing years. An inherited taint of mental instability is significantly frequent. The sexes are affected about equally (51 per cent. of the patients are women).

Psychopathology. Understanding of the symptoms is aided by a consideration of the psychological alteration that normally accompanies advancing years. There is a diminution in energy, with a diminution in working capacity and a corresponding withdrawal of interest from the outside world to the self. Consequently an increasing interest is displayed in health, and death has to be contemplated as an increasing possibility. Cherished ambitions which have not been fulfilled have to be relinquished. Retrospection and misoneism become the habit (the " good old days "). From these conditions result increasing egocentricity, manifesting itself in the developed psychosis in a lack of emotional responsiveness, and actual peevishness. Hypochondriasis is in one of its aspects, an exaggeration of the preoccupation with health, while miserliness and delusions of poverty crystallise out from the financial anxieties. The failure of cherished ambitions for the patient himself or for his children leads to depression. Unwillingness to accept the fact of prospective dissolution appears in the psychosis as a fear of death, which is envisaged as full of terrors. An important further factor enters here, that ideas with a strong emotional colouring which the young healthy person may be able to keep in the background (by " repression ") are apt to break into consciousness, in a form all the more distressing because they have been distorted in the process of repression. Feelings of guilt of long standing about sexual and other misdeeds, real or only fantasied, give rise to delusions of unworthiness, and to apprehension of impending retribution (torture, damnation, etc.). The hypochondriacal delusions also rest not infrequently upon a feeling of guilt—that certain practices, especially masturbation, have ruined the patient's health. The loss of interest in life, betokened by increasing egotism, implies also a longing for death ; on the other hand, egotism resents the idea of death ; and so these patients both seek for death and fear it, hence the combination of apparently contradictory symptoms like delusions of impending death and attempts at suicide. Projection of the loss of interest leads to nihilistic delusions—that nothing exists, that every one else is dead, that nothing is real.

Mental Symptoms. After a prolonged period of sleeplessness, restlessness, worry and headache, the patient becomes definitely depressed and usually apprehensive. With the depression go ideas of unworthiness, which often reach the intensity of delusions of unpardonable sin, ostensibly and characteristically over masturbation in youth. The depression may be well concealed by the patient: he may smile in conversation, and a short time afterwards attempt suicide. Increase in the depression and apprehension leads to continuous agitation, the patient pacing up and down, wringing his hands, biting his nails, weeping, moaning, pressing his forehead, sighing, digging his nails into his hands or throat, and pulling his hair. This may be continuous or intermittent with periods of quiet resignation, or actual apparent cheerfulness and even elation (rarely). There is often stereotyped activity, such as repeated requests for reassurance: " Are they going to take me away ? " The patient shows delusions of impending persecution, often of a bizarre kind. He is to be shot, executed, roasted alive, etc.

The activity seems to depend largely on the nature of the delusional content. The above description applies to agitated depression. In others hypochondriacal delusions are the most prominent feature. Again, there is apt to be a grotesque kind of exaggeration, probably of metaphorical import. The bowels are rotten, the brain is dust, etc. In others a quiet inactivity goes with a nihilistic belief that all the world is dead, including (or excepting) the patient. In these sluggish inactive cases there may be some slowness in answering questions, the replies

being monosyllabic; the condition closely resembles a manic-depressive psychosis. Others refuse to answer at all (mutism) and refuse food under the influence of delusions that they must not eat or speak (delusional control), often reinforced by hallucinatory commands to the same effect. There is usually no complaint of difficulty in thinking; but some patients complain of perplexity—they cannot understand what they see.

The intellectual and sensorial functions are unimpaired except in persons with extreme agitation, in whom clouding of consciousness may appear, with terrifying hallucinations. A toxic superaddition is to be suspected here.

Suicide is a risk always to be borne in mind in these patients. It is more common in involutional depression than in any other psychosis.

The physical signs consist in emaciation, constipation, hyperactive knee-jerks, and tremor of hands, as well as the physical accompaniments of advancing years, especially arteriosclerosis.

Course and Prognosis. There is often considerable fluctuation in the intensity of symptoms, and a patient apparently recovering may commit suicide. The course is prolonged, from at least many months to years. Recovery has occurred after eight years. The prognosis depends to some extent on the affective condition. The more the emotional disturbance of depression and anxiety fills the picture the more favourable the outlook. Peevishness and marked hypochondriacal preoccupation are said to be ominous. The presence of signs of senile cortical deterioration (memory defect) or of focal arteriosclerotic brain disease vitiates the prognosis.

Treatment. There are two guiding principles: the maintenance of physical strength and the prevention of suicide. Both require constant supervision; the second means that the patient cannot be left alone day or night. Hence, unless he has means enough to allow of the provision of nurses day and night at home, treatment in a mental hospital is necessary. Rest in bed is indicated at first to facilitate nutrition. If the treatment can be carried out in the open air, restlessness is favourably influenced. Tube-feeding should be resorted to if the patient refuses food. Sleep can be secured in the usual way, but hydrotherapeutic measures are often contra-indicated on account of the patient's debility and active resistance. After the physical condition has been restored simple occupations should be devised. Sometimes these afford the first step in the patient's convalescence. Psychotherapy should usually be of a simple kind; deeper probing may have disastrously upsetting results.

SCHIZOPHRENIC REACTION TYPES

(*Dementia Præcox*)

Schizophrenic patients compose 25 per cent. of the admissions to mental hospitals, and 40 per cent. of their permanent population. Kraepelin first collected the somewhat heterogeneous clinical material into one group and called them all "dementia præcox," but Bleuler's term, "schizophrenia," is to be preferred for various reasons: that many patients of this kind do not become demented, but recover, some completely, some partially; that "precocious" is not a correct description, since neither does the condition necessarily occur early in life, nor is dementia, when it occurs, always rapidly attained; and, finally, the root-meaning of schizophrenia, "splitting of the mind," is well adapted to describe what is sometimes considered to be the fundamental schizophrenic process, namely, a lack of the usual harmonious co-operation between the different mental functions. There has been a tendency to extend the term "schizophrenia" to cover nearly every psychosis, not of demonstrable organic origin, that could not be included under the manic-depressive psychosis; but this is to be deprecated, although it is conventional and permissible to speak of schizophrenic symptoms complicating other psychoses (**7**).

Definition. Schizophrenia involves an alteration, commonly but not invariably progressive to a more or less profound and permanent deterioration in the patient's personality. The process reveals itself in change in feeling, thinking and behaviour, leading, on the one hand, to an attitude of apparent indifference to the external world, and, on the other, to an internal disorganisation of some of the mental processes, especially an incongruity between feeling and thinking, but with preservation of the intellectual and sensorial functions (memory, comprehension and orientation).

Ætiology. Incidence:—The condition first appears as a rule in adolescence; hence Clouston's term "adolescent insanity." Most cases are admitted to mental hospitals between twenty and forty, but they are not all by any means admitted at the time of onset. Schizophrenia has been reported as early as the age of four, and schizophrenic symptoms, colouring other psychoses, as late as the senile period. But schizophrenia in the sense described above is uncommon after forty-five. Males are affected more often than females (16 per 100,000 of population to 12·8 per 100,000). The fact that schizophrenia is more frequent in cities than in rural districts, and among the foreign-born population of the United States rather than among the native-born, gives some support to the conception of schizophrenia as a reaction to special stresses in adjustment. There is some in conclusive evidence that race and country of birth are predisposing factors, *e.g.* that Slavonic races are relatively prone to schizophrenic reactions.

Hereditary taint, in the form of psychoses, nervous diseases, alcoholism, epilepsy, senile dementia, abnormal character and suicide, prevails more in the ancestry of schizophrenics than in that of normal persons. Psychoses in antecedents and collaterals are especially frequent, being three times commoner than in the ancestry of normals. In addition to definite psychoses, abnormalities of temperament and character are significantly common in the blood-relatives of schizophrenics. The heaviest hereditary taint falls, however, on indirect (collateral) antecedents and in grandparents. Alcohol has little or no direct effect in producing a schizophrenic illness. Sometimes it acts as if it released latent schizophrenic tendencies; more often alcoholism is a symptom of schizophrenia, being resorted to by an individual already mentally ill.

Theories of the ætiology of schizophrenia are numerous. It has been suggested that schizophrenic psychoses result from a metabolic disturbance, from the presence of a toxin, from structural brain disease, or from focal sepsis, with consequent poisoning of the central nervous system. It has also been considered that the psychosis is a manifestation of a general "regressive atrophy" of the cells of the body generally, especially the small pyramidal cells of the brain and the cells of the endocrine glands, especially the testes. None of these theories has so far succeeded in establishing itself as the accepted explanation.

A constitutional predisposition probably exists. This is held to be demonstrated on the physical side by the frequency with which "dysplastic" types of physique are found among schizophrenics, and also by the post-mortem finding that in the majority of cases there is a hypoplasia of many of the viscera, together with an unusually high incidence of chronic inflammatory lesions.

More directly related to the clinical manifestations of schizophrenia are the traits of personality which so often exist before the onset of frank schizophrenic symptoms. It has been recognised that a certain kind of person is more prone than others to develop schizophrenic symptoms. This type of personality has been called shut-in, schizoid, introvert, or narcissistic, terms which have different shades of meaning but refer to the same class of persons. The "shut-in" personality exists in approximately two-thirds of schizophrenic cases. These patients have always been shy, seclusive, reticent, hard to influence, sensitive and stubborn, with little interest in the pleasures and pursuits of the average person, but living instead in phantasy. Other peculiarities exist, such as shallow-

ness of emotion, lack of consideration for their environment, abnormal precision, or a poorly balanced sex-instinct.

How does the transition from a disposition of this kind to a full-blown schizophrenic psychosis occur? The psychosis is regarded as the result of a long-continued series of maladjusted reactions to environmental and inner stresses. The individual concerned, instead of facing his problems squarely, shirks them and adopts subterfuges ("substitutive reactions"), like amnesia, fault-finding, day-dreaming, prayers and other expedients. These subterfuges unfortunately tend to gain an automaticity of their own; they become more easily resorted to (habit deterioration), and ultimately more or less uncontrollable. The fact that the onset of a schizophrenic psychosis may be sudden is not against this view; the suddenness is equivalent to the rupture of compensation that may lead to the appearance of dyspnœa, œdema, etc., in a person whose damaged heart has hitherto performed satisfactorily. There is no question, on this theory, of any specific disease-entity; each individual is a case by himself. This does not preclude general similarities that make it possible to speak of a group of people having certain morbid reactions in common as belonging to the schizophrenic reaction-type; some people tend to become mentally diseased, as others develop normally, along one or other of several lines. Nor is the notion of inevitable dementia at all justified; it is merely that certain reactions are so pernicious as refuges that if they become habitual a reversal to normal is hardly possible (**2**).

Psychopathology. The disorder of thought, leading to the utterance of what often appears to be mere nonsense, is one of the clinically striking aspects of many schizophrenic patients. It is not such a surprising phenomenon when it is remembered that many of them have lost all desire to communicate with other people, and so need not make themselves understood. Hence they may, with satisfaction to themselves, use a language of their own. Furthermore, the disintegration of the personality that occurs in the schizophrenic implies that many feelings and tendencies that normally remain unconscious come to conscious expression, either directly, as, for example, simple delusions of grandeur, which are the naïve expression of ambitious day-dreams common to all men, or delusions of being loved, which are the counterpart in women; or indirectly, as, *e.g.* hallucinations or delusions of persecution, which are the joint result of unconscious tendencies and of an attempt to repress them, with the consequence that these tendencies reach only a qualified distorted expression; *e.g.* homosexual liking *for* another person may reach conscious expression as a delusion of persecution (dislike) *by* that other person.

Another quality that makes the schizophrenic's mental processes seem so disorderly is the symbolism in which his thoughts are so often disguised. The disguise may be an attempt at repression, *i.e.* refusal to recognise certain tendencies within himself; or it may be regarded as a regression (return to an earlier stage of development) to a type of thinking found more prominently among primitive races. Lack of clearness in thinking is also responsible for some of the disorderliness of the schizophrenic's statements. Any one becomes slovenly in the expression of his thoughts who does not continually test them against reality. In his sensitive self-centredness (introversion), the schizophrenic cannot bear to do so; his illness in one sense is the result of a turning away from the unpleasant reality of an unfriendly world to a world of phantasy where everything is as he wishes it, where he receives "perfumes and flowers that fall in showers, that lightly rain from ladies' hands" (**6**).

Mental Symptoms. It is usual to describe four main types of schizophrenia —the simple, the hebephrenic, paranoid and catatonic types—according to the relative preponderance of certain symptoms. But there is no decisive line of demarcation. All of them are characterised by a loss of interest in the external world of reality, and by a corresponding absorption of the patient in his own

inner experiences; all of them show also an apparent discrepancy ("intra-psychic ataxia") between emotional and thinking processes (a discrepancy which may perhaps be more apparent than real) and a disorder of the process of thought itself (*vide* "Psychopathology"), which makes the utterances of these patients seem incoherent and absurd. There is usually a preliminary period of vague uneasiness and gradually increasing change in personality and behaviour, which may be simply the further development of the traits already mentioned. The patient is less and less inclined to mix with other people, and he becomes inactive, sitting for hours perhaps doing nothing. On the other hand, impulsive outbursts of activity may occur, *e.g.* in the form of a fugue or of personal violence. He neglects his appearance; when remonstrated with he is irritable and even dangerous. He complains of unpleasant feelings, especially in his head, and makes odd, unfounded remarks, often to the effect that certain people are watching him or are interested in him in a special way (ideas of reference). True depression of spirits is often felt, and at this stage it is sometimes difficult to distinguish the condition from an attack of cyclothymic (manic-depressive) depression. On the other hand, an elation of a thin and unconvincing kind may be the only mood-change, and this may go, for example, with an attempt to write high-sounding prose, or to construct a fantastic philosophical or mechanical scheme. Insomnia and disturbances in the general health (loss of weight, etc.) accompany the mental symptoms. Sometimes the onset is sudden, especially after acute infections. The catatonic form is apt to have a more dramatic onset than the others.

Schizophrenia Simplex. The principal feature of this type is the falling off in external interest, the patient becoming solitary and apparently preoccupied. There are often illusions and hallucinations of a fleeting kind, but commonly the impression is of such impoverishment of energy and interest that even autistic activity is reduced to a minimum. Ultimately the patient sinks into a quiet, docile state, in which he may be capable of routine work of the simplest kind under supervision. Such persons may remain outside of institutions, and furnish a proportion of life's failures following upon early promise. They swell the ranks of the idle and unemployable and of tramps and prostitutes.

Hebephrenic schizophrenia is characterised especially by the fantastic and fleeting nature of the delusions, the prominence of hallucinations, the striking incoherence of thought, and the emotional deterioration showing itself in apathy (indifference to environmental stimuli) and disharmony of thought and emotion, so that for example, alarming and distressing ideas are received or related in a matter-of-fact way. Alternation of depression and excitement, the latter often with wild impulsive and suicidal activity, is also characteristic. Mannerisms (fantastic ways, *e.g.* of eating) and stereotypy of speech, movement, and posture (tendencies to repeat certain phrases and motions and to maintain awkward bodily attitudes), silly laughter (*i.e.* laughter without apparent justification), and fantastic self-decoration, are all frequent. The persons in whom this type develops have often been imaginative and unpractical, romantic and artistic, lacking in self-confidence, suggestible, timid, unsociable, with narrow interests, but kindly and mildly cheerful. The general impression in the fully developed condition is one of incoherent fatuity in a setting of complete disintegration of the previous personality.

The paranoid form is common in persons in whom definite schizophrenic signs develop after thirty years of age. The relationship of paranoid schizophrenia to paranoia and paraphrenia is best expressed by arranging the conditions in a series—paranoia, paraphrenia and paranoid schizophrenia—in that order of increasing disintegration of the mental life. The characteristic signs of paranoid schizophrenia are the prominent delusions, the lack of systematisation (in contrast to paranoia), their fantastic, transient and changeable nature, and their association with hallucinations, often of a fatuous kind, and like the delusions themselves, usually persecutory or grandiose in nature. The other signs and

symptoms are those held in common with the other forms of schizophrenia. The type of personality in whom paranoid schizophrenia ultimately develops is commonly stubborn, seclusive, rigid, "bending the facts rather than to the facts," and self-conscious. An appearance of self-confidence marks in them a decided lack of it. Often in childhood these people have been unusually disobedient, not open to advice or correction, and insistent on having their own way. Others have been bashful and retiring, lacking in initiative and always on the defensive.

Catatonic schizophrenia is especially characterised by stupor and negativism (resistance to impressed movements or actual carrying out of an action opposite to that requested) alternately with outbursts of impulsive excitement. Stupor comprises mutism and general immobility, together with lack of response to stimuli, so that the patient does not attend to the calls of nature, and even saliva is allowed to collect in his mouth until it is putrid. Stupor is commonly associated with, and may in itself be a manifestation of, negativism, including the refusal of food and resistance to passive movements. On the other hand, the limbs may remain in any position in which they are placed by an observer (*flexibilitas cerea*), and may not fall, even under the influence of gravity. This may be regarded psychologically as the opposite of negativism. Similarly, the patient may obey in apparently automatic fashion whatever he is told to do (command automatism), and may repeat automatically what he has heard (echolalia), or imitate exactly whatever movements he sees others perform (echopraxia). Perseveration is exhibited not only in the maintenance of postures of the limbs, but also in the classical *schnautzkrampf*, the patient holding his lips pursed like a pig's snout. From this condition of stupor and neuro-muscular tension there is often a gradual or rapid change to wild excitement, in which the patient is impulsively violent, suicidal and homicidal. In this condition he may go on for days or weeks, taking no heed of the injuries he inflicts on himself, tearing off dressings, neglecting food or eating it ravenously, talking incessantly and sleeping little. Such attacks of over-activity are often short-lived, the patient relapsing quietly into stupor.

It will be seen that all the symptoms of the stuporous phase of this condition can be considered as various expressions of negativism, in the sense of an attempt to shut out the external world, and of its opposite, extreme suggestibility (echolalia, etc.), together with perseverative phenomena (stereotypies).

Physical signs are more prominent in the catatonic than in the other varieties, but are not characteristic or significant in any way except of general physical unfitness. Especially common is cyanosis of the extremities, sometimes with œdema (the result of immobility). The tendon reflexes are usually very active. There are also constipation and retention of urine and saliva (all to some degree negativistic phenomena).

Course and Prognosis. The following statements are of general application; individual cases produce surprises. The majority of schizophrenic patients deteriorate, quickly or slowly, to a chronic deep dementia. Others recover to, or are arrested at, a state of mild dementia, consisting of more or less apathy, with poverty and disorder of thought and slight oddities of behaviour. These and others make what is called a "social recovery"—they are sufficiently well to live outside hospital, although recognisably not fully normal. The outcome is related to some extent to the nature of the symptoms. When there is much confusion the prognosis is less hopeless than when the sensorium remains clear. The more profound the emotional symptoms in the form of depression or elation —*i.e.* the more the picture resembles that of a manic-depressive psychosis— the more hopeful the outlook. Patients in whom the onset has been acute have a better chance of recovery than those with long prodromata. (The probability of overlooking the latter has to be remembered.) The previous personality has to be weighed—the better "stuff" a patient is made of the better his chances of

a favourable adjustment. Patients with a catatonic schizophrenia of acute development show a higher recovery rate than occurs with other types. Previous attacks with remission suggest the possibility of a further remission, but the general tendency in remitting cases is to a progressive inadequacy.

Prevention by mental hygiene in early life suggests itself as the most likely line of treatment, in view of the volume of evidence in favour of predisposition by faulty attributes of temperament and character. Parents and educators must be instructed as well as the children. Foresight in planning a suitable career instead of the present largely hit-or-miss method is likely to lessen the chances of maladaptation.

Treatment is in a very unsatisfactory state. When a recognisably schizophrenic condition has established itself, institutional treatment is usually necessary, on account of the odd and sometimes even dangerous behaviour, and the patient's neglect of his own physical needs. The *régime* of hospital, with its insistence on cleanliness, appointed meals, regular evacuations and sleep, helps not only the general health, but corrects deterioration in habits to some extent. Occupation of a suitable kind (rug-making, weaving, basket-making, etc.) helps to stimulate the flagging external interest and to re-establish self-respect. The more the physician can get into touch with the patient, and enter into his perplexities, the more hope there is. Precautions must be taken against impulsive suicidal and homicidal outbursts and attempts at self-mutilation (*e.g.* self-castration as expiation for some sin, real or phantastic). Tube-feeding has sometimes to be resorted to, either by stomach-tube or (in very resistant patients) by nasal tube. Isolation in a single room is only to be resorted to when the patient is too disturbing to others. The control of excitement demands isolation and skilled nursing (male nurse for excited male patients), with, if necessary, sedative and hypnotic drugs and, rarely, mechanical restraint to prevent self-injury. It has to be remembered that measures such as these can only legally be carried out in licensed houses and certified institutions, recognised by law for the purpose. Special indications in the physical health (teeth, tonsils, sinuses, or any other foci definitely known to be infected) should be attended to. The general physical unfitness that has been demonstrated in such patients calls for exercise, hydrotherapy, and the open air. If sleep can be arranged out of doors so much the better.

Empirical methods of all sorts have been tried—the induction of an aseptic meningitis, of febrile conditions (by malaria, nucleinate of soda) and of prolonged sleep (with trional or somnifen, etc.). Protein shock, vaccines, endocrine preparations, calcium, and testicular extracts have all been tried with little evidence of success. Some put thyroid medicinally in; others surgically take it out, in both cases without specific effect.

PARANOIA AND PARANOID STATES

The essence of paranoia, paranoid states and paraphrenia is the presence of delusions in a setting of clear consciousness. These conditions were previously known as "delusional insanity." *Paranoia* was defined by Kraepelin as consisting in the insidious development of a permanent and unshakable delusional system resulting from internal causes, accompanied by perfect preservation of clear and orderly thought, will and action. Hallucinations are absent. Recovery does not occur, but neither does dementia. *Paranoid states*, *i.e.* states characterised by delusions, are sometimes of acute onset, often transitory, often precipitated by some exogenous factor (infection, war, imprisonment, operation). The delusions do not reach the extreme systematic development of paranoia; but hallucinations may be present (hallucinatory paranoid states), and their content harmonises with that of the delusions.

Ætiology. The condition becomes obvious usually in middle life, and in

males more commonly than in females, in the proportion of seven to three. Paranoia itself accounts for only about one in 100 admissions to mental hospitals, but the condition is more frequent than the figures would indicate, a number of patients succeeding in preserving a sufficient social adjustment to remain outside of hospital. While paranoid symptoms or even a full-blown paranoia sometimes become apparent in relation to organic disease, as if the injury to the personality as a whole uncovered or released underlying trends, paranoia itself, in the accepted sense of the term, is found in persons organically healthy in every way. The *rôle* of heredity is uncertain. It is said that in the descendants of paranoics, paranoid schizophrenia is apt to appear.

The evidence is much stronger for the existence of peculiarities of temperament and character in the patient himself long before the appearance of the psychotic symptoms. The " paranoic constitution " has been described as one with a tendency to see always a biassed meaning in things and to be suspicious. There is a failure to recognise and admit adverse facts : such people are always in the right, haughty, vain, sensitive and easily offended, sulky, irritable, and often very ambitious, with a high opinion of their own worth and deserts. Some are obstinate and revengeful, others over-scrupulous and over-conscientious and self-centred. Some have the notion of being born for something special ; others cherish a phantasy of exalted birth, or of being loved by some one higher in the social scale. Some, being sexually dissatisfied, develop a morbid jealousy of the spouse ; others show principally a morbid concern about health (hypochondriacal preoccupation). In the psychoanalytic view, the essential determinant, alike of the constitution and of the subsequent psychosis, is a repressed homosexuality ; in the psychosis, the repressed tendencies are projected (*i.e.* attributed to people in the environment and disowned by the patient) in a disguised form as delusions of persecution (**10**).

Mental Symptoms. It is out of some such personality as a rule that a paranoic psychosis develops, usually with insidious slowness. There is often a prodromal stage, in which the patient complains of nothing but general malaise, or of peculiar sensations, not yet attributed (openly at least) to any external agency.

Commonly there follows a stage of ideas of reference : people are looking at the patient, or talking about him ; small actions in the environment are misinterpreted ; people cough as they pass him, or cover their mouths with their hands, etc. From these the passage is easy to delusions, which connect up and explain all that the patient believes he has observed. The delusions are worked up into a more or less coherent system. There is a plot against the patient on the part of the Masons, or the Roman Catholics, or Scotland Yard. Gradually the delusions extend to cover a large part of the patient's everyday experiences, and no amount of persuasion makes the slightest impression on the patient's unshakable belief in his interpretations. The delusions are persecutory and grandiose (megalomanic), but frequently the former exist apparently alone ; they practically always precede the development of grandiose delusions, which may therefore be looked on as compensatory to the persecution. The patient must be someone important, else he would not be persecuted. Out of this egotistical self-estimation develop notions of royal birth, of divine mission, of great wealth, and the like. The patient believes he is a prophet, or a prince, or the heir to millions, or that he has invented a *perpetuum mobile*. A number of crank inventors belong to this class. The mood varies. Memory and the intellectual functions generally are intact. Pseudo-memories, in the form of falsifications of events in the patient's life, become increasingly numerous as time goes on, so that it is impossible to be sure that a patient's story gives a reasonably accurate account of the beginning of his psychosis. He misinterprets events long past in the light of his delusional beliefs, and suddenly sees meanings in events which had puzzled him at the time. The behaviour may be outwardly unaltered, the

patient passing for socially normal so long as he is not speaking of his delusions. But not infrequently he betrays himself by attempts to interview M.P.'s and other personages, by letters to editors or (much more rarely) by assaults on persons whom he blames for the persecution. Frequent changes of occupation or residence, or emigration to another country, are the expressions of an attempt to flee from persecution. Three stages of the condition were in fact described: "Il fuit; il se défend; il attaque"; but the sequence is not at all invariable. Delusions of jealousy (unfaithfulness of spouse) are less common. Hypochondriacal delusions are frequently present, but are not predominant.

"Abortive" paranoias or "*formes frustes*" have been recorded. These are sometimes mild manic-depressive conditions with a paranoid colouring: at other times they are the response of a paranoid personality to a sudden stress, the delusional symptoms subsiding when the stress disappears.

There are no characteristic **physical signs.**

Course and Prognosis. The condition is chronically progressive. Recovery in a full-blown case is practically unknown. There is little tendency to deterioration in the sense that, although the delusions may increase and influence conduct more, intellectual operations on neutral topics are intact and the patient takes care of his outward appearance.

Treatment is a matter of judicious arrangement. To attempt to argue the patient out of his beliefs is fatuous. He must be listened to and his confidence gained as far as possible. It is then feasible to give some practical advice calculated to prevent the patient coming into open conflict with society, but without letting him feel that his ideas are profoundly disbelieved. The provision of occupation of an interesting kind is very necessary. It is advisable for this purpose to keep the patient in his own environment, unless there is a reliable hospital or home where truly adequate interests and occupations are provided for the patient. There are a few cases where, on account of anti-social trends of a violent kind, removal to a mental hospital is obligatory. Certification as insane is then imperative, since the patient's lack of insight prevents his realising the necessity for safeguarding.

PARAPHRENIA

This has been distinguished from paranoid schizophrenia on the one hand and paranoia on the other. It occurs at a later age than paranoid schizophrenia, as a rule (after about thirty-five), and the deterioration in affect, the discrepancy between affect and thought, and the incoherence in thinking, are much less pronounced. The delusions are more consistent with each other than in schizophrenia, but, on the other hand, are more fantastic and less carefully knit together than in paranoia. The paraphrenic suffers from hallucinations, and the paranoic is supposed classically not to do so. But all these distinctions break down in practice. The course is more slowly deteriorative than that of paranoid schizophrenia.

ORGANIC REACTION TYPES

These comprise the following:—

(A) Psychoses with toxins or infections. Toxins: (i.) Endogenous, *e.g.* uræmia, eclampsia, acute yellow atrophy; (ii.) Exogenous, *e.g.*, alcohol, opium (and its derivatives), cocaine, bromides, etc., metals (lead, etc.), gases (carbon monoxide, chloroform, etc.). Infections: (i.) General—pre-febrile, febrile and post-febrile deliria from bodily infections; (ii.) Local brain infections—syphilis: (*a*) general paralysis, (*b*) meningeal and vascular syphilis; encephalitis, including epidemic encephalitis; meningitis; abscesses.

(B) Psychoses with primary degenerative brain changes: Senile dementia, pre-senile cerebral degeneration, Alzheimer's disease, presbyophrenia, arteriosclerotic brain disease, Huntington's chorea.

(C) Psychoses with general metabolic deficiency: Pellagra, myxœdema, cretinism.

(D) Psychoses with brain trauma: Traumatic delirium, constitution, mental enfeeblement, behaviour disorders.

(E) Psychoses with other brain diseases: Brain tumour, multiple sclerosis, thrombosis, embolism, etc.

(F) Psychoses with chronic general diseases: Cardio-renal disease, pernicious anæmia, etc.

All these except infection exhaustion states, presbyophrenia and Alzheimer's disease have been described in the preceding sections.

Symptoms. The essential symptoms of the organic reaction-type in general are those attributable to disease, toxic or structural, of the brain. They are principally defects of the sensorial and intellectual functions, and consist of impairment of memory, attention, perception, comprehension, and retention: recent events are rapidly forgotten; there is difficulty in activation of old memories; fluctuation in the level of attention, and probably diminution in the span of attention, so that the patient cannot hold isolated facts simultaneously before his mind; difficulty in comprehension, new events not being readily assimilated with the old, or with each other; and, in consequence of all this, lack of social capacity.

Secondly, there is frequently affective disorder in the form of emotional instability, the patient laughing and weeping without sufficient cause or being explosively irritable. There may also be depression, or anxiety, not the direct result of the brain-disease, but the outcome of the patient's realisation that he is ill. More rarely there is euphoria, as in G.P.I. and disseminated sclerosis, an anomalous result perhaps related to the special toxins.

Thirdly, behaviour disorders, out of keeping with the previous personality, may appear, doubtless in part as a result of release from higher control (failure of cortical inhibition). In this way indecent exposure, sexual misdemeanours, petty and fatuous thefts, foolish extravagance, violent assaults, and the like, may arise episodically.

The typical acute organic reaction is a delirium. In this attention fluctuates with extreme rapidity; perception is so much impaired that disorientation is usually complete; illusions appear; and hallucinations are common. When emotional disturbance occurs, it is commonly, but not invariably, fear.

INFECTION EXHAUSTION PSYCHOSES (*including Neurasthenia*)

Infection exhaustion psychoses include a variety of symptom-pictures, accompanying or following acute infections, poisoning by an exogenous or an endogenous toxin, hæmorrhage and extreme physical stress of any kind. The infection exhaustion psychoses, properly so-called, belong to the organic reaction-type; but similar causes, in predisposed individuals and sometimes in persons in whom no predisposition is discoverable, may release or activate a mental disorder of a manic-depressive, schizophrenic or paranoid kind. In these instances, however, there is apt to be an admixture of organic symptoms (*e.g.* disorientation out of proportion to the intensity of a manic excitement) which will suggest to the observer an infective or organic origin of the condition.

There is no specific correspondence between the types of infection or other stress and the type of psychosis produced. Any type of infection, etc., may be associated with any type of psychosis, the result being dependent largely on the psychic constitution of the individual attacked. When infection is the cause, mental symptoms may occur either in the pre-febrile, febrile or post-febrile stage, and there is no hard and fast distinction between the symptoms at any of these stages. The commonest reaction is delirium, but a hallucinosis (without disorientation), a catatonic state (either with or without hallucinosis), and stupor may also occur, and at any stage. Intellectual enfeeblement, amnesia, some-

times of the Korsakow type, apathy and depression occur in the post-febrile stage. Such conditions are one of the types of "neurasthenia," as that comprehensive word has been used, the term being applied especially when, in addition to depression or apathy, there are fatigability, mental and physical, headache, vague pains, and anorexia with loss of weight. Influenza is especially apt to be followed by this type of depression, in which suicidal attempts are not uncommon and convalescence is very slow.

The characteristic delirium of the febrile period is ushered in by restlessness and insomnia, with terrifying dreams and feelings of numbness and confusion in the head. This is followed by the symptoms of delirium proper—disorientation, failure of attention and comprehension, inability to sustain a train of thought, and hallucinations, often but not invariably accompanied by intense fear, which may prompt assaults in self-defence or homicidal attempts at escape. Violent psychomotor excitement sometimes ensues, and in severe cases coma. In the post-febrile stage a "collapse delirium," with extreme prostration as well as hallucinatory phenomena and restlessness, has been described.

The physical signs are those of the provocative physical condition. Examination of the blood may show an acidæmia, and sometimes there is nitrogen retention.

Treatment should be directed to discovering the underlying physical condition and to combating any infection, general or focal, which may be found. Symptomatic treatment consists in rest in bed, preferably in the open air; hydrotherapy; adequate feeding (by stomach-tube or nasal-tube if food is persistently refused) with milk, cereals, sugar and fruit-juice; elimination by the bowels (calomel, followed by milder medicaments); alkalis well diluted by mouth or bowel; and where toxæmia is profound, physiological salt solution by the bowel (Murphy drip) or even intravenously.

"*Central neuritis*" (Meyer) denotes an acute inflammatory change in the cerebral neurones, occurring as a terminal stage in a variety of conditions, especially pellagra. Clinically there are spastic paralysis with contractures; confusion, often with hallucinations, illusions and noisy restlessness. The confusion merges into coma, and death is the inevitable termination.

PRESBYOPHRENIA

This is a condition of cortical degeneration occurring in middle life and in the pre-senile period, especially in women. It is characterised clinically by progressively complete failure of retention, so that recent memory disappears, and therefore in the course of time much of the more remote memory also; by lack of comprehension, and consequent increasing disorientation; by lack of insight; and by a fatuously happy mood with facile laughter and occasional irritability. The gap in memory is commonly filled by invention (confabulation), again without insight. There is a deterioration in the general behaviour: the patient no longer takes ordinary care of her clothes, etc., and, although in some cases still a young woman, she becomes incapable of the simplest household responsibility. She is very talkative, rattling on in an incomprehensible way, the question that prompted her to begin to talk having been quite forgotten. Cases of this sort not infrequently end with focal signs, *i.e.* with a clinical picture indistinguishable from Alzheimer's disease.

ALZHEIMER'S DISEASE

This depends upon a degenerative change in the brain cortex, beginning usually in the pre-senile period, *i.e.* in the fourth decade (sometimes as early as the thirties). There is a diffuse cortical atrophy of senile type. Microscopically there are wedge-shaped cortical foci showing loss of cells, from gradual occlusion of the smaller blood-vessels which run from the meninges into the cortex. The occlusion of these vessels results in numerous small hæmorrhagic

softenings, or in atrophic areas. Gross focal lesions such as occur in arteriosclerosis are wanting. The lost nerve-cells are replaced by whorls and tangled masses of fibrils (which are held to be the intracellular fibrils of the degenerated nerve-cells).

Clinically the patient exhibits loss of memory, recent and remote, with impairment of comprehension and lack of insight. Focal disturbances such as aphasia appear early. Indeed, the clinical picture of Alzheimer's disease is that of presbyophrenia plus focal signs. Later the patient becomes restless and talkative, singing and laughing. The aphasia reaches a profound degree, speech becoming a senseless jargon. Walking becomes impossible. Other focal signs appear (paralysis of the limbs). Epileptic attacks occasionally occur, and the pupillary reactions may be lost. The course is progressive, but slowly so, towards death.

Pick's Disease is clinically indistinguishable from Alzheimer's disease, but is characterised by a more definitely familial incidence, brain atrophy that falls more in certain areas (frontal and temporal) and comparatively greater loss of white matter.

PSYCHOPATHIC REACTION TYPES

Temperamental instability (sometimes called "constitutional psychopathic inferiority") is a factor common to the predisposition to many mental illnesses; but in some persons it reaches such a pitch in itself that, even apart from any incidental complicating mental illness to which the instability renders its possessor prone, it may be a serious factor in producing maladaptation and general inefficiency. When combined with some degree of intellectual defect, it is still more prone to produce failure in life, alcoholism, drug addiction, or actual antisocial behaviour (suicidal attempts, delinquency and crime). Persons suffering from this degree of temperamental instability, and being thereby far too readily depressed, just as they are too easily elated or made suspicious (with ideas of reference) or antagonistic or rebellious, are more prone than their normal neighbours to develop definite mental illness when faced with some difficulty in life; but just as such psychoneurotic or psychotic episodes are more easily provoked in them than in normals, so these episodic manifestations more readily subside. Such individuals often betray themselves, even on superficial inspection, by their frequent change of occupation and by their lack of concrete plans. Some of them have great aims, but all of them lack persistence.

In a number of them much improvement can be effected if they are treated early enough. There is evidence that in some at least the instability is not innate, but acquired in response to early influence of environment, especially of the family. Apart from intensive psychotherapy, the treatment is one of practical arrangement and, as far as possible, safeguarding. The selection of the most suitable occupation after an examination of the patient's abilities, intellectual or manual, is especially important. Any one finds it more easy to stick to a job he is naturally fitted for. This, together with sufficient social and other provision and more or less supervision by some one in whom the patient has confidence, is the best prophylactic of serious consequences of the instability. When the temperamental instability has brought the patient in contact with the law, full use should be made of probation, coupled with investigation into the circumstances and motives of the delinquent act, and a subsequent attempt to place the patient in a suitable environment.

In children and adolescents temperamental instability produces special problems which are at the same time more hopeful than at a later age. In such patients of the hospital class full use should be made by the practitioner of the out-patient clinics (psychiatric and pediatric) of general hospitals, which are equipped to deal with them; of child-guidance clinics, of school authorities, social workers and of the appropriate charitable organisations, as well as, in delinquency, probation officers, some of whom are now specially trained in this branch

of the work. Instruction of the parents is an important part of the treatment. Faulty attitudes of over-solicitude, etc., must be corrected after their influence on the child has been explained.

"*Folie à deux*," or "communicated insanity," is the term applied when two persons closely associated with one another suffer simultaneously a psychosis in which one member of the pair appears to have influenced the other in his delusional ideas. The condition is not, of course, necessarily confined to two persons, and may involve three or even more ("*folie à trois*," etc.). It is commonest in persons living secluded lives and in elderly people. Husband and wife, brother and sister, or parent and child, or friends of the same sex living closely together are the usual subjects of the condition. It is commonly a paranoid one—delusions of persecution, sometimes mingled with delusions of grandeur (royal birth, etc.). Occasionally there is a collective hallucinosis (*e.g.* of infection by insects which are seen). One or other patient has the predominant *rôle* and plays unwittingly upon the suggestibility of the other, who may be over-suggestible either from affection, ignorance or hysteria.

MENTAL DEFICIENCY

(*Amentia*)

Mental defect, or "amentia," as it is often called in this country, refers to defective intellectual endowment, existing either in the germ-plasm (primary amentia) or acquired as the result of intercurrent disease at any time after conception (secondary amentia).

The causes of mental defect are mainly these: (1) Heredity. There is a form of defect which is heritable, probably as a Mendelian recessive. (2) Blastophoria: parental alcoholism, syphilis, tuberculosis, or debility from any cause, devitalising the germ-plasm. (3) Birth injury. (4) Disease in early life, especially toxic and inflammatory conditions of the brain (meningitis, encephalitis, etc.).

Physical accompaniments are common, especially in the primary form, as the so-called "stigmata of degeneracy." These consist in anatomical malformations—of the skull, as microcephaly, macrocephaly, hydrocephalus, steeple-skull, etc.; of the palate and teeth; and of the eyes and ears; and in physiological disturbances (usually dependent on anatomical lesions), such as paralysis, tremor, stammering, clumsy speech and choreiform movements, strabismus, nystagmus and epileptic attacks.

It is usual to classify mental defectives according to the degree of their defect. In the Mental Deficiency Act of 1913 they have been divided into idiots, imbeciles, feeble-minded and moral imbeciles (**14**).

The criteria which have been used clinically and legally (as in the definitions given below) have been principally those of conduct and capacity, *e.g.* whether the patient could learn at school and whether and to what extent he was afterwards capable of earning his own living. But in 1906 Binet and Simon, two Parisian psychologists, devised "tests of intelligence" which, with various modifications, have since been much employed to facilitate more accurate diagnosis and classification. These tests enable a "mental age" to be assigned, according to the number of tests passed. Adult defectives having a mental age less than that of a normal child of two are idiots; those with a mental age between three and seven correspond to imbeciles; and those above seven, but not more than about ten in mental age, are feeble-minded. The upper age-limit for feeble-mindedness depends a good deal on associated temperamental factors. A degree of mental development which would allow its possessor to earn a living and keep a place in the community under ordinary conditions may be insufficient for these purposes by reason of associated temperamental instability, which, along with the intellectual defect, renders the patient legally and socially classifiable as feeble-minded. Defectives of all grades are therefore further divisible

into " stable " and " unstable." The mental age of the average normal adult on the above scale is now assumed to be fourteen years. To make comparison at different ages possible it is necessary to express the mental age as a function of the chronological age, and the expression $\frac{\text{mental age} \times 100}{\text{chronological}}$ is known as the " intelligence quotient," or I.Q. On the whole, the latter remains remarkably constant throughout the development of a given individual. To reach an approximate estimation of an individual's capacities, it is necessary not only to apply tests of intelligence, so called, like the Binet-Simon tests, but tests of practical ability, such as " performance tests," " maze tests," and tests of mechanical aptitude, for all of which special apparatus and formulæ have been devised. Tests of temperament are much more difficult; the best criteria of temperament are obtained from the history **(12)** **(15)**.

The following is the classification according to the **Mental Deficiency Act of 1913,** with the corresponding **symptoms.**

Feeble-minded or Morons " Persons in whose case there exists from birth or from an early age mental defectiveness not amounting to imbecility, yet so pronounced that they require care, supervision and control for their own protection or for the protection of others, or, in the case of children, that they by reason of such defectiveness appear to be permanently incapable of receiving benefit from the instruction in ordinary schools " (Mental Deficiency Act, 1913). By the Mental Deficiency Act of 1927, " early age " was defined as not exceeding eighteen years.

" Stigmata of degeneracy " are frequent in the feeble-minded. Delay in learning to walk and to talk is the rule in early childhood. Enuresis and sometimes fæcal incontinence up to a late age are more frequent than in the normal. There is also abnormal susceptibility to infections. The mental functions show distractibility of attention, which itself makes learning difficult, in addition to a defect of comprehension and of ability to reason abstractly. The defect of association capacity which underlies the defect in comprehension is responsible, together with a lack of persistent emotional drive, for a defect in imagination, which even in the adult feeble-minded is childlike in its simplicity. The males do not get much beyond the stage of picturing themselves as engine-drivers, and the day-dreams of the girls do not surpass the fairy-princess level. Emotionally, many are stable and docile, but their very docility makes them easily led into delinquency, illegitimacy or actual crime. A few are unstable, passionate and uncontrollable. At school the feeble-minded, even at the best, hardly perform work equivalent to the average Standard II. The lowest grade of feeble-minded are incapable of any scholastic attainments at all: they cannot master words of even one syllable, or perform the simplest addition or subtraction. Fortunately, in the higher grades many are capable of being useful at handicrafts of a simple kind, and of supporting themselves in adult life; and a considerable proportion of those classed as feeble-minded at school cease to be so classed as adults, since they prove to have sufficient manual ability to earn a living and sufficient common-sense to manage their lives on a simple level. The corresponding mental age is seven to ten years.

Imbeciles are " persons in whose case there exists from birth or from an early age mental defectiveness not amounting to idiocy, yet so pronounced that they are incapable of managing themselves or their affairs, or, in the case of children, of being taught to do so." Imbeciles as a class show a higher incidence of stigmata than do the feeble-minded, since a large proportion of them belong to the group of primary aments. They are clumsy in movement and fatuous in expression. Their vocabulary is very limited, and scholastic ability almost *nil*. Some are exceedingly restless. The unstable variety may exhibit simple cunning, violent anger, jealousy, careless habits, immodesty and unrestrained masturbation. Not a few are childishly vain. The corresponding mental age is three to seven years.

Idiots are " persons so deeply defective in mind from birth, or from an early age, as to be unable to guard themselves against common physical dangers." In idiots physical degeneracy reaches such a degree that they may be recognised at a glance. They are stunted, misshapen, suffer from various paralyses, and if they can speak at all, can utter only a few words, and then in a clumsy way. They do not attend to the calls of nature, but constantly wet and soil themselves. They do not eat, but rather " wolf " their food. Some are destructive of everything within their grasp. Many of them are bedridden of necessity from locomotor defect; those that can get about by themselves are exceedingly clumsy. Even more than imbeciles they are subject to infections, and they fortunately, as a rule, die young. Intellectual processes are virtually absent. Only the most primitive emotions—rage, cruelty, fear and bodily pleasures—are evinced. The corresponding mental age is less than two years.

Moral imbeciles are " persons who from an early age display some permanent mental defect coupled with strong vicious or criminal propensities on which punishment has had little or no deterrent effect." The term " moral imbecile " is unfortunate, because in a considerable proportion of cases so designated there is little or no intellectual defect. The morbidity is in the emotional sphere. Such persons appear to have none of the emotions that are such important constituents of the moral sentiments. They lie, steal, drink to excess, are sometimes violent and even cruel without provocation, and are unprincipled and untrustworthy in every way; yet they never at any time show any compunction or any genuine feeling of regret. Punishment has no effect in mending their ways. Treatment is mainly by way of control. It is well for their relatives if " moral imbecility " is diagnosed early (although it should not be diagnosed earlier than late childhood), and steps taken to segregate the patient by certification under the Mental Deficiency Act. Later they are still more difficult to deal with. The principal hope of getting control of them then becomes this: that they should commit some crime and so be dealt with by imprisonment, or that they should develop a psychosis and become certifiable under the Lunacy Act.

Pathological Classification. Defectives are also classified as follows: (1) *Primary aments*, who fall into three main groups: simple, microcephalic and mongolian. (2) *Secondary aments*, who are divisible into (*a*) those having gross cerebral lesions—amaurotic, syphilitic, hydrocephalic, porencephalic, sclerotic, paralytic, and other after-effects of gross inflammatory or vascular lesions, such as epidemic encephalitis; and (*b*) those without gross cerebral lesions, but who suffer from general arrest of neuronic development, epileptic, cretinous, or nutritional. Many of them have been described in earlier sections of this book. The result of disease of sense-organs and corresponding lack of cerebral development (" isolation amentia ") is dealt with below. All of these types of amentia may exist in any of the degrees of feeble-mindedness, imbecility and idiocy.

Below is a description of certain well-defined types:—

Microcephalic amentia is the term applied to a condition in which the mental defect is associated with an obviously small skull, commonly less than 17 inches in circumference. But if the shape of the skull rather than the skull size be made the criterion, patients with skulls of a circumference 2 inches or so more than this may be included. The typical pointed or " bird-like " shape is produced by recession of the frontal and flattening of the occipital region, with which are associated hypoplasia of the cerebral hemispheres and immature development of individual neurones and fibres. There are imperfect development of gyri, and local areas of agenesis. The shape of the skull gives the microcephalic a bird-like appearance. In addition he is usually of small stature. The brain has fewer cells than normal, but shows numerous embryonal and heterotopic cells. The majority of microcephalics belong to the idiot and imbecile classes; a few are merely feeble-minded. As a group they are vivacious, restless, affectionate and well behaved.

Mongolian aments are so called because the eye-slits shape obliquely upwards and outwards. The epicanthic fold of skin at the inner canthus is strongly developed. In addition the tongue is large and marked by transverse fissures—the " scrotal tongue " ; and the skull is brachycephalic from flattening of the frontal and occipital regions. The first dentition is delayed; the teeth are small and decay early. The nose is short, the hands and feet broad, the thumbs and little fingers shorter than normal, while the latter are slightly concave towards the ring fingers. The palms often possess only a transverse furrow—the so-called " simian line." The ligaments are lax, so that the joints can be hyperextended. Congenital abnormalities of all kinds, and especially congenital heart disease, are common.

Mentally the majority are of imbecile grade. Many are feeble-minded, and a few are idiots. They are placid, given to grimacing and mimicking. They often show a good appreciation of rhythm and a pleasure in music. The cause of mongolism is still in dispute. The one factor that is definitely correlated is maternal age—mongols are born mainly to elderly mothers.

Sclerotic Amentia. Amentia is dependent in a small proportion of the cases upon neuroglial lesions either in a diffuse or in a circumscribed (nodular or tuberous) form. In both instances the picture of mental defect is complicated by various paralyses, by tremors, and, especially in the tuberous form, by convulsions. In a few cases of tuberous sclerosis, adenoma sebaceum and tumours of various internal organs have also been present. To such a combination of lesions the term " epiloia " has been given. In the hypertrophic diffuse form of sclerosis headaches are a prominent symptom.

Sense Deprivation and Mental Defect. It is now realised that the mental defect commonly associated with a lesion of one of the organs of special sense is more apparent than real, and is dependent not on innate deficiency, but lack of education through the missing organ. Recent special tests of the intelligence of children completely deaf from an early age have shown that they are no less intelligent on the average than the normal child.

Idiots savants are persons who, although suffering from a general mental deficiency, yet exhibit an unusual aptitude in one direction. For example, some imbeciles and feeble-minded persons have a phenomenal memory.

Incidental Psychoses and Psychoneuroses complicating Mental Deficiency. Mentally defective persons, even more than ordinary people, are liable to develop mental illness of some kind or another in face of difficulties. But just as they more easily develop incidental psychoses or psychoneuroses, so they recover, on the whole, more readily. The emotional disturbance of the psychosis may however leave the patient even less socially adequate than before, so that for example a defective who before the onset of a schizophrenic episode was able to live in the outside world may, in spite of the subsidence of schizophrenic symptoms, have to remain permanently thereafter in an institution. Hysterical manifestations in defectives are apt to be more gross than in individuals of normal intelligence. The patient has visions and hears voices with great readiness, and the hallucinations have a childlike simplicity; while paralysis of entire limbs is preferred to the tremor and aches and pains so common in the average hysteric.

Treatment of Mental Defect. The problem of mental defect arises principally in three spheres: of education, social control, and occupation. Any child who is a year or more behind the average intellectual development of his age (the " dull and backward " group) is best taught in a special class. When the defect amounts to three years or more, a special school is desirable, with special methods of teaching and special attention to simple handicrafts, and only as much instruction of the scholastic kind as the child can assimilate. Home control revolves round two factors in the child: his intellectual and his temperamental status. Often the parents are annoyed by his apparent stupidity,

while his brothers and sisters tease him. They must be taught to make allowances. Temperamental difficulties may be controlled by wise parents, but if, as too often happens, one or both of the latter are themselves defective, a foster home may be necessary. Legal provision is made for placing defectives under " guardianship " or in approved homes.

Where the defect reaches an intensity which makes these methods inapplicable, resort must be made to institutional care after certification as detailed in the section on legal aspects.

The question of occupation after leaving school is very important. A suitable choice may produce a useful citizen ; an unsuitable choice may result in, first, frequent change of job, and, later, chronic unemployment and sometimes also delinquency or crime. The choice has to be made on the basis of a knowledge of the child's school achievements, supplemented, if necessary, by special tests of industrial aptitude.

LEGAL RELATIONSHIPS

LUNACY CERTIFICATION

Certification that a person is a " lunatic " or " of unsound mind " involves, besides the actual problem of certification, the question of the legal responsibility of a medical man for any certificate he may write. Certification is fundamentally a legal proceeding. It is not merely a step towards treatment, but a certified lunatic is *ipso facto* deprived of some of his civil rights, including his liberty. Furthermore, it is necessary to remember that not only are there direct legal consequences of certification, but there may be indirect civil consequences as well ; for example, if a business man has once been certified, and knowledge of the fact comes to his professional colleagues, he may find himself deprived, if he recovers, of his right to serve on a board of directors or to hold some similar position of trust. Accordingly, in certifying a patient the following points must be carefully considered : (*a*) whether certification of the patient in question is medically desirable ; (*b*) whether it is legally possible ; and (*c*) whether, if (*a*) and (*b*) are satisfied, certification will grievously handicap him in his business after his recovery. It should be observed that the practitioner certifies not only that the patient is of unsound mind, but " a proper person to be detained under care and treatment." The reasons for certifying that the patient is such a person were detailed by Sir Claud Schuster, Permanent Secretary to the Lord Chancellor, in his evidence before the recent Royal Commission, as follows : (1) to protect the public from injury ; (2) to protect the patient from self-injury ; (3) to give treatment with a view to cure or amelioration which cannot otherwise be given ; (4) to protect the patient from injury due to want of care.

Any disorder of conduct resulting from disorder of mind, which disables the patient socially to such an extent that he is incapable of looking after himself or his affairs, is sufficient ground for certification. But it is to be noted that there must be disorder of mind, and there must be disorder of conduct involving either conflict with society or unnecessary loss to himself, or there must be disorder involving neglect of his personal health and safety. Mere disorder of mind, if the conduct remains socially normal, is not a ground for certification. Thus a patient who firmly believed over a period of twelve years that he was in daily communication with the rulers of this country and the commanders of its armies, but who carried on a successful business and lived a happy family life the while, did not become certifiable till, as the result of business reverses, he became depressed and attempted suicide by thrusting a hat-pin twice into his abdomen. In other words, the mere presence of delusional beliefs does not give ground for certification. On the other hand, the absence of demonstrable abnormal mental trends does not make certification impossible, for abnormality of conduct alone

can form a valid basis. A patient who, in the absence of physical reasons, becomes inactive, refusing to eat and to attend to the calls of nature, may have to be dealt with by certification to enable adequate methods of feeding to be instituted.

The patients most difficult to certify are (1) those who are antagonistic and have sufficient control and insight not to give themselves away in the presence of the examiner; this group includes paranoid states especially; (2) those who have a disorder of conduct only exhibited in special circumstances or in relation to certain persons, and who show little or no demonstrable mental defect or disease apart from such conduct, and who deny the conduct; such are certain chronic alcoholics who shamefully misuse their wives and families; (3) those with intermittent or episodic attacks of mental illness, *e.g.* epileptics and alcoholics who are still sufficiently well in the interval not to show any disorder of a degree that would carry conviction to the lay mind (which for these purposes is also the legal mind); it is, however, not justifiable to certify a chronic alcoholic patient during an attack of delirium tremens, if he is not certifiable in the interval; (4) the mildly excited patient, who may be extravagant and lacking in finer discrimination and may play havoc with his business in consequence, but who in an interview is suave and plausible when questioned about his business transactions.

In any case a mentally sick patient should be certified only for his own safety and protection or for the protection of society, and only where no other method medically as efficacious presents itself. Such another method may fortunately be found in the provisions that are made for voluntary patients in mental hospitals. This method requires that the patient himself shall sign a letter in which he states that he wishes to place himself under care and treatment in a certain hospital which he names. No other formality is necessary. In the case of patients under sixteen, there is a special form which is signed, not by the patient, but by his parent or guardian, to which is appended a recommendation by a medical practitioner. This, whenever the patient can be persuaded to sign, is the method of choice. It has none of the drawbacks of certification. It has, however, some disadvantages of its own. (1) It is precisely the patient most difficult to certify who cannot be persuaded to sign a voluntary document—the paranoid, the chronic alcoholic and the hypomanic. (2) A patient placed in hospital on a voluntary basis is permitted to leave on seventy-two hours' notice. This can be very inconvenient, harmful and even dangerous in a patient who, for example, is suicidal. In such an event, the only procedure that is fair to the patient is to have him certified, although no one would like to persuade a patient to enter a hospital as a voluntary boarder and then to detain him by certification if he insists on leaving. The better method is to discharge the patient to the care of friends before certifying. In England, by the Mental Treatment Act of 1930, the voluntary method now applies to both private and rate-aided patients; the latter cannot afford to pay anything at all. The lowest rate for board, lodging and medical attendance for a private patient in a private mental hospital is usually about £3 3*s.* a week; but in several public (*i.e.* rate-supported) mental hospitals, in and outside London, voluntary boarders are admitted as private patients for £2 2*s.* a week.

The legal sanction to certify a patient as of unsound mind is given in the Lunacy Act, 1890. There are various forms of procedure in committing a patient to a mental hospital, designed to meet different cases. Method (1): by *Reception Order on Petition.* This applies only to private patients who have been living in their family or with their friends. For rate-aided patients the method (2) is by *Summary Reception Order.* This second method is also applicable to private patients who (*a*) are not under proper care and control (*b*) are cruelly treated or neglected by their relatives, or (*c*) are wandering at large. Method (3) is by *Urgency Order,* and method (4) by *Inquisition.* The latter is a special and

elaborate method rarely used nowadays, and reserved for instances where a large estate is involved (**13**).

Method (1). For the complete legal process of certification by *Reception Order on Petition* five documents are required: (1) the petition of the nearest relation or the nearest available relation or, failing them, of any other person; but failing the nearest relation, the reason why the latter is not the petitioner must be stated; (2) a statement of particulars, consisting in answers to a series of printed questions; (3) and (4) two medical certificates, described below; (5) the reception order, signed by the appropriate judicial authority, authorising the patient's reception in a recognised mental hospital or home.

Method (2). In procedure by *Summary Reception Order* the necessary documents are similar, but there is no form of petition, since the relations or friends are not available. The statement of particulars is signed by the civil authority, *e.g.* any constable, relieving officer, or overseer of the parish in which the alleged lunatic is found. The form of the medical certificates is in all cases the same as in method (1). Two certificates are required for private patients, and one certificate for a rate-aided patient.

Method (3), by *Urgency Order*, is intended to be used only if it is essential that the patient shall be moved to hospital at once. Only one medical certificate is required, together with an order, signed by the nearest relative, or if the nearest relative is not available by some responsible person, the reason for the absence of the nearest relative's signature preferably being stated. A statement of particulars must be enclosed, and signed by the person signing the Order. If the person signing the Order is not the same as the signatory of the statement, the reason must be stated. An Urgency Order remains in force for only seven days, by which time, if the patient has not recovered, it must be replaced by a certificate under methods (1) or (2). The practitioner signing the certificate to accompany the Order must have seen the patient within two clear days before signing, or preferably (according to comments in the recent case of *Hume-Spry* v. *Smith and Another*, *Times*, 1927) on the same day. Similarly the relation or other person signing the Order itself must have seen the patient within a similar interval.

The Mental Treatment (England) Act of 1930 introduced a further method of placing a mentally ill person in a recognised hospital or home, without actual certification. This is the method of Temporary Recommendation, and applies only to the so-called non-volitional cases, *i.e.* the patient who is judged incapable of either giving or withholding his consent to be placed in hospital. Strictly interpreted the operation of the section is confined to delirious or stuporous patients, but judging from the official attitude of encouragement revealed in the Board of Control's Reports, some latitude is allowed in the clinical interpretation, so that, *e.g.* manic excitements not of delirious intensity may be included. The method requires that a request be signed by a relative in the case of a private patient, or by the civil authority (Public Assistance Officer) in the case of a rate-aided patient, and that two medical recommendations should be signed, one by a medical man specially recognised by the Board of Control for the purpose.

Medical Certificates. One of the certificates for the Reception Order on Petition must be signed by the usual medical attendant of the patient, unless some valid reason for being unable to obtain such certificate is mentioned in the petition, when both certificates may be given by independent medical practitioners. The two certifying practitioners must make their examinations separately. Mr. Justice Hawkins in *Weldon* v. *Semple* said: "The statute requires separate examinations by the medical men, and here they both go together—as gross an evasion of the Act as could be conceived. . . . Anything more calculated to excite suspicion could not be supposed than both the doctors meeting and going together." But where one of the certifying doctors has not previously seen the patient—as is usually the case, since both cannot be the

patient's "usual medical attendant"—it is obvious that he must be made acquainted with the previous and the present conditions before he proceeds to his examination. It is therefore suggested that to conform to the law in the letter as well as in the spirit, a certain interval, say of a day or at least of several hours, should be allowed to elapse between the visit of the consultant and the visit for purposes of certification of the usual medical attendant.

There are certain *statutory prohibitions* which should be known to the medical man signing a certificate—prohibitions which are designed to eliminate the entrance of self-interest into the examination. The medical certificates must not be signed by any of the following persons: (1) a practitioner related by blood or business to the other certifying practitioner—father or father-in-law, mother or mother-in-law, son or son-in-law, brother or brother-in-law, sister or sister-in-law, partner or assistant; (2) a practitioner who is at the same time either the petitioner himself or the superintendent, proprietor or medical attendant of the asylum, hospital or house to which the patient is sent; (3) a practitioner interested in the payments on account of the patient; (4) the husband already named, or wife, father or father-in-law, etc., of any of the persons.

The Medical Examination. The examination with a view to certification must be made separately, as stated above. A physician is sometimes asked by relatives labouring under a mistaken idea of tactfulness to see the patient under a false guise, and not as a medical man at all. He should never be persuaded to do this. It is essential to be quite frank with the patient, and if he asks point-blank whether the intention is to certify him, the practitioner should state that he has come to see the patient about the state of his health, especially his mental health; that there is no intention of certifying him if it can possibly be avoided; and that in any case certification is only performed by medical men when it is definitely necessary for purposes of treatment.

The medical practitioner should always *take notes* of the interview, either while it is going on, or, if that is impossible on account of the patient's suspicion or of his conduct, such as the rapid flight of his ideas, he should make notes immediately after leaving the patient. These notes should contain all the relevant facts that have been elicited. Some verbatim samples of significant portions of his stream of talk are invaluable. The necessity for taking notes—and preserving them—of every case which one certifies seems to be shown very clearly by the strictures of the Judge upon Dr. Fisher in the recent case of *Harnett* v. *Fisher*. Dr. Fisher certified Mr. Harnett to be insane in 1912, and Mr. Harnett brought an action for negligence resulting in wrongous certification in 1926, fourteen years later. The Judge asked, "Tell us one single question you asked him." Dr. Fisher replied, "I must have asked him something, but I do not remember what the phrases were." The Judge said: "I should have thought you would have told us the questions you asked him," and commented, "He says he put such small questions, he cannot tell what they were."

The examination itself should be conducted as any other mental examination is conducted, in a systematic fashion, taking each topic in turn as far as possible. A careful physical examination should always be included (*cf.* case of *Hume-Spry*). It is necessary also to inquire about the mental condition of the patient before the onset of his illness. Valuable confirmatory evidence may be obtained in this way, and, on the other hand, rash conclusions may be avoided. It has been pointed out that great religious activity may be a fairly normal characteristic of one individual, *i.e.* of some one who has previously been of a religious turn of mind, but totally foreign to another individual's mentality and so a symptom of illness.

There are certain points which are specially telling in a certificate, and which should be stated if they are observed. Strangeness of conduct is one of these, *e.g.* mutism and resistiveness. The presence of morbid ideas is another, especially if they have developed to the extent of being delusions. But it is insufficient

to state in the certificate that the patient has delusions. The delusions, or some of them, must be specified in detail, and further (what is equally important) the medical practitioner must be reasonably certain that they are in fact delusions. Thus a man may be jealous of his wife and say that she is having an affair with another man. This may be true, and it is very difficult to disprove, so that the physician has only the presumption of its falsity to go on. A patient said that every one was looking at him and talking about him in the workshop in which he was employed. This was true, and not a delusion. His erratic conduct had drawn their attention on numerous occasions. In reporting a delusional idea, therefore, it is necessary for the practitioner to add some such phrase as " which I believe to be false," or " which I know to be false." Hallucinations are useful evidence for a certificate, being convincing to the layman. It is, however, not infrequently impossible to state their content, and their presence is often a matter of more or less expert inference from the patient's behaviour. Nevertheless, as they are very generally accepted evidence of insanity, the evidence of their presence should be included in the certificate.

Neither delusions nor hallucinations may be present, and the affective condition alone may be sufficient for certification, provided it is abnormal enough to influence behaviour in the direction either of inactivity, of agitation, or of attempts at suicide. Merely the expression of suicidal ideas, if in a setting of considerable depression, is sufficient for a certificate to be written, since in such a setting they are very apt to be carried out. Suicidal determination, in the absence of demonstrable mental disorder, can apparently only be dealt with in law by the police if ordinary persuasion fails. Defects of memory, of orientation, and of comprehension are very useful corroborative evidence. They are not usually considered sufficient in themselves to establish the validity of a certificate, but they are not infrequently made to serve in the case of old people who cannot be looked after at home and who require special care on account of their increasing mental inadequacy.

It is very unwise to put a diagnosis in a certificate. It adds nothing to the facts, and it may be wrong (*cf. De Freville* v. *Dill*, *Times*, May 19th, 1927, where the certifying practitioner wrote that the patient was suffering from acute mania, and where it was subsequently proved that within twenty-four hours of the certificate being written to that effect the patient was perfectly normal).

The second division of the certificate is for " facts communicated by others." A valid certificate can never be made on these facts alone, and this section may be left blank entirely. But where the facts observed by the practitioner himself are not very conclusive, the " facts observed by others " may be of considerable value. The full name, address and occupation of the informants must be given. It is probably better to make a rule of placing information in this section whenever it is available. It helps to show " reasonable cause." The patient should evidently be questioned on these facts alleged by others. In the *Harnett* v. *Fisher* action, already referred to, the judge asked Dr. Fisher, " Why did you not take the trouble to ask him about matters the brother had spoken of—whether they were correct or not ? You answered he was incapable of telling you anything because he could not speak. How could he tell you anything unless you asked him ? " Also in the case of *Hume-Spry* v. *Smith and Another* the plaintiff complained that in certifying him the defendants relied on his having fixed delusions that his wife had committed misconduct, and on statements that he had tried to murder his wife and to commit suicide. The plaintiff contended that the infidelity was a fact, and that the allegations about himself were false. The defendants had to admit that they had made no attempt to discover whether the patient's statements were true and that they had omitted to question the patient on the topic of his alleged attempts at murder and suicide. Counsel for plaintiff asked, " How can you determine whether a man is wrongly charged with using threats unless you ask him about them ? " (*Times*, March 12th, 1927).

Finally, the practitioner signing a certificate of unsoundness of mind must be in actual practice as well as being registered. The date of examination stated in the certificates (not only the date given at the foot) must be within seven clear days of the petition. All blanks on the certificate must be filled in.

Protection of Practitioners. Since certification deprives the person certified of his civil rights, it is an act which involves great responsibility and should never be undertaken without the most careful consideration. It is a step also which may have serious legal complications, for the person certified may, in indignation at the deprivation of his liberty, ask for a trial by jury as to his alleged insanity. Furthermore, when a person who has been certified recovers sufficiently to be set at large, he may take action for " wrongous " certification. Lunacy certification involves apparently greater risks than most other forms of medico-legal work. There is even a small class of patients in whom litigiousness is the main symptom—namely, the so-called "litigious paranoiacs." Further, patients recovered sufficiently to be discharged from certification have often incompletely recovered and may continue to have delusions which may very well be directed towards the medical men who were the apparent " *agents provocateurs* " of the detention. It would therefore seem *a priori* probable that a medical man certifying a patient undergoes a peculiar risk of actions for damages. This has been a very prevalent impression, but, notwithstanding some recent alarms, it is not the case in practice that the certifying practitioner is peculiarly liable to actions at law. Only one action for wrongous certification has ever been brought in Scotland, and " that action should never have been brought " (Robertson). The practitioner is now more adequately protected by the Mental Treatment Act of 1930. By Section 16 of this Act, it is necessary for the complainant to lay a petition before a Judge in Chambers, and to show that the certifying practitioners acted in bad faith and without reasonable care. It is still very desirable that every medical practitioner should join a medical insurance society. Otherwise he may find himself involved in litigation which is ruinous to him as a private individual depending on his own financial resources.

When there is any doubt in the practitioner's mind as to the desirability of certification, a second visit to the patient may be helpful, and certainly will help to forestall any allegation of want of reasonable care.

On the other hand, refusal to certify may also carry legal responsibility for the practitioner. This point is not legally settled. Mr. Justice McCardie suggested that, while a doctor might owe such a patient care about certification, he might not be liable to the patient for negligence if he refused to certify a person actually of unsound mind who afterwards injured himself (*De Freville* v. *Dill*; editorial, *Times*, July 8th, 1927).

Appointment of Receiver. When a person has been certified as of unsound mind, and has property or a business which must be administered, and when it is considered that his mental disorder makes him incapable of business transactions, application is made to the Judge in Lunacy by the petitioner for the appointment of a receiver. The latter may be the nearest relation or a solicitor, or other person elected by the Judge. When the patient is decertified he has to make application to the Judge for the termination of the receivership.

When a person who is not actually certified is considered to be incapable of managing his affairs, and when it is necessary that some one should be appointed to manage them, either the patient may grant a power of attorney to some person approved of by him or, where this is inadvisable or not permitted by the patient, the usual medical attendant of the patient may, at the request of the patient's representatives, make an affidavit that the patient is, " by reason of mental infirmity arising from disease or age," incapable of managing his affairs (sect. 116 of the Lunacy Act of 1890). A receiver is appointed accordingly by the Judge in Lunacy after he has satisfied himself of the necessity for the step.

MENTAL DEFICIENCY

Mental defectives are dealt with under the Mental Deficiency (England) Acts of 1913 and 1927.

Certification of a person as mentally defective under the Acts is carried out as follows: (1) If the patient is an idiot or imbecile of any age, the parent or guardian signs a statement of particulars. In addition, two medical certificates are required, one preferably by the usual medical attendant and the other by a medical practitioner specially approved for the purpose by the Board of Control. (2) If the patient is feeble-minded or a moral imbecile and is under the age of twenty-one, the procedure is as with idiots and imbeciles, but a certificate from a judicial authority is required in addition. (3) If he is a defective of any class or age, under *special circumstances*, as (*a*) neglected, abandoned, without visible means of support, or cruelly treated; or (*b*) found guilty of any criminal offence, or ordered or liable to be ordered to be sent to a certified industrial school; or (*c*) undergoing imprisonment or detention, or in an institution for lunatics; or (*d*) is a habitual drunkard (and some other provisoes), certification is carried out as follows: (i.) by petition with two medical certificates, one of which must be by a medical man specially approved by the local authority or Board, with a statement of particulars, and a statutory declaration by the petitioner, and a judicial order by a county court judge, a magistrate (police or stipendiary), or a justice of the peace specially appointed; (ii.) by order of the court, on conviction, or on a child being found liable to be sent to an industrial school; (iii.) by order of the Home Secretary (on imprisonment, detention in a reformatory or in a criminal lunatic asylum), with two medical certificates. In certification for this class of patient, the precautions and forms to be observed are very similar to those in lunacy certification, but the class to which the defective belongs must also be stated. General statements, such as "he is lacking in judgment," must be supplemented by the mention of actions or statements of the patient himself.

TESTAMENTARY CAPACITY

The practitioner is sometimes asked to adjudicate on a patient's mental capacity to make a will. The tests he has to apply are not identical with those required in matters of certification. All that is needed for testamentary ability is that the testator "shall understand the extent of the property of which he is disposing; shall be able to comprehend and appreciate the claims to which he shall give effect"; and shall not have such a disorder of mind that his sense of right or his affections are perverted—so that, for example, delusions influence him in disposing of his property; or a gross defect of memory prevents him from exercising his natural faculties. Hence a patient may be certifiably insane (from the point of view of his own safety), yet be capable of executing a valid will. On the other hand, he may suffer from such a disorder of mind that he can live at home, yet be incapable of making a will. This occurs principally in persons suffering from senile cortical deterioration, in whose case there is a gross defect of memory and comprehension.

CRIMINAL RESPONSIBILITY

The problem of criminal responsibility is the most debated of those concerning the social relations of psychological medicine. Medicine and the law have a difficulty in seeing eye to eye in regard to it. This is not surprising, and is usually held to arise from the divergence in social outlook of the lawyer from that of the medical man. The former is concerned for the safety of society, the latter for the welfare of the individual. "When I am tempted to pity the criminal, I remember also that there is a pity that is due to my country" (Sir Matthew Hale). But this is not the principal point. The difference lies rather in the

divergence of the legal from the medical concept of mind and mental disorder. The legal concept is of mind dominated by reason and freewill; the medical concept is of functions actuated by emotion and determined by intrinsic factors. In the legal mind everything is consciously known; in the medical mind much in unconscious and unknown. Hence come certain differences in medical and legal criteria of responsibility (**5**).

The plea of insanity (in bar of trial or in bar of sentence) is confined almost exclusively to murder trials. This does not mean that murder is almost the only criminal act which mentally ill persons commit. Arson, sexual offences, larceny, and so on are commoner among them than murder. But the defence of insanity in these conditions, if successful, leads only to compulsory detention in an asylum; and the net result is not profitable for the patient, since he could have gained his liberty just as soon if he had not been found a lunatic by the court. In capital crimes, on the other hand, a successful plea of insanity saves the patient from hanging. The law presumes that every person is innocent until he is proved guilty, and likewise that every person is sane until he is proved insane, in both cases to the satisfaction of the jury. The burden of proof of insanity rests therefore upon the defence. For proof of insanity there must be fulfilled the following conditions according to the current law of England.

McNaghten Rules. The accused must be proved at the time the action was committed, first, to have had disease of the mind; second, not to have known the nature and quality of his act, or (not " and "), third, not to have known that the act was wrong. These conditions are not actually embodied in a statute, but they are the substance of the answers in the McNaghten case (1843), and they have been the basis of all legal decisions as to criminal responsibility since that date. They refer to the time of the act of which the person is accused. They refer specifically to that act and the knowledge of it, and not to crime in general. The knowledge required is not of legal right or wrong: the accused person is not assumed to know any more of legal right and wrong than is the common property of the community. It is in effect the capacity to determine the moral quality of the act that determines responsibility. The McNaghten Rules partake of the medically out-of-date doctrine of the mental faculties and its corollary, partial insanity, the mind being regarded as divided up into a series of independent compartments, the cognitive faculty being one of the large subdivisions. Medicine has come to recognise that the mind is a whole, one and indivisible. There is no mental disorder, however partial in appearance, that does not have its reverberations throughout the rest of the affected mind. Consequently the purely intellectual criterion of responsibility falls to the ground, for the intellect as intellect may be unimpaired, but an emotional disturbance will alter or impede or nullify its effect on conduct. Conversely, intellectual defect means deficient emotional control. The influence of the doctrine of partial insanity on the judges who propounded the McNaghten Rules is shown in their reply to the fourth question put to them: " If a person under an insane delusion as to existing facts commits an offence in consequence thereof, is he to be executed ? " " The answer," said the judges, " must, of course, depend on the nature of the delusion; but making the same assumption as we did before—namely, that he labours under such partial delusion only, and is not in other respects insane—we think he must be considered in the same situation as to responsibility, as if the facts with respect to which the delusion exists were real. For example, if, under the influence of his delusion, he supposes another man to be in the act of attempting to take his life, and he kills that man, as he supposes, in self-defence, he would be exempt from punishment. If his delusion was that the deceased had inflicted a serious injury to his character and fortune, and he killed him in revenge for such supposed injury, he would be liable to punishment." The insane person may then kill a man with impunity if he believes that he is doing it in self-defence, while he is punished by death for a homicidal act which results from the belief

that the victim was reading his thoughts or tampering with his genitals. No account is taken of anything but apparently intellectual operations and their influence on conduct. No apparent allowance is made for such well-known phenomena as post-hypnotic and epileptic automatisms.

The practical issue is this: that, whereas it is nominally required in the trial of a person pleading insanity in extenuation of a crime that evidence be taken bearing both on his general state of mind at the time of commission of the crime and on his particular knowledge of the moral nature of the act, it is to the latter, the knowledge of the criminal act, that attention is principally or entirely devoted by the court. Consequently it not infrequently happens that a person who, from a general survey of his mental state, was undoubtedly insane at the time, is found sane in respect of the commission of one particular act, the criminal one. "It follows that a man can legally be hanged for murder and yet be regarded by the same court as unfit to take care of himself or his property" (Singer and Krohn). Fortunately for the insane criminal under sentence of death, there is a proviso in the Criminal Lunatics Act, 1884 (sect. 2, sub-sect. 4), that when the Secretary of State is informed by any means that there is reason to believe that a person under sentence of death is insane he shall appoint two or more legally qualified practitioners to examine such prisoner and to inquire as to his insanity. If the medical men or a majority of them find he is insane, the Secretary of State may, if he thinks fit, direct the prisoner's removal to an asylum (for criminal lunatics). In the end then the prisoner may be judged at his trial insane, but worthy of punishment, only to be exempted from it while awaiting execution of his sentence.

The law has taken some cognisance of the inconsistencies revealed in these ways by the exercise of wide powers of discretion by the judge in his instructions to the jury, and, more recently, by the appointment of a special committee under Justice Atkin (following the trial of Ronald True). The Atkin Committee made the following recommendation: "It should be recognised that a person charged criminally with an offence is irresponsible for his act when the act is committed under an impulse which the prisoner was by mental disease in substance deprived of any power to resist."

This recommendation, if adopted, would avoid certain difficulties arising out of the unqualified application of the McNaghten Rules. But it does not remove or supplant these rules, and consequently does not correct the antiquated theory of mind and mental disorder which they represent. The position of medical men who appear as witnesses in trials of criminal responsibility where a plea of insanity is put forward is beset with difficulties and disadvantages. First, the medical witness (an expert, and not an ordinary witness to fact) appears on one or other side of a case in which he is summoned. He is therefore, in the eyes of the court, to that extent biassed. He is obliged to gather his evidence partly retrospectively from the accounts of biassed persons (the patient and his friends). His personal direct observations of the prisoner's mental condition are made under the least favourable conditions—the accused person is in prison, and the time and opportunity for observation is limited by the circumstances of incarceration and of the fixing of an early date for the trial. In court he is asked to direct his attention less to what his training best enables him to judge, namely, the general mental state of the prisoner, and more to the much more difficult question of responsibility for a particular act, which is a matter of opinion.

The first of these difficulties the practitioner can do something in himself to mitigate. When asked to see a prisoner on behalf of one or the other side, he should reply that he will see him and examine him, that he will submit his report in accordance with the facts he finds, and that if, on the basis of his report, the legal advisers who made the request desire him to appear, he will do so.

To meet the other disadvantages, suggestions have been made, that to avoid

medical witnesses appearing on opposite sides, a panel of impartial experts should be appointed who will make a combined report to the court. But this does not yet occur in this country. To give time for sufficient examination, provision is made in certain countries for transfer of the patient to a psychopathic hospital for observation for a time. As an answer to the final objection—that medical witnesses are asked to testify to presence or absence of specific responsibility—it has been urged that responsibility is for the jury to decide. The British Medico-Psychological Association in a recent recommendation suggested that, in addition to the question laid down in the McNaghten Rules, the jury should be asked whether they considered the prisoner was insane at the time, and whether his act was related to his insanity.

REFERENCES.

1 DUNTON, W. R., Jr. "Prescribing Occupational Therapy." London, 1928.
2 FLOURNOY, H. "L'Enseignement Psychiatrique d'Adolf Meyer," *Archives de Psychologie*, 1926, xx. 81.
3 FREUD, S. "Introductory Lectures." London, 1922.
4 HART, B. "Psychology of Insanity." Cambridge, 1919.
5 HENDERSON, D. K., and GILLESPIE, R. D. "Text-book of Psychiatry." London, 3rd ed., 1933.
6 JUNG, C. "The Psychology of Dementia Præcox." New York, 1909.
7 KRAEPELIN, E. "Dementia Præcox," translated by Barclay. Edinburgh, 1919.
8 „ „ "Manic-depressive Insanity and Paranoia." *Ibid.*
9 MACCURDY, J. T. "Psychology of Emotion." London, 1925.
10 MEYER, A. Article on "Paranoia." Modern Treatment of Nervous and Mental Diseases, New York, 1913.
11 ROSS, T. A. The Common Neuroses. London, 1924.
12 TERMAN, L. M. "Measurement of Intelligence." New York, 1916.
13 THEOBALD, H. S. "The Law relating to Lunacy." London, 1924.
14 TREDGOLD, A. F. "Mental Deficiency." London, 1929.
15 WELLS, F. L. "Mental Tests in Clinical Practice." New York, 1927.

DISEASES OF THE SKIN (DERMATOSES)

It is not possible in a general text-book of medicine to present a complete review of the diseases of the skin, and in the following section much of importance has been omitted. It has been thought advisable, for example, to refer the reader to text-books of dermatology and surgery for descriptions of many tumours of the skin, both innocent and malignant, and no account will be found of the various diseases of the nails or of radiodermatitis. Dermatology has unfortunately in the past been regarded as a subject apart, and has been both neglected by the general physician and misunderstood by professed dermatologists. In reality it is clinically one of the most important of the special branches of medicine, since the skin is the mirror in which the state of the general health can be read, and a knowledge of the ætiology of its commoner disorders provides the key to the proper understanding of the pathology of disease. Of recent years dermatology has become more and more a part of general medicine, and it is as essential nowadays for the physician to acquaint himself with modern dermatological teaching as it is for the dermatologist to keep abreast with the advances made in medical pathology.

The skin is liable to the same pathological conditions as other organs and structures in the body, and the classification of its diseases is based upon these.

Thus there are changes in vascularity, inflammations, new growths, structural changes due to the presence of micro-organisms, such as those of tubercle or leprosy, lesions resulting from the circulation of disease-toxins, such as those of scarlatina and other exanthemata, the invasion of animal and vegetable parasites other than bacteria, hypertrophy and degeneration of the separate structures of the skin, and changes of pigment.

We have to consider also the disorders of certain organs contained in the skin, namely, the hair, the sebaceous glands, and the sweat-glands or coil-glands.

Many disorders of the skin have been already described, as, for instance, the eruptions characteristic of the exanthems, the cutaneous lesions of syphilis, lepra, glanders, actinomycosis, and elephantiasis, and the forms of hæmorrhage known as purpura.

The discrimination of the various diseases is based upon a careful observation of the local changes, or lesions, which take place in the skin, combined with a consideration of their distribution, duration, and associated and antecedent circumstances.

PRIMARY LESIONS

Blebs or Bullæ. Large vesicles, from 5 mm. to an inch or more in diameter. The fluid contents are clear, or slightly turbid, or bloodstained. They are often situated on an inflamed base: they heal by discharge of the contents, and the drying and shedding of the epidermic scale. ***Chaps, Rhagades, or Rimæ.*** Cracks or fissures through the epidermis, reaching the stratum mucosum or corium beneath, very sore and apt to bleed. ***Excoriation.*** A patch of skin deprived of the upper layer of the epidermis, and exposing the stratum mucosum. It is of a vivid red colour, and tender to the touch; and it secretes a small amount of serum, which may dry into a crust. ***Hæmorrhages.*** Cutaneous hæmorrhages

form larger or smaller spots of bright red, dark red, or purple colour: they do not disappear on pressure. As a rule, the blood is gradually absorbed, and the colour fades into brown or brownish-yellow, or becomes successively brown, green, and yellow, in the larger subcutaneous hæmorrhages. A yellowish-brown stain may be left for a long time. The smaller spots are called *petechiæ*, the larger *ecchymoses;* if they form streaks they are called *vibices.* In *capillary ecchymosis* a very fine mottling is produced, which looks like a hyperæmia, until it is found to persist under pressure. Exceptionally the skin involved in hæmorrhage sloughs and leaves an ulcer. ***Hyperæmia.*** This consists of redness, of varying extent, due to the blood vessels being distended with blood. It may be: (1) an *active hyperæmia* from vasomotor action; (2) an *early inflammatory hyperæmia,* with slight swelling, tenderness, and some indications of pyrexia; or (3) a *venous hyperæmia,* or passive congestion, with a more blue or livid colour than in the other forms. In all cases the redness disappears on pressure, to return when the pressure is removed—quickly in the first two cases, slowly in the last. ***Macules.*** Small areas of discoloration of the skin, which are unaccompanied by alteration in its surface or consistence. They may arise from a preceding hyperæmia, and then disappear shortly. They are generally more permanent if arising independently. ***Nodules.*** Solid elevations larger than papules. ***Papules.*** Small elevations of the skin, solid, or at least not visibly containing fluid. They arise mostly in the cutis, but may be imitated by accumulations of epidermic scales. They may be pointed (acuminate), obtuse, or flat (plane). ***Pustules or Pustulæ.*** Vesicles or bullæ containing pus. ***Scabs or Crusts.*** Irregular flat masses of dried serum, pus, or blood, or a mixture of these materials, forming upon and adherent to the raw surface which has secreted them, and frequently the result of a vesicle, pustule, or bulla. ***Scales or Squamæ.*** Collections of epidermic cells in the form of flakes. Sometimes, as in dandruff, there is a large admixture of the fatty matter of sebum. Scales vary from the small branny particles of measles (furfuraceous) to the large exfoliations seen in exfoliative dermatitis and in some cases of scarlatina, or the thick adherent masses of psoriasis. ***Scar or Cicatrix.*** The new growth of connective tissue, which results from the healing of sores, involving the papillary layer and deeper corium. When recent, they are pink or bluish in colour. Finally they become dead white, and contract in size. ***Scratch Marks.*** Linear or, if at the apices of erected follicles, punctate, produced by the nails, and bearing small crusts of blood. Ultimately, if deep enough, they may become linear or fusiform cicatrices. Their direction generally bears a definite relation to the position of one or other hand. ***Sore or Ulcer.*** A loss of substance involving the whole epidermis and part or the whole of the corium. The base is covered with granulations, and secretes pus. It heals by scarring. ***Telangiectases.*** Dilated superficial venules of the subpapillary plexus. They are often seen on the malar regions and nose, particularly in rosacea and in those who have been much exposed to cold and sunlight. They are a feature of radiodermatitis and lupus erythematosus. ***Vesicles or Vesiculæ*** Small blisters from 1 to 5 mm. in diameter, due to the accumulation of clear fluid under the upper layer of the epidermis. They are frequently inflammatory, seated upon an inflamed base, and contain a yellow albuminous serum. ***Wheals or Pomphi or Hives.*** A circumscribed œdema of the corium, producing a pale pink or white elevation of the skin.

The following Diseases are caused by Infective Organisms

Diseases caused by ultra-filterable viruses.

It is probable that further research will show that several diseases of the skin of unknown ætiology are caused by a filter-passing virus—pityriasis rosea, for example. At present the following have been proved to be of this nature, namely,

molluscum contagiosum, the common wart, herpes simplex and zoster, and lymphogranuloma inguinale.

MOLLUSCUM CONTAGIOSUM (*See Plate 58, D, p. 833*)

This name is given to small tumours on the skin, which are from $\frac{1}{10}$ to $\frac{1}{8}$ or $\frac{1}{2}$ inch in diameter, lenticular or hemispherical in shape, occasionally globular or pedunculated, somewhat irregular or nodulated on the surface, and of a yellowish-white colour. In the smaller tumours there is a minute opening in the centre: in the larger there are several; and if the tumour be firmly squeezed, a soft gelatinous mass of degenerated cells exudes from these apertures. Examined under the microscope, this is seen to consist of minute oval glistening bodies, the *molluscum corpuscles* or *bodies*. A vertical section through the tumour shows it to have a structure somewhat like that of a racemose gland. There are lobules separated by fibrous tissue; each lobule has externally a row of columnar cells, within this are more oval epidermic cells, and in the centre of each lobule is a collection of the glistening opaque molluscum bodies. The lobules in the larger tumours do not converge to a central duct or opening, but rather lie side by side, and open separately upon the surface.

The process appears to begin by a conversion of the prickle cells of the rete Malpighi into the molluscum bodies, which are stated to consist of keratin. The adjacent part of the rete enlarges downwards into the corium, and the septa between the apparent lobules are the fibrous remains of the papillæ. There is no necessary connection with sebaceous glands or hair follicles.

The growths are thus really benign epitheliomata, and are of interest in that they are caused by an infecting organism which is so minute that it passes through a Berkefeld filter. It may be inoculated by smearing the cheesy contents of the growth into an abrasion on the skin, or, better, by injecting intracutaneously a sterile saline filtrate, made by grinding up the tumours, removed with a curette, with saline solution, and passing the resultant emulsion through a Berkefeld filter. After an incubation period of from five weeks to six months tiny molluscum growths make their appearance along the site of injection.

Molluscum contagiosum is common in birds, from which it may be communicated to man. It occurs both in children and adults, and the tumours are seen most commonly on the face, the arms or hands, the mammæ of women, and the genitals of men. They are apt to suppurate, and may disappear spontaneously; otherwise they may last indefinitely and multiply by auto-inoculation. Very large numbers may occur on the trunk of persons who take Turkish baths frequently, the infection being acquired from the fingers of a masseur or possibly from bath-gowns.

Treatment. The tumours may be caused to disappear by expressing the contents and applying pure carbolic or iodine to the interior, or " by boring into them with a grooved needle dipped into melted silver nitrate, so that it becomes charged with a sheath of the salt " (Whitfield). A simpler method is to scrape them away with a small curette, and paint the affected surface with weak tincture of iodine.

WARTS

(*Verruca*)

There are several distinct varieties of verruca or wart, of entirely different ætiology. Thus the common wart (*V. vulgaris*) is due to a filter-passing virus, the venereal wart (*V. vel condyloma acuminata*) is probably caused by a spirillum (*see* p. 888), the seborrhœic wart (*V. seborrhœica*) is possibly a nævoid growth of late development, and the senile wart (*V. vel keratosis senilis*) is a pre-cancerous degeneration of the skin. The last two are often wrongly confused, and neither has any connection with the verruca vulgaris.

Common warts are excrescences from the skin, consisting of hypertrophied papillæ capped with horny epidermis. They vary in shape and size; thus they may be small and flat (*V. plana*), hemispherical, pointed, or pedunculated, and the larger ones may be lobulated or digitate. In colour the flat ones are pale yellow or pinkish, the larger ones darker and of a greyish-brown tint. They occur most commonly on the backs of the hands, on the fingers, and on the face, particularly around the mouth, owing to the tendency of children to bite the original, or "mother-wart," situated on the hand. They also occur on the eyelids and scalp, and on the soles (*V. plantaris*). Large numbers of flat warts are not infrequently met with on the face in children, and sometimes in adults. In the former they are situated chiefly on the forehead, the temples, the cheeks and the chin, and children with seborrhœa and pityriasis of the scalp and face appear to be especially predisposed. In men both flat and pedunculated warts may occur on the beard region, and are spread by the shaving brush and razor. The nail-folds are sometimes involved, the warty growth often extending underneath the nail. *Plantar warts* are very common, and of importance owing to the intense pain they may cause; they are often mistaken for corns. They are usually situated over the heads of the metatarsals or on the heel. They are surrounded by a horny ring, in the centre of which the papillary vegetations can be observed through the transparent corneous layer.

Ætiology. Common warts are seen in children and adolescents more frequently than in adults. They are contagious and auto-inoculable. The infecting organism has been shown to be a filterable virus; plane warts were reproduced by inoculating the juice of crushed common warts, filtered through a Berkefeld filter (1).

Anatomy. There is an enormous hypertrophy and elongation of the papillæ, with thickening of all the epidermal layers. There is no inflammatory change in the dermis.

Treatment. Warts of moderate or large size are easily removed by freezing with a stick of carbon-dioxide snow, after previously softening them with a fomentation. They may also be destroyed with the thermo- or galvano-cautery, by electrolysis, or, if very numerous, by ionisation with magnesium sulphate. Plane warts will often disappear with moderate doses of the X-rays, and also by the repeated application of a 1/1000 solution of biniodide of mercury in 75 per cent. spirit containing 2 per cent. of salicylic acid.

Plantar warts are sometimes difficult to cure, but, as a rule, large doses of X-rays —one-and-a-half to two pastilles,—the surrounding normal skin being carefully protected, are successful. A more certain method is to scrape out the wart from its bed with a Volkmann's spoon under local or general anæsthesia, and to pack the cavity with gauze soaked in tinct. iodi or a 5 per cent. solution of silver nitrate. Internal treatment with magnesium sulphate, the green iodide of mercury, or increasing doses of arsenic is very unreliable. A remarkable fact, since they are caused by a known infective virus, is that warts may sometimes be rapidly cured by suggestion, and this method is currently employed on the Continent and in America. The claims of "wart-charmers" are, indeed, often justified.

HERPES SIMPLEX

Under the term *Herpes* are commonly included two conditions, *H. simplex* and *H. zoster*. The French prefer to restrict it to the former, and to label the latter *Zona*. Unfortunately it has also been applied to a variety of conditions which bear no relationship either to each other or to true herpes, *e.g. H. gestationis* (*Dermatitis herpetiformis* occurring in pregnancy), *H. circinata*, or tonsurans (ringworm), *H. iris* (a variety of erythema multiforme), *H. cretacea* (lupus erythematosus): these terms should be abandoned.

Herpes simplex is an acute eruption consisting of a varying number of vesicles,

grouped together on an erythematous base. There may be one or several such patches. An attack is usually heralded by a feeling of tension, tingling, or burning, in the part to be affected. After a few hours there appears an œdematous patch of erythema, upon which the small clear vesicles rapidly develop : they may be few or very numerous, and, when closely set, often become confluent ; occasionally they are hæmorrhagic. Their clear contents become turbid, and then dry into scabs, which fall, leaving a temporary stain, but never a scar. Not infrequently a secondary invasion with a streptococcus takes place, and herpes may be the starting point of an attack of impetigo contagiosa. The adjacent lymphatic glands may be slightly swollen, but not to the extent that obtains in *H. zoster.*

Herpes simplex may occur almost anywhere, but the sites of election are on the face around the lips and nose, and on the genital organs ; not infrequently it is also met with on the ears, the nipples, the mucous membrane of the mouth, and on the buttocks. Its tendency to recurrence is notorious, and it usually affects the same region in the person affected. Darier has recorded profuse eruptions on various parts occurring as a sequel to antityphoidal inoculations.

Herpes facialis seu labialis is the commonest variety. It occurs in association with acute infections, such as the ordinary cold, lobar pneumonia, influenza, cerebrospinal meningitis, and malaria. It is extremely rare in encephalitis lethargica and in typhoid fever. Sometimes it accompanies a sharp pyrexial attack with rigor (herpetic fever), and epidemics of this type have been recorded. In many cases, however, one or repeated outbreaks are seen independently of any acute infection.

Herpes genitalis. This is met with in both sexes. In the male, the eruption affects the inner surface of the prepuce, less often on the outside, the glans, the balano-præputial sulcus, the meatus, or even the urethra. In the female, it may occur on any portion of the vulva, and occasionally in the vagina and on the cervix uteri. Acute and profuse attacks of recurrent herpes in women are met with, in which not only the vulva, but also the inner surfaces of the thighs, the mons veneris, the internatal cleft, and the buttocks, are affected. There is fever, swelling of the parts and neighbouring glands, and severe pain and discomfort, which may necessitate confinement to bed. In both sexes the herpetic lesions are transformed into erosions, which may become covered with a diphtheritic-like membrane, or discharge a fœtid muco-purulent liquid. Herpes genitalis in this erosive stage is often confounded with soft sore or a primary syphilitic chancre, and it naturally predisposes to such infections in those who expose themselves to the risk. Moreover, it may mask a syphilitic infection until secondary symptoms develop.

Herpes buccalis is usually seen in conjunction with herpes labialis. Like the latter it is often bilateral, and may affect the mucous membrane of the cheeks, the palate, or the tongue. The vesicles are quickly transformed into erosions. Herpes of the pharynx occurs rarely, and is usually accompanied by fever, intense local pain, and swelling of the cervical glands. The eruption also occasionally involves the conjunctiva.

As has been said, herpes simplex is very apt to recur, and the apparent provoking causes differ in different cases. The most frequent is the common cold. Chronic foci of infection are also often predisposing factors—of the teeth, naso-pharynx, nasal sinuses, or middle ear, in labial, nasal, or aural herpes ; urethritis, prostatitis, metritis, in herpes genitalis. Treatment of such foci may lead to a cessation of the attacks. Apart from infective conditions, however, certain articles of food, *e.g.* cheese, may appear sometimes to be provocative. In women, apart from the outbreak that may follow defloration, recurrent attacks, either on the lips or vulva, may accompany nearly every period. In men, herpes genitalis may constantly follow intercourse with a certain woman. Reflex irritation, *e.g.* from cutting teeth or dental operations, is also apparent in some cases.

Certain varieties of recurrent herpes may be distinguished. In children and adolescents repeated attacks on one or other cheek are not uncommon. In adults the same is true of the buttocks. Less frequent, but of greater interest, is recurrent herpes of the hands and fingers, which simulates *H. zoster*. The lesions arise along the course of a nerve-trunk, and may be accompanied by sensory and vasomotor disturbances, or even by muscular wasting. In a woman under the writer's care the eruption appeared at every period on the middle finger of the right hand.

Ætiology. As a result of recent researches, it is now established that herpes simplex, whatever the provoking cause may be, is due to infection with an ultra-microscopic filtrable virus. Inoculation of the contents of a vesicle of herpes in man into the cornea of a rabbit produces a characteristic keratitis. This keratitis is transmissible from rabbit to rabbit, and in some cases is followed by severe and even fatal encephalitis. It would appear that a large proportion of persons harbour the virus on their mucous membranes, even though they may not suffer from herpes (**2**). Keratitis and encephalitis have been produced in rabbits by inoculating the saliva of herpetic and even non-herpetic subjects. Although a mild disease in man, attacks of herpes may be accompanied by lymphocytosis in the cerebrospinal fluid. The question as to the identity of the virus of herpes with that of encephalitis lethargica is still *sub judice*.

Morbid Anatomy. The vesicles are formed in the deeper portion of the rete malpighii by necrosis of the prickle cells, without the " ballooning " that is seen in *H. zoster*, and intercellular œdema. In the corium there is vascular dilatation with œdema, and infiltration with polymorphonuclear leucocytes, which invade the cavities of the vesicles, connective-tissue cells, and a few mast-cells.

Treatment. The early lesions may to some extent be aborted by frequent sponging with alcohol or eau-de-Cologne, followed by the application of a simple dusting-powder or calamine lotion. Ointments should be avoided. In cases of recurrent herpes the predisposing factor or factors must be determined if possible, and dealt with. Radiotherapy, and autohæmotherapy, or other methods of desensitisation, are sometimes partially successful in preventing these recurrent attacks. Recently, varying success has been achieved by subcutaneous injections either of vaccinial virus (calf-lymph diluted 1 in 10), or of an emulsion of the herpetic virus in doses gradually increasing from 0·1 to 1 c.c. at weekly intervals (**3**).

HERPES ZOSTER (*See Plate 61, A, p. 922*)

(*Zona, Shingles*)

This is an eruption of vesicles, arranged in groups, which generally correspond in position to the distribution of a cutaneous nerve. The name zona, or girdle, is taken from the most common or intercostal variety, in which the groups of vesicles extend from the spine round one-half of the body to the middle line in front. The eruption is preceded sometimes by pain, tingling, or smarting, and it may be a little malaise or slight pyrexia ; then appear groups of closely set papules, forming red patches, 1 or 2 inches in diameter ; and upon these the vesicles quickly arise, with thin walls, clear contents, not very tense, and, when numerous, acquiring a polygonal form from mutual compression. The patches do not all appear simultaneously—for instance, one may form first near the spine, then later one in the axilla, and later again one near the sternum ; some patches also—that is, the later ones—may fail to produce any vesicles, the process, as it were, subsiding early or aborting. After a time the contents of the vesicles become opaque or milky, and the vesicle dries into a scab which drops off, leaving a red stain. The milkiness may amount to the formation of pus, and the superficial layer of the skin may be destroyed, so that scars result. Scars may form in each group, but not from every vesicle of a group. Quite rarely extensive sloughing of the skin takes place, leaving deep ulcers, which heal

slowly. Although the patches are obviously related to nerves, on the trunk they form a band from 2 to 4 inches broad, the direction of which is more horizontal than the true course of the ribs ; and the vesicles may transgress the middle line both in front and behind. Occasionally vesicles occur, even abundantly, in parts of the body remote from the nerves primarily concerned (*aberrant vesicles*, or *generalised herpes*).

H. frontalis occupies the area of the supraorbital nerve on the forehead, scalp, upper eyelid, and side of the nose. Herpes of the ear and neighbouring parts may arise from implication of the sensory branches of the fifth nerve, of the facial (*nervus intermedius*) and of the ninth and tenth nerves and their corresponding ganglia. *H. cervicalis* lies over the neck, clavicle, and deltoid ; *H. brachialis* follows the course of the nerves of the arm ; and other similar groupings on the abdomen, thigh, and leg are occasionally seen. An intercostal zona may be accompanied by herpes of the inner side of the arm (intercosto-humeral nerve), or a gluteal by an anterior crural, representing posterior and anterior branches of the lumbar nerves. The eruption is nearly always unilateral, and its bilateral occurrence has very rarely been recorded. An important feature of *Herpes zoster* is that the lymphatic glands corresponding to the affected area are enlarged and tender even before the eruption appears.

The duration of the eruption is from four to ten days, but the disease does not always end here. Especially in old people, neuralgic pain in the course of the affected nerve may continue for months or years, and be a source of serious trouble ; and in a few cases motor nerve fibres are involved as well as the sensory, and paresis of the corresponding muscles has been observed, most often in those supplied by the facial, sometimes in those supplied by the third, fifth or sixth cranial nerves, and by the nerves to the deltoid and abdominal muscles. Frontal herpes may be accompanied or followed by conjunctivitis, ulceration of the cornea, or iritis.

Ætiology. The eruption occurs about equally in the two sexes, and, although very rare in infancy, is seen almost at any age. There would seem to be a seasonal incidence to some extent, more cases being met with in spring and autumn than at other times. There is no doubt that in some instances it is contagious, but less so than varicella. Accumulated clinical and pathological observations suggest that the essential lesion in *H. zoster* is involvement of the spinal posterior root, the Gasserian, or geniculate ganglia, with degenerative changes in the posterior roots, the posterior columns of the cord, and the peripheral nerves ; such involvement may be due to a variety of causes, which may be tentatively classified as follows :--

(*a*) The relationship of zoster to varicella is no longer in doubt. Suggested first by Bokay in 1892, and insisted on by Le Feuvre and others, it has been confirmed by numerous observations all over the world. The evidence in its favour may thus be summarised : (1) An attack of zoster may be followed by varicella. In a case observed by the writer, that of an elderly man who had not previously had chicken-pox, a typical outbreak of zoster on the trunk was followed about a week later by a generalised eruption of varicella ; at the beginning of his attack of zoster he visited a niece, who a fortnight later developed varicella. (2) Conversely varicella may be succeeded by zoster. (3) Zoster in one person may be followed after an interval of twelve to seventeen days, which corresponds to the incubation period of varicella, by an attack of the latter in children or others who have been in his company, or the converse may occur. (4) The identity of the two infections has been further established by Netter and Urbain, and more recently by Brain (**4**), employing the complement-fixation test. The serous contents or the crusts of the lesions of the two eruptions provide the antigen. Experiments with other vesicular eruptions, including herpes simplex, were negative. (5) The micropathology of the vesicles in herpes zoster and varicella is identical.

It is probable that in those cases of *H. zoster*, in which, apart from the main part of the eruption with radicular distribution, aberrant vesicular patches occur on various parts of the body, the cause is infection with the virus of varicella. As might be expected, in such cases the eruption appears to be part of a specific infective disease, there being prodromal fever, general malaise, and a leucocytosis with eosinophilia.

(*b*) Apart from the specific virus of varicella, it would seem certain that other infective organisms, reaching the ganglia by the blood-stream and causing inflammatory changes in them, may be causative. It is claimed that *H. zoster* has been produced in animals by injecting streptococci isolated from tonsils or infected teeth in persons suffering from the eruption. The writer has observed the case of a lady with supraorbital zoster, accompanied by rheumatoid arthritis, in whom injections of a vaccine prepared from streptococci isolated from her septic tonsils, provoked not only exacerbations of the arthritis, but also recurrent outbreaks of the herpes. Sande found gram-positive cocci in sections of the Gasserian ganglion taken from a case of herpes frontalis. No doubt the organisms of acute infections, such as pneumonia, may also invade and set up inflammation in the ganglia, thereby being the cause of zoster in some instances.

(*c*) Tuberculosis and syphilis of the spinal meninges may involve one or more posterior root ganglia. The writer has seen two cases of spinal caries, in which an attack of zoster occurred over an area corresponding to the nerve-roots of the affected part of the vertebral column. In syphilis it may be met with during the secondary period (sometimes, of course, being provoked by injections of salvarsan), there being signs of meningeal involvement; or it may accompany a syphilitic meningo-myelitis; and lastly, it is not uncommon in tabes and general paralysis. Cases of tabes have been observed in which *recurrent* attacks of zoster have taken place over a period of many months in an area affected by lightning pains.

(*d*) Certain toxic chemical substances may be responsible, *e.g.* arsenic, carbon monoxide, bismuth and mercury. Many cases were noted in the epidemic of arsenical poisoning among beer-drinkers that occurred in Manchester in 1900. It is sometimes met with in cases of psoriasis or other diseases, which are being treated by the oral administration of arsenic, but is more likely to be provoked by injections of the organic arsenical compounds.

(*e*) Traumatic zoster is sometimes seen, *e.g.* after injuries to the head or spinal column, lumbar puncture or spinal injections, and manipulation of the spine.

(*f*) New growths of the spinal column and meninges may invade the posterior root ganglia, as in the case recorded by Head and Campbell (**5**), in which an attack of zoster accompanied sarcoma of the vertebræ; post-mortem, invasion of the corresponding ganglia by the growth was revealed. In other cases it may occur in association with disease of the ribs; in one described by Dubler—tuberculous necrosis of the ribs—the ganglia were not involved, but an inflammatory neuritis of an intercostal nerve was found.

Morbid Anatomy. In the affected posterior root ganglia there is destruction of the ganglion cells, and degeneration in the posterior roots and columns and peripheral nerves. The vesicles of the eruption, which arise on an erythematous base, are structurally identical with those of varicella. They are formed in the rete Malpighii by intercellular œdema, and the epithelial cells undergo a peculiar "balloon" degeneration, whereby they become swollen and their nuclei multiply. In the corium there is vascular dilatation and œdema, with leucocytic infiltration, and some degree of necrosis, which may be intense enough to leave deep cicatrices. It has been suggested that these lesions in the skin, which clearly result from irritative changes in the sensory ganglia or the nerves distal to them, are due to the slow and continuous release of H-substance (probably histamine) in the area of skin affected (**6**).

Treatment. In mild cases all that is necessary is to keep the lesions dry and

clean by the application of a boro-talc dusting-powder, calamine lotion, or a simple zinc paste. Ointments, fomentations, and poultices should be avoided, since they favour secondary infection of the vesicles, and increase the liability to scarring. Intramuscular injections of a solution of pituitary extract, 0·5–1 c.c., have a remarkable effect not only in relieving pain, but also in shortening the duration of the attack. The injections may be repeated daily until pain has ceased. Pregnancy is the only contra-indication. Autohæmotherapy also appears to be of value. For the severe and intractable pain that may persist long after the attack, as a rule in old people, driving the patient even to suicide, deep radiotherapy of the corresponding roots is sometimes strikingly successful.

Bacterial Diseases. I. Micrococcal

In the great majority of diseases of the skin, in which the pathological changes are due to the active growth in it of micro-organisms, infection takes place from without; it must be remembered, however, that even the healthiest and cleanest skin is never sterile, but harbours on its surface, and particularly at the mouths of the pilo-sebaceous follicles, at the muco-cutaneous junctions, and in its natural folds, a large number and variety of organisms. There are three organisms that are so constantly found in human skin, at any rate under civilised conditions, that they may, perhaps, be regarded as its normal habitants. They are the *Staphylococcus albus*, the *microbacillus of acne*, and the *pityrosporon of Malassez*, which is also wrongly termed the " bottle-bacillus " ; it is a yeast-like fungus, nearly related to *Monilia*. It cannot, however, be too strongly emphasised that the healthy skin must not be regarded as a hot-bed of microbial growth ; on the contrary it is remarkably amicrobial. Microscopical sections through absolutely normal skin show that organisms occur *as isolated units* on *the surface* of the horny layer, never penetrating even its superficial layers ; they are also seen lying at the mouths of the pilo-sebaceous follicles, but never in the sweat-ducts. However it is clear (7) that a distinction must be drawn between the mere presence of micro-organisms on the surface and their occurrence *in a state of active growth ;* except in certain moist folds, such as between the toes and in the axillæ, where organisms are normally in a state of vigorous multiplication (without, however, in health producing any effect beyond decomposing the secretions), there is no active microbial growth on healthy skin, whereas in the most minute pustule or other infective lesion organisms are present in enormous numbers. Moreover, in seborrhœa and comedo the sebaceous follicles contain myriads of acne bacilli, and in the scales of pityriasis simplex the pityrosporon can be seen in profusion.

The horny layer forms a natural protection against microbial invasion of the skin. When this is damaged, however slightly, an opportunity for such invasion occurs, and any micro-organisms present, either normally, *e.g.*, staphylococci, or accidentally, *e.g.*, streptococci, are liable to take on active growth and produce pathological effects. The pilo-sebaceous orifices may be looked on as weak points in the horny barrier, and the staphylococci that lurk there are likely to set up a folliculitis when the skin is damaged by an irritant.

It will thus be understood that diseases of the skin, caused by external infection, may arise from (1) active growth and invasion of organisms, already present in an inactive state, owing to damage to the skin or some other factor which lowers its resistance, *e.g.*, many forms of staphylococcal, and, to a less extent, streptococcal infections ; (2) direct or indirect contagion with virulent organisms from an infected person or animal, *e.g.*, impetigo contagiosa, ringworm, syphilis, warts and lupus verrucosus ; (3) invasion of the skin from infected mucous membranes, *e.g.*, impetigo from rhinitis or otorrhœa, sycosis of the upper lip from rhinitis or from spread, *viâ* the nasal duct, of a staphylococcal blepharitis. It is, moreover, obvious that once a focus of virulent bacterial growth has been established, the risk of invasion of other parts of the skin is greatly increased.

The skin may be invaded by organisms *viâ* the blood stream, *e.g.*, in pyæmia and septicæmia, in tuberculosis, syphilis, leprosy, suppurative ringworm, certain of the exanthemata, and probably, at least in some cases, in eruptions such as erythema multiforme, erythema nodosum, and purpura.

By far the commonest eruptions caused by external infection are those due to the pyogenic cocci, the acne bacillus, and the pityrosporon of Malassez, and the conditions caused by these organisms will be dealt with first. With regard to the pyogenic cocci certain differences between staphylococcal and streptococcal infections may be tabulated as follows :—

Staphylococci.	*Streptococci*
(1) Some strains may be considered as natural habitants of the skin.	(1) Are more likely to invade the skin either from some previous host, or from mucous membranes.
(2) Tend to involve the pilo-sebaceous follicles, so that most staphylococcal eruptions are primarily follicular.	(2) Have no predilection for the follicles, but tend to involve the natural folds of the skin and to form fissures.
(3) Do not, as a rule, cause lymphangitis or adenitis.	(3) Are prone to invade the lymphatics and cause adenitis.
(4) Are powerfully chemiotactic for polymorphonuclear leucocytes, thus producing "laudable pus."	(4) Are less pyogenic, and tend to provoke an exudation of serum containing only a few cells.
(5) Staphylococcal lesions tend to remain *pure, i.e.*, do not usually become secondarily infected with other organisms.	(5) Streptococcal lesions always become secondarily infected with staphylococci, which may then form primary follicular lesions—*e.g.*, a staphylococcal sycosis may follow a streptococcal impetigo.

STREPTOCOCCAL INFECTIONS

Impetigo is the term given to a superficial infection of the skin with pyogenic organisms, and is characterised by the formation of pustules or bullæ, appearing rapidly on healthy skin, the contents of which dry up to form crusts under which healing takes place. Instead of developing on healthy skin, infection with the same micro-organisms may complicate some pre-existing pathological lesions, particularly eczema, resulting in pus formation and subsequent crusting. Under these circumstances the lesions are said to have become secondarily *impetiginised.*

Of primary impetigo there are two distinct varieties : (1) *Impetigo contagiosa* (Tilbury Fox), due to infection with the streptococcus pyogenes longus ; (2) *impetigo of Bockhardt,* due to staphylococcal infection. It is preferable to reserve the term *impetigo* exclusively for the streptococcal variety ; the impetigo of Bockhardt may be conveniently named *porofolliculitis.*

IMPETIGO CONTAGIOSA (*See Plate 58, A*)

In this variety infection of the skin with the streptococcus takes place just beneath the horny layer. The primary lesion is a minute red spot, which very rapidly becomes a superficial vesicle or bulla, owing to the exudation of fluid, and the vesicles or bullæ may be considered as the characteristic lesions of the disease. Where the horny layer is thin, as on the face, they are flaccid, but in other parts, particularly on the palms and soles, they may be tense. In the early stage the contained fluid is clear serum, and from it the streptococcus may often be grown in pure culture, but secondary infection with staphylococci soon takes place, and the fluid then becomes cloudy from the presence of leucocytes ; in this stage the

vesicles are surrounded by a red halo of hyperæmia. The fluid may escape owing to rupture of the roof of the vesicle, or may dry up spontaneously; in any case the dried serum forms characteristic crusts, which are yellow, or amber coloured, or sometimes brown from admixture with blood or dirt. After a few days the crusts fall, leaving a pink stain to mark the site of the original lesion. Should a crust be removed before healing has taken place beneath it, a raw, oozing, and sometimes bleeding surface is exposed, which soon becomes encrusted again. Healing takes place by complete regrowth of normal epithelium and no scar is left. The subjective symptoms are usually slight, but there may be some itching or burning, and in children fresh lesions are produced by scratching. Various types of impetigo contagiosa have been described.

In *impetigo circinata* there is comparatively little exudation, and the lesions tend to spread peripherally while healing in the centre, thus forming circinate patches with crusted margins; the condition is often mistaken for circinate ringworm. By confluence of the patches extensive gyrate figures may result (*I. gyrata*).

Impetigo bullosa. In this variety the lesions form large bullæ, the roofs of which are flaccid, except where the horny layer is thick, as on the palms and soles.

Impetigo pityrodes. There is, as Sabouraud insisted in 1904, a dry, attenuated form of streptococcal impetigo, situated as a rule on the face, in which the lesions consist of dry, furfuraceous patches usually of irregular shape. They correspond probably to the majority of cases of the *dartre volante* or tetter of older authors. They are met with towards the end of an attack of ordinary impetigo, and one may see in the same patient all stages from the crusted, oozing lesions, to the dry, scaly patches referred to. They are, however, also very common in children suffering from chronic nasal catarrh, in whom there has been no definite attack of ordinary impetigo, and are then frequently associated with streptococcal fissures at the angles of the nostrils or mouth. Their occurrence is predisposed to by the use of strongly alkaline soaps, which damage the protective horny layer, but such soaps may of themselves give rise to dry, scaly patches apart from infection. Impetigo pityrodes is contagious, and many epidemics of it have been described. It has to be differentiated from the scaly patches caused by the pityrosporon of Malassez, which are usually seen in older children and adults, and from the eczematoid tuberculide.

Ætiology. The primary phlyctenule of streptococcal impetigo rapidly becomes secondarily invaded by the staphylococci always present in the mouths of the pilo-sebaceous follicles, and, as these organisms grow much more readily and abundantly than streptococci in ordinary media, cultures made even from early lesions of impetigo may give pure growths of staphylococci. In order to obtain the streptococcus, the serum from the early phlyctenule, or from the raw surface exposed after removal of a crust, is drawn up into a small glass pipette half-full of serum-broth, the ends are sealed, and the pipette incubated at 39° for about eight hours. If then the lower end of the pipette be broken, the first few drops of the medium will be found to contain the streptococcus in pure culture, whereas the fluid in the upper part in contact with air will contain staphylococci. The streptococcus, being a facultative anaerobe, will grow alone in the lowest portion of the pipette. When the phlyctenules or bullæ of impetigo occur on the palmar surface of the hand, where there are no pilo-sebaceous follicles and consequently staphylococci are less numerous, secondary staphylococcal invasion occurs relatively late, the serous contents of the phlyctenule tend to remain clear, and the streptococcus may be obtained in pure culture even on ordinary media. Culture media containing crystal-violet, which inhibit the growth of staphylococci, may also be used (**8**). By this means abundant growths of a streptococcus longus in ordinary impetigo and ecthyma are obtained, whereas in cultures from normal skin and from various other skin

eruptions, not of streptococcal origin, either no streptococci grow at all, or only a few isolated colonies. Sabouraud's contention as to the streptococcal causation of impetigo pityrodes is thus confirmed. The chief factors predisposing to impetigo are trauma of all kinds, whereby the horny layer of the skin is damaged, and exposure to infection with virulent streptococci. As its name implies, it is contagious, and is apt to be communicated from one member of a family to another by indirect and direct contact, and also occurs in epidemic form in schools and other communities. The so-called *scrum-pox* is impetigo contagiosa spread by contact on the football field. Apart from contagion, it may arise spontaneously, and is apt to complicate itching conditions, such as scabies, and particularly pediculosis capitis. Impetigo of the scalp is frequently due to the latter cause. It may begin around the nostrils, or on the upper lip, by infection of the skin with a streptococcus derived from an acute rhinitis or purulent nasal discharge, and around the ear from the discharge of a chronic otitis media. It frequently arises from fissures at the angle of the mouth (*la perlèche*).

Morbid Anatomy. Microscopical section through a vesicle shows that this is situated at the level of the stratum granulosum, so that the roof is formed by the stratum corneum and the base by the upper part of the prickle-cell layer. The fluid consists of serum containing leucocytes; chains of streptococci may be seen along the floor of the vesicle, and groups of staphylococci near the roof and sides. The epidermis beneath is œdematous, and leucocytes may be seen in the intra-epithelial lymph channels. The capillaries in the papillæ are dilated and there is slight inflammatory infiltration.

Prognosis. The prognosis varies according to the individual case. An acute attack of the disease occurring in a child or adult, otherwise in good health, tends to run a definite course of some three to six weeks' duration, recovery taking place spontaneously owing to the gradual development of immunity to the infecting streptococcus. On the other hand, in debilitated persons, particularly in those who suffer from a chronic streptococcal infection of their mucous membranes, so common among children of the poorer classes, or from otorrhœa, impetigo, usually associated with streptococcal fissures and intertrigo, may become a chronic disease. It is in these cases that, apart from chronic fissures at the muco-cutaneous junctions and in the natural folds of the skin, the dry scaly form of impetigo, already described, is likely to occur.

Treatment. *Local.* One of the best local applications for streptococcal impetigo is the eau d'Alibour of the French, of which various formulæ are employed. Sabouraud recommends:—

℞ Zinci Sulphatis . . . . . 1·0
Cupri Sulphatis . . . . . 4·0
Aq. dest. . . . . 1000·0

This solution should be applied vigorously with swabs of cotton-wool, so as to remove the crusts and bring it in contact with the underlying infected surface. The applications should be repeated several times daily, until under their influence the thick yellow crusts are replaced by dry, superficial scales. The desiccating effect of this lotion may be mitigated by applying a weak ichthyol cream.

An alternative method is to swab the infected areas, after removal of crusts, with a solution of perchloride of mercury in 75 per cent. spirit (1 in 4,000). In either case, when desiccation of the lesions has occurred, a mercurial ointment or paste should be employed, *e.g.*,

℞ Hydrarg. Ammoniat. . . . . gr. v.–x.
Ung Paraffini . . . . . ad ʒi.

or ℞ Hydrarg. Oxidi Flavi . . . . gr. v–x.
Pasta Zinci Comp. B.P. . . . ad ʒi.

In extensive cases with much crusting preliminary applications of boric-starch poultices are of value, and, when the eruption is widespread, a tablespoonful of

zinc sulphate should be added to the daily bath. It is of great importance to treat infection of the adjacent mucous membranes and any fissures that may be present.

As has been said, recovery from an attack of impetigo probably depends more on the development of immunity than on the efficacy of local treatment. In early cases it is worth while trying to abort the attack by the judicious employment of a mixed streptococcal and staphylococcal vaccine, prepared from strains of organisms obtained from impetigo lesions. A vaccine is also of value in cases in which fresh lesions continue to appear despite adequate local measures, and in those of long-standing. A completely out-of-door life by the sea or in a bracing climate should be enjoined when possible, and is almost imperative in chronic cases, in which the most careful local treatment usually fails to prevent recurrence.

As has been said, impetigo contagiosa is often spread by indirect contact through the medium of towels, shaving brushes, etc.

ECTHYMA

This condition may be regarded as a deep form of streptococcal impetigo, in which destruction of the epidermis occurs, and an ulcer results. The lesions begin as pustules or bullæ containing serum, which, as in ordinary impetigo, is either cloudy or, more rarely, frankly purulent according to the degree of secondary staphylococcal infection; the serum dries to form a thick, adherent crust of a dirty yellow colour, or reddish-brown from admixture with blood, and sometimes almost rupial in character. Around the crust may be seen in comparatively early lesions the shrivelled roof of the original bulla, and beyond this a red area of inflammation, with sometimes considerable œdema. On removal of the crust the underlying ulcer is exposed. It is not, as a rule, very deep, its borders are sharply defined, and its base is red; from it exudes a purulent or sero-sanguinous fluid, containing tissue-*débris*, elastic fibres, altered red blood corpuscles, leucocytes, and cocci. Under suitable conditions and treatment the lesions dry up, the crusts are shed, and the ulcers heal, leaving scars, usually surrounded by a pigmented border. Ecthyma is most frequently seen on the legs, the buttocks, particularly in infants, and the back; circulatory stasis is an important contributory factor, so that it is apt to occur on varicose legs, and may be the starting point of a varicose ulcer. General debility, acroasphyxia, alcoholism, and diabetes are predisposing causes, and the condition may complicate a pruritus, scabies, and pediculosis. During the war it was a cause of much disability among our louse-ridden soldiers, and the streptococcus fæcalis appeared often to be the infecting organism (MacCormac).

Morbid Anatomy. The ulcerated lesion shows necrosis, leucocytic infiltration and intense congestion of the dermis, with dilatation of the vessels, which are surrounded by sheaths of cells.

Treatment. The local treatment should be carried out along the lines already suggested for impetigo. In obstinate cases exposure of the lesions to sunlight or the ultra-violet rays will usually hasten healing. In debilitated persons prolonged rest out of doors, and the administration of tonics, particularly the Syr. ferri iodidi B.P. and the Syr. calcii lactophosphatis B.P., are indicated.

DERMATITIS GANGRENOSA INFANTUM

This very rare condition has already been referred to under the name of *varicella gangrenosa* (*see* p. 35), but, although it is usually a sequel of chicken-pox, it may follow other eruptions, such as vaccinia and the infective dermatitis known as "napkin-rash." It occurs usually in marasmic infants, enfeebled by previous acute disease, improper feeding and neglect, rickets or tuberculosis, but

it has been seen in well-cared-for children. The lesions consist of sharply punched-out ulcers often covered by a black slough; they may heal, but in severe cases extend peripherally, producing vast areas of gangrenous ulceration. The children as a rule are acutely ill, with high fever; death results from pyæmia and septic bronchopneumonia. In cases that recover permanent widespread scarring is, of course, present throughout life.

Ætiology. Probably the original infecting organism is, as in ordinary ecthyma, a streptococcus pyogenes longus, but secondary invaders, such as staphylococci, doubtless play an important and sometimes predominant part. There is considerable evidence that infection with the *Bacillus pyocyaneus* may in some cases, at any rate, be responsible for the development of the condition.

Treatment. The same principles should be followed as indicated under pemphigus neonatorum.

INTERTRIGO

The eruption known as intertrigo (*erythema intertrigo, eczema intertrigo*) is the inflammatory redness which occurs in the natural folds of the skin, for example in the groins, between the buttocks, in the axillæ, under the mammæ, behind the ears, and in fat people in the hypogastric fold and around the neck. In its simplest form the eruption corresponds closely to the parts of the skin that are in contact; the surface is raw, denuded of the upper layers of the epidermis, and it secretes a whitish, turbid fluid, different from the yellow serum or sero-pus of eczema, and not drying into crusts, unless mixed with the medicinal substances applied to it. At the bottom of the fold is often a fissure, which is easily seen when the opposing surfaces are separated. Intertrigo may give rise to no subjective symptoms, but sometimes itching is complained of, and secondary eczematisation, with lichenification, may result from constant scratching.

Ætiology. The mechanical friction of two opposed surfaces of skin, the accumulation and decomposition of secretions, and the moisture of the parts are predisposing factors; it is obvious, therefore, that lack of personal cleanliness and obesity favour the development of intertrigo. Apart from these predisposing factors, however, the essential cause of intertrigo is infection of the surface of the skin in the fold or folds involved, and this may be due to different kinds of organisms. Thus we recognise varieties due to infection with (1) a streptococcus, (2) certain species of ringworm fungus, *e.g.*, the epidermophyton inguinale (eczema marginatum, tinea cruris) and the microsporon minutissimum (erythrasma), (3) yeast-like organisms of the genera monilia (or oïdium), cryptococcus, saccharomyces or endomyces—the oïdiomycoses—including the pityrosporon of Malassez. The diagnosis of erythrasma and of epidermophytosis is not, as a rule, difficult; they will be dealt with in a later section. On the other hand, the differentiation between a streptococcal intertrigo and that due to the oïdiomycoses may be impossible without careful microscopical examination of scrapings and cultural investigation.

Probably, as Sabouraud maintains, the majority of cases of simple intertrigo are of streptococcal origin. Certainly is this so in retroauricular intertrigo. In the axis of the fold is found a fissure, on either side of which the appearances are those of a streptococcal impetigo, or of a simple intertrigo as seen in other folds; that is to say, there may be impetiginous crusts, removal of which exposes a moist, pink surface, as in ordinary impetigo, with extension of the infected area beyond the actual fold, or the infection may be strictly limited to the fold, with no crust-formation. Such a streptococcal intertrigo may also be seen in the groins, the hypogastric fold, the internatal cleft, where it may be the cause of pruritus ani, the axillæ, and submammary fold in women. In intertrigo due to the yeast-like group of organisms, there is a greater tendency to extension of the infection, and a widespread dermatitis far beyond the limits of the folds may

result. This variety will be described later. It must be remembered that *psoriasis* may involve the flexures, and in some cases closely imitate an intertrigo of infective origin

Treatment. In streptococcal intertrigo it is essential that the central fissure be completely healed, as otherwise relapse is certain to occur. One of the simplest and most effective methods is to apply a 1 per cent. solution of iodine in spirit vigorously on a cotton-wool swab once or twice daily to the infected area, and after each application a simple zinc cream may be smeared in the fold. The treatment must be continued until the new horny layer is completely restored. In some cases, particularly if the central fissure is deep and resistant, a 2 per cent. solution of silver nitrate in spt. ætheris nitrosi is to be preferred to the iodine. In mycotic intertrigo the iodine solution is also very effective.

Needless to say, scrupulous cleanliness, the separation of the opposing surfaces of the fold, and the use of a mild antiseptic dusting powder are indicated as prophylactic measures. There is no doubt that a sedentary life, an excessive dietary, particularly of carbohydrates and fats, and overclothing are often predisposing factors in the intertrigo so common in the folds of obese persons, and, apart from dietetic restrictions and regular exercise, the internal administration of alkalies often seems to be of value.

Chronic retroauricular intertrigo is common in children, and is usually seen in those suffering from chronic nasopharyngeal catarrh, impetiginous anterior rhinitis, and the dry, scaly form of impetigo of the face. An open-air life by the sea, a generous dietary of vitamin-rich foods, and a course of real or artificial heliotherapy should be prescribed for these cases.

STREPTOCOCCAL FISSURE

As has already been stated, streptococci are prone to infect the folds of the skin, and to produce fissures therein and at the mucocutaneous junctions; in the latter situations the mucous membrane is often the primary source of infection. Thus fissures in the naso-labial folds are usually secondary to an acute or chronic rhinitis, and those at the labial commissures—which form the starting point of *la perlèche*—may result either from a streptococcal stomatitis, gingivitis, or pyorrhœa, or from maceration with infected saliva in children who dribble. Fissures are also common in the retroauricular region (retroauricular intertrigo) and beneath the lobes of the ears.

Retroauricular intertrigo is often wrongly diagnosed as eczema, or seborrhœic dermatitis; it provides a very good example of chronic streptococcal infection of a natural fold. Behind one or both ears is seen a moist, crusted area, and beneath the crusts the surface is bluish-red; at the angle of the fold is the fissure, which divides the infected area into two halves, and is exposed on drawing the ear forward. Sometimes at the margin may be seen remains of the original streptococcal vesicle in the form of a shrivelled fragment of the raised horny layer.

La perlèche, or intertrigo of the labial commissures, may be confused with the mucous patches of syphilis and with labial herpes. It consists of a fissure at one or both angles of the mouth with a V-shaped inflammatory area spreading outwards, and covered with macerated greyish-white epidermis. It often co-exists with impetigo contagiosa, and may, like other streptococcal fissures, be a source of reinfection. It is contagious, being spread by kissing or by the exchange of pens and pencils, which have been held in the mouth of an infected person. It is often associated with dyspepsia of the fermentative type, due to an excessive carbohydrate dietary.

Treatment. A streptococcal fissure should be painted with a 2 per cent. solution of silver nitrate in spirit, ætheris nitrosi, and then smeared with a mercurial paste. In resistant cases fractional doses of X-rays are of value.

RELAPSING STREPTOCOCCAL LYMPHANGITIS

This condition occurs most commonly on the face or around the ears. The malar regions and upper lip are common sites. Clinically it resembles ordinary erysipelas, the affected area being swollen, reddened, and somewhat shiny. There is usually little or no constitutional disturbance, owing to the slight virulence of the infecting streptococcus. Exposure to cold wind may provoke an attack. From repeated attacks permanent blocking of the lymphatics may result, with the production of one form of elephantiasis nostras. Persistent swelling of the upper lip and malar regions is not uncommon from this cause. Recurring attacks of lymphangitis involving the feet, ankles and legs, are also met with in association with streptococcal fissures between the toes. These fissures are almost always secondary to epidermophytosis of the feet (*q.v.*). Unless permanent blockage of the lymphatics has already occurred, efficient treatment of the epidermophytosis will be curative.

Ætiology. The condition is due to streptococcal infection of the lymphatics of the part. In most cases there is present a streptococcal fissure from which reinfection periodically takes place. In some cases there is no external fissure, but, as a rule, some chronic focus of streptococcal infection in the mucous membranes of the mouth or nasopharynx, or in the nasal sinuses, is present.

Treatment. If a streptococcal fissure is responsible, its cure will lead to a cessation of the attacks. In other cases any source of streptococcal infection in the mouth, nose, or nasopharynx should be sought for and treated. When persistent elephantiasis has supervened, removal of the original source of infection may be followed by a gradual disappearance of the swelling, but not always. Repeated small doses of X-rays to the area affected are sometimes of benefit. Intradermal injections of a streptococcal vaccine, either autogenous or prepared from various stock strains, are of undoubted value, even when persistent blockage of the lymphatics is present. The initial dose should be small—one to two million organisms—and the subsequent dosage depends on the degree of local reaction at the site of injection, which is usually severe, often leading to abscess-formation and necrosis. So long as this is marked, the dose should not be increased.

ECZEMATOID STREPTOCOCCAL ERUPTION OF THE SCALP

(*Fausse teigne amiantacée d'Alibert*)

This condition is frequently seen on the scalp in association with streptococcal retro-auricular intertrigo, but may occur without any infective lesion of the skin. It may be widespread over the surface of the scalp, or localised, often to the vertex. It is characterised by a whitish lamellar crust, composed of silvery scales, which mat the hairs together, and, when the entangled hairs are lifted up, the scales become dissociated and cling to the hair-shafts. The under surface of the crust is yellowish, in contrast with the silvery whiteness of the upper portion, owing to admixture with serum. After removal of the crust, the underlying epidermis appears smooth and slightly pink, and droplets of serum exude when this is gently scraped.

The eruption is therefore eczematoid in nature, but the serous exudation is minimal, whereas the formation of parakeratotic scales is the striking feature.

Ætiology. Its frequent association with retro-auricular intertrigo, particularly when the infection tends to spread upwards to the lateral surfaces of the scalp, indicates its streptococcal origin, and Sabouraud states that streptococci appear in cultures from the deeper layers of the squames. When this is so the condition may be regarded as an eczematoid reaction to the local growth of streptococci. In some cases, however, cultures have yielded only a *Staphylococcus albus* even when special media have been utilised and when streptococci

have been grown in abundance from the neighbouring intertrigo. Moreover, similar cases have been observed in which the latter was absent, but a chronic focus or foci of streptococcal infection were present elsewhere, *e.g.*, in a nasal sinus, successful treatment of which appeared to benefit the eruption. It is therefore likely that it may be sometimes a true eczematoid streptococcide, *i.e.*, an epidermal reaction to streptococcal toxin absorbed from a distant focus of infection either in the skin or elsewhere.

Treatment. The scales should be removed and to the affected area should be applied an ointment containing oil of cade, or ammoniated mercury and liq. picis carbonic B.P. If retro-auricular intertrigo be present, this should be treated along the lines already suggested. In every case other possible foci of streptococcal infection should be sought for.

INFANTILE ERYTHEMA OF JACQUET

(*Napkin Rash*)

Under this title is known a form of dermatitis, which is common in the napkin area of infants, and which may be considered as a variety of intertrigo. The eruption occurs on the buttocks, lower abdomen, genitals, and inner sides of the thighs, *i.e.*, on the areas in which there is friction from the napkin. It may also be seen on the calves and on the parts of the thighs opposed to them when the child lies with its legs drawn up, and also on the heels. In the early or erythematous stage the appearance is that of ordinary intertrigo, but the colour may be of a curious reddish-coppery hue ; vesicles may then appear, leading to the formation of erosions, which, in turn, may be transformed into flat red papules, resembling somewhat those of congenital syphilis ; lastly, the erosions may terminate in punched-out ulcers, which often coalesce.

Ætiology. In the majority of cases the condition is associated with "the ammoniacal diaper." It has been shown (**9**) that the ammonia is produced by a saprophytic organism present in the fæces of many infants as well as of older children and adults, the *Bacillus ammoniagenes*, which possesses the power of forming free ammonia from urea [$CO(NH_2)_2 + 2H_2O = (NH_4)_2CO_3 = 2NH_3 + H_2O + CO_2$]. The primary causal factor is the irritation of the skin by the ammonia thus produced in napkins soiled with urine and fæces, and consequently the dermatitis is limited to those areas of skin that come in contact with the wet napkin.

The eruption is relatively rare in breast-fed infants, as in them the normal acid stools are less favourable for the growth of the *B. ammoniagenes*. On the other hand, in infants fed on a rich protein diet, and with alkaline stools, this organism thrives, and it is in them that the condition is most commonly met with. Infrequent changing of the napkins and carelessness in keeping the buttocks clean are naturally predisposing factors. The irritation by the ammoniacal diaper at first causes an erythema, which may be followed by desquamation ; in long-standing cases the action of the alkali renders the skin harsh, dry and thickened, the appearances resembling those of "washerwoman's dermatitis." The damage sustained by the horny layer naturally favours invasion by pyogenic organisms, particularly streptococci, which are probably responsible for the secondary lesions—vesico-papules and pustules, and ecthymatous ulcers. Sabouraud, in fact, regards Jacquet's dermatitis as a streptococcal impetigo and ecthyma, but the primary damage to the skin by ammoniacal diapers is the essential cause. It should be remarked that an identical condition may arise in older children with nocturnal enuresis, and in adults with urinary incontinence ; the ulceration that may occur around the meatus of circumcised male infants is also due to irritation of the exposed glans by the ammoniacal diaper.

Diagnosis. The importance of the eruption lies in the fact that in its severer forms it may easily be confused with a congenital syphilitic eruption,

and Parrot, who first described it, wrongly attributed it to syphilis. The main points in the differential diagnosis are that a napkin rash occurs on parts exposed to pressure and friction, and not on the flexures, which are protected from contact with the napkin ; there are no lesions on the palms and soles, the colour of the eruption is less coppery, and mucous patches on the anus and at the angles of the mouth are absent. Nevertheless, doubtful cases are met with, and careful investigation for syphilis should then be made both in the parents and child.

Treatment. Cooke has shown that the impregnation of the diapers with an antiseptic, thus inhibiting the growth of the *B. ammoniagenes*, is rapidly effectual. He recommends that, after washing, the diapers should be rinsed in a 1 : 4,000 solution of mercuric chloride, prepared by dissolving one 7½ grain tablet in two quarts of water. They are then wrung thoroughly, and allowed to dry. As an alternative a saturated solution of boric acid may be used in the same way, which, though less efficacious, obviates the risk of careless handling of so harmful a poison as mercuric chloride. Mild cases respond to this preventive treatment alone, but when erosions and ulceration are present, Lassar's paste, to which ammoniated mercury (5 grains to the ounce) may be added, should be freely applied. The diet should be modified with a view to restoring the normal acid reaction of the stools.

STAPHYLOCOCCAL INFECTIONS

The great majority of staphylococcal lesions of the skin are primarily follicular, and, in order clearly to understand their morbid histology, the general structure of the pilo-sebaceous follicle must be considered. It is formed by an invagination of the epidermis, like the finger of a glove, extending obliquely from the surface through the dermis, in which it is embedded. The depth of the follicle is proportional to the size of the hair that it contains, the larger the hair the deeper the follicle. Many of the deepest follicles extend to the subcutaneous fatty layer. The sebaceous gland arises obliquely from the follicle at a point situated one-third of its depth from the surface. At the bottom is the dermic papilla, from the epithelial covering of which the hair is formed. A pilo-sebaceous follicle may conveniently be divided into three portions : (*a*) The mouth or *ostium*, at the point of emergence of the hair ; (*b*) the *infundibulum*, lying between the ostium and the opening of the sebaceous gland—this constitutes the upper third ; (*c*) the portion between the infundibulum and the papilla. In this, the lowest two-thirds, the hair is closely in contact with the epithelial lining, but in the infundibulum there is a virtual space between the two, and it is here that the acne bacillus grows in seborrhœic persons. The ostium is the widest part of the follicle, forming a cup-like depression on the surface of the skin, and often separated from the infundibulum by a slight constriction. In the ostium are found, lying amidst the epithelial *débris*, a few staphylococci, which under favourable conditions multiply and produce inflammatory lesions. Moisture and heat are particularly likely to excite active germination of these staphylococci ; hence the frequency of pustulation in regions such as the groins and armpits, and the noxious influence of poultices and fomentations.

Staphylococci are divided into three main groups, according to the colour of their growth on artificial media, viz., *S. albus*, *S. aureus*, and *S. citreus*. The depth of colour is to some extent an index of their virulence, as is their hæmolytic power. The *S. albus*, the least virulent, is a normal habitant of the human skin. Different strains or modifications of this organism have been described and it varies in virulence from a harmless saprophyte to a definitely pyogenic organism (**10**). It is found in a state of active growth, in association with the pityrosporon of Malassez, in the so-called *Pityriasis steatoides* and in *Seborrhœic dermatitis* (*q.v.*) ; it is the cause of the common and mild follicular pustule, of the

pustules that often arise after epilation for hypertrichosis, of some cases of porofolliculitis, and of some stitch-abscesses. Very rarely it may be the causal organism in sycosis. The *S. aureus* is almost constantly responsible for the more serious and chronic staphylococcal lesions of the skin, and, of course, for osteomyelitis and staphylococcal septicæmia. It is the cause of the more severe form of porofolliculitis (impetigo of Bockhardt), of boils and carbuncles, sycosis, the majority of cases of infective eczematoid dermatitis, hydradenitis, the multiple abscesses of infants, many cases of perionychia, granuloma pyogenicum, pemphigus neonatorum, and, in association with the microbacillus of acne, of acne necrotica. The *S. citreus*, intermediate between the other two species as regards virulence, is occasionally found in place of *S. aureus*. A characteristic of the more virulent staphylococci is their tendency to produce *necrosis*, such as occurs in boils, carbuncles and, more superficially, in some cases of porofolliculitis, and in acne necrotica.

Although the *S. albus* is constantly present in the skin, this is not true of the other two varieties. The *S. aureus* may sometimes be cultivated from the clean skin of normal persons, but its presence usually indicates either that the subject is suffering from some active pyogenic lesion, or that he has been in contact with some one thus infected. In either case he has become a "pyococcus-carrier." Once an active infection with a pyogenic staphylococcus has occurred, the organism becomes, so to speak, sown in the mouths of the pilosebaceous follicles, not only in the neighbourhood of the actual lesions, but also in parts widely distant from them. This fact is of the highest importance, both because fresh lesions, *e.g.*, boils, are likely to arise in different parts of the body so long as the pyococcus is present in the skin, and because the subject is a potent source of infection to others. As will be seen later, the pyococcus-carrier is the cause of most if not all the epidemics of pemphigus neonatorum. It follows from this that in cases of recurrent pyogenic infection of the skin, such as furunculosis, surface antisepsis is the first essential of rational treatment.

STAPHYLOCOCCAL PUSTULE

(*Porofollilitiicus*)

The simplest and commonest staphylococcal lesion of the skin is the small, superficial pustule, formed at the ostium of a pilosebaceous follicle, and caused by a *S. albus*. The organisms, lying latent in the ostium, under the influence of some trauma, *e.g.*, the application of an irritant, friction, shaving, etc., begin to grow actively, and form a mulberry-like mass. With their multiplication their toxins are presumably liberated, and cause a migration of polymorphonuclear leucocytes from the vessels in the dermis, which pass through the deeper layers of the epidermis, squeezing themselves between the Malpighian cells, towards the site of infection, and forming an *intra-epidermic* cavity—the *pustule*—having for its roof the horny layer and for its base the underlying rete Malpighii. This pustule usually arises at the side of the ostium, but quickly surrounds it, thus forming a ring around the hair, which pierces its horny roof. At the point of emergence of the hair the dome-like roof is umbilicated. Healing takes place by the desiccation of the pustule with the formation of a crust, which is exfoliated as a new horny layer is formed beneath it.

The simplest and most benign pustules of this type arise owing to the awakening into activity of the *S. albus*, already present at the mouths of the pilosebaceous follicles. The so-called *impetigo of Bockhardt*, better termed *acute porofolliculitis*, is merely an eruption of numerous follicular pustules due in mild cases to the *S. albus*, in the more severe to the *S. aureus*. The eruption usually follows the application of some irritant, such as liniments, plasters and blue ointment, particularly to hairy parts. An acute outbreak is often provoked around a discharging boil or septic ulcer as a result of fomenting or poulticing, the moisture,

heat, and maceration of the skin providing the staphylococci with conditions ideal for their active growth. In children, recurrent acute attacks on the scalp are not infrequent, and due, as a rule, to *S. aureus*. Each fresh attack is heralded by enlargement and tenderness of the occipital glands, and this is followed by the appearance of numerous pustules of varying size, yellowish or greenish-yellow, and each pierced by a hair. With their development the glandular enlargement subsides. In some of the pustules the infection spreads deeply and produces an area of *necrosis* in the dermis. This is revealed clinically by the presence of a greenish plug, embedded in the follicle, which cannot, unlike the overlying pustule, be wiped away after incising the horny layer. This plug or sphacelus is comparable to the core of a boil, and like it is the result of necrosis—consequently when the lesions heal there are left small circular pitted scars similar to those of acne necrotica. Another complication that may result from the simple, superficial follicular pustule is the development of an abscess, which is formed in the dermis around the follicle at a point about midway between the ostium and the bulb—the so-called hour-glass abscess. From this point the infection may spread laterally and produce an abscess of considerable size.

Treatment. In the treatment of superficial staphylococcal pustulation it must be emphasised that one's object is, first, to aid the desiccation of the lesions and, secondly, to disinfect both the area involved and the surrounding skin. For this purpose, as a rule, all that is necessary is to paint on once or twice daily a dilute solution of iodine in spirit, *e.g.* ℞. Tinct. iodi mitis, 1·0; Spt. vini meth. indust., ad 5·0; and to keep the infected area powdered with the pulv. acidi salicylici comp., B.P.C. If there is much pain or discomfort, calamine lotion, should be substituted for the powder. In the more severe or recurrent form of porofolliculitis, which is often accompanied by boils or abscesses, everything possible should be done to raise the patient's resistance to infection. An out-of-door holiday with judicious sun-bathing is the best treatment; failing this, total ultra-violet light baths should be ordered. It is important to attempt to disinfect the whole skin by antiseptic baths as in furunculosis.

MILIARIA RUBRA

(*Prickly heat: Lichen tropicus*)

This eruption is most commonly seen in Europeans who inhabit tropical countries, but negroes are never affected. It occurs in temperate climates in those who perspire freely and who are seborrhœic. It consists of innumerable minute red spots, with tiny central vesicles containing a turbid fluid. These spots are hardly elevated, and they are not as a rule follicular. The trunk and the proximal segments of the limbs are the sites of predilection. Histologically there is seen to be congestion, with the presence in the rete of minute vesicles, formed either, as in impetigo, by cleavage or, as in eczema, by spongiosis; these vesicles contain numerous polymorphonuclear leucocytes, and arise frequently, though not invariably, around a sweat-duct; they are not, as Pollitzer stated, due to dilatation of the ducts.

Ætiology. The eruption is commoner in males than females, and appears suddenly after profuse sweating, provoked by a rise of temperature, the taking of hot alcoholic drinks, a hot bath, or violent exercise. The vesicles contain staphylococci in a state of active growth, and Darier's view that the eruption is due to an auto-inoculation of the skin with these organisms, caused by maceration of the epidermis with sweat, is probably correct. As he points out, there is frequently present some active infective focus, such as a boil, impetigo, seborrhœic dermatitis, acne pustules, etc. As predisposing factors may be mentioned the seborrhœic state, the wearing of excessive clothing (and particularly of flannel next the skin), overeating and dyspepsia, and the abuse of alcoholic

drinks. The fat, plethoric, cocktail-drinking European in the tropics is the commonest victim.

Treatment. A brisk purge, twenty-four hours' starvation, copious drinks of barley water and fresh lemon juice, and the administration of alkalies in large doses will rapidly cut short an attack. Locally, tepid baths containing zinc sulphate (¼ lb.), followed by the application of a boro-talc powder, will suffice. Recurrence can be prevented by instituting a rational dietary, the avoidance of alcohol, the wearing of light, porous clothing, the taking of alkaline drinks, regular bathing, and the habitual use of a boric dusting powder.

BOILS

(*Furuncles. Furunculosis.*)

A boil is a massive folliculitis, due almost invariably to the *Staphylococcus aureus* (rarely *S. citreus*), and characterised by the intensity of the inflammatory reaction and by necrosis. It commences with a painful, red, and slightly raised spot, which gradually enlarges, becomes hard and tender to the touch, and is accompanied by induration and sometimes by a considerable œdema of the surrounding skin. The colour becomes dusky red, and after a few days the apex softens, a little pus being extruded and later a greenish-yellow slough of necrosed tissue—the *core*. When this has separated the inflammation subsides, and the sore gradually heals by granulation, leaving a small scar.

Boils may be situated on any portion of the skin where hair-follicles are present, but their sites of election are the back of the neck, the buttocks, the back, the thighs and forearms. Of particular importance are those occurring on or near the upper lip, owing to the fact that infection may spread to the cavernous sinus, and result in septic thrombosis, with ultimate pyæmia and death. In the external auditory meatus they give rise to intense and radiating pain; in this situation they often complicate a chronic seborrhœic dermatitis of the meatus.

Morbid Anatomy. A boil arises in a manner comparable to the more severe necrotic form of porofolliculitis. The staphylococci, growing first at the mouth of the follicle and producing a superficial and transitory pustule, spread downwards along the hair in long chains to form another centre of activity in the deeper part. Here they give rise to an enormous colony, around which necrosis of the follicular tissue and surrounding part of the dermis occurs. This necrotic mass, which is the *core*, has for its centre the colony of staphylococci, included in the remains of the follicle, and around this is a mass of fibrin, enmeshing masses of polymorphonuclear leucocytes, together with the disintegrated connective and elastic tissue of the dermis. The leucocytes nearest to the microbial colony are broken up, while in those further away the contours and nuclei are still intact. The mode of formation of a boil shows that it always results from an *external* infection of a follicle, and that the infection remains intrafollicular, but produces necrosis of tissue at a distance.

Ætiology. The *S. aureus* cannot be regarded as a normal habitant of clean healthy skin, but exposure to contamination with it must be very frequent. Although not so contagious as streptococcal impetigo, active lesions due to this organism are certainly a potent source of infection to others either by direct or indirect contact. Nurses and doctors not infrequently develop furunculosis from attending patients with this disease. Boils, porofolliculitis, and sycosis are also often contracted in the barber's shop. Once the skin is contaminated, irritation of the follicles, in which the staphylococci lurk, predisposes to their active growth; boils are therefore common at sites of friction, such as the back of the neck and the buttocks, and hence their frequency in the latter situation in horsemen and oarsmen, and on the forearms and backs of the hands in those who follow certain trades. The seborrhœic skin undoubtedly favours the growth of

the *S. aureus*, as well as of the *S. albus*, pityrosporon, and acne bacillus. Hyperglycæmia, too, is a notorious predisposing factor, but it must be remembered that boils and carbuncles, like other infections, may themselves cause a rise in blood-sugar, which falls to normal when the active infection subsides. An unhygienic indoor life, overwork, anæmia, an excessive or inadequate dietary, and chronic infections elsewhere are also factors operative in certain cases. A localised pruritus, *e.g.*, pruritus ani, is sometimes a predisposing cause, for which inquiry should always be made. In such cases the boils occur chiefly in the neighbourhood of the irritable area—on the buttocks and in the perinæum with pruritus ani—the constant or repeated scratching of the parts causing abrasions of the skin and disseminating the staphylococcus.

Treatment. The presence of a boil implies the probability of a widespread dissemination of the *S. aureus* in the ostia of the pilosebaceous follicles, and the first essential of treatment is to disinfect the skin over a considerable area around the boil by painting daily with diluted tincture of iodine, as recommended for porofolliculitis, and to attempt a more general disinfection of the whole skin by the addition of an antiseptic to the daily bath, *e.g.*, 4 oz. of zinc sulphate, or of such preparations as lysol, cyllin, monsol, etc. Many chronic cases of furunculosis respond to this simple method of surface antisepsis, when more elaborate treatment by means of vaccines, collosol manganese, etc., have failed. An incipient boil may sometimes be aborted by making a small incision with a fine von Graefe knife, and plunging through this into the centre a sharpened match-stick dipped in pure carbolic acid, monsol, or lysol. When the active stage of inflammation has subsided, the greatest care must be taken to remove the core entire—to break it up on the surface of the surrounding skin is to risk disseminating living staphylococci contained in its centre. *In no circumstances should a boil be treated by poultices or boric fomentations*, for reasons already stated; if pain is very intense in the early stages, hot fomentations with a 1/4,000 solution of perchloride of mercury for a short period are admissible, but they should not be employed if the skin has already been painted with iodine. It is preferable to apply a layer of pure ichthyol to a developing boil and cover with cotton wool, or it may be dressed with magnesium paste (magn. sulph. exsicc. 2·0, glycerine 1·0). In addition to the local application of dilute iodine and ichthyol, and a daily antiseptic bath, the pulv. acidi salicylici comp., B.P.C., should be dusted on the skin surrounding the boil and in the joint flexures.

General Treatment. Although local and general disinfection of the skin is of primary importance, and often alone suffices, there may in many cases be indications for internal treatment. It is important to examine carefully for focal infection in the teeth, tonsils, nasal sinuses, or elsewhere, for this is sometimes responsible for lowering the resistance to the staphylococcus. Hyperglycæmia must, of course, be dealt with by suitable dietary and, if necessary, injections of insulin. In plethoric seborrhœic persons a restricted carbohydrate dietary and full doses of alkali are indicated; on the other hand, in debilitated, anæmic persons, in whom phosphaturia is common, iron should be given and acidosis produced by acid sod. phosph. (see p. 538). In obstinate cases a complete holiday in the open air must be insisted upon, and this should be combined with real or artificial sun-baths. Given in suitable and increasing doses, heliotherapy provides one of the best methods of raising the resistance to staphylococcal infection. Injections of a stock or autogenous staphylococcal vaccine, provided the dosage be carefully controlled, are of undoubted value in furunculosis, but cases are met with in which they fail or actually do harm. Less certain in their effect are injections of collosol manganese or manganese butyrate, and the oral administration of tin (stannoxyl). Fresh brewers' yeast, 1 to 2 oz. per diem, may be tried with advantage. Lastly, autogenous whole-blood injections have been claimed as almost a specific in resistant cases. To sum up, the successful treatment of furunculosis depends first on local and general disinfection of the

skin, and secondly on the correction of any factors that are lowering the patient's general health, combined, if necessary, with specific vaccination and heliotherapy.

CARBUNCLE

This is a similar infection by staphylococci, leading to extensive inflammation, induration, and necrosis of the skin and subcutaneous tissue. It differs from a boil in its extent, and in the fact that there are numerous foci of suppuration, leading to discharge through several openings instead of one. The patients are generally of middle age or older, and diabetes mellitus is a very common antecedent. The common seat of the lesion is the back of the neck, but it also occurs often on the back. It begins as a flat, indurated area of red or purplish-red colour; this extends and becomes more elevated above the level of the skin, spots of softening occur, and discharge of pus takes place. The hard mass forms a slough, which comes away, leaving a deep ulcer; and this ultimately heals by granulation, producing a scar. A carbuncle may be from 1 to 3 inches in diameter, and occasionally very much more. There is much constitutional disturbance, with pyrexia; septic infection is likely to occur, or death may take place from exhaustion.

Treatment. In the early stages, both of furunculosis and carbuncle, intramuscular injections of *aolan*—a proprietary preparation of lactalbumin—which produces a leucocytosis, will as a rule mitigate the severity and hasten the evolution of the lesions. From 5 to 10 c.c., or more in threatening carbuncle, should be injected into the muscles of the upper and outer quadrant of the buttock daily or every other day, three to five injections being given. In severe cases of carbuncle, particularly in debilitated persons, complete excision may be advisable; otherwise the measures advised for boils should be employed.

PEMPHIGUS NEONATORUM (*See Plate 58, C, p. 833*).

This disease, first described in France by Ochène, is a comparatively rare contagious affection of the newly-born, and has by many been regarded merely as a variety of bullous impetigo occurring in infants. Sabouraud still inclines to this view, and considers that, like ordinary impetigo, it is primarily of streptococcal origin. That a bullous *streptococcal* impetigo may occur in infants, as well as in older children and adults, is certain, but the independent observations of several workers indicate that the true pemphigus neonatorum, like the rare form of bullous impetigo described by Jadassohn, is usually, at any rate, due to infection with *Staphylococcus aureus*.

The eruption, which appears, as a rule, from the fourth to the fourteenth day after birth, consists of hemispherical bullæ, containing at first almost clear serous fluid. The bulla, which, like the vesicle of ordinary impetigo, is formed between the stratum corneum and the rete, soon ruptures, exposing a red, moist, glistening surface from which serum continues to ooze until it dries to form a yellowish, thin crust. Extension of the infection at the margins of the ruptured bullæ occurs, the horny layer being stripped up, thus increasing the denuded area. Confluence of adjacent lesions also takes place, and in this way large tracts of skin become deprived of their horny layer. In favourable cases extension and the formation of new bullæ gradually cease, the crusts dry up and separate, and reconstitution of the horny layer proceeds without scarring, as in impetigo contagiosa. More rarely, however, the infection continues to spread, the mucous membranes of the conjunctiva, mouth and nose are invaded, ecthymatous ulceration and abscesses may occur as complications, and the infant dies with symptoms of a general septicæmia and collapse. It would seem that a fatal result has often followed involvement of the incompletely healed umbilical

scar, the infection spreading along the recently clotted vessels and causing a pyæmia.

Distribution. The eruption may begin at almost any site, most commonly perhaps on the neck, chin, fingers or toes. It may spread widely over the trunk and flexor surfaces of the limbs, but in contradistinction to the bullous congenital syphilide, it spares the palms and soles. It is probable that the condition labelled by Ritter von Rittershein as *dermatitis exfoliativa infantum*, and sometimes known as "Ritter's disease," was merely a severe form of pemphigus neonatorum, in which there was widespread exfoliation. Ritter described epidemics, occurring in a foundling hospital in Prague between 1878 and 1880, in which out of 274 cases, about 50 per cent. died.

Prognosis. The mortality has varied greatly in the different epidemics recorded. Of recent years it has been slight, largely no doubt owing to early isolation of infected cases and greater care in the treatment of the umbilical scar.

Ætiology. The eruption has all the characters of an acute streptococcal impetigo of the bullous type, but a number of careful independent observations tend to incriminate the *S. aureus* as the causal organism (**11**). *S. aureus* is not a normal habitant of clean, healthy skin, but once an active infection with this organism occurs it may be cultivated even from parts of the skin widely distant from the active lesions, and the patient is a "pyococcus-carrier." Moreover, persons who have been in close contact with such a carrier may themselves harbour the organism on their skins, without necessarily developing active lesions. Probably in most cases of pemphigus neonatorum the eruption is due to direct contact of the infant with a "pyococcus-carrier" A point of importance is that although the *S. aureus*, isolated from cases of pemphigus neonatorum, does not apparently differ in its cultural reactions from the ordinary variety obtained from boils and carbuncles, nevertheless it is characterised by a tendency to produce vesicular lesions, not only in the newly born, but also in adults who have been infected from an infant. We are thus forced to the conclusion that, although in the great majority of cases staphylococcal lesions are follicular and pustular ab initio, *S. aureus*—perhaps a special strain—is capable of producing, like the *Streptococcus pyogenes longus*, vesicular and bullous lesions. It is thus responsible for the bullous form of impetigo described by Jadassohn and for pemphigus neonatorum.

Treatment. The infant should be immediately isolated, and the greatest care taken to prevent spread of the infection either by direct or indirect contact. Unless the general condition forbids it, a daily boric or zinc sulphate (1 in 10,000) bath should be given, the skin being afterwards dried by dabbing and then powdered copiously with a boro-talc dusting powder. When the lesions have dried up, a weak mercurial ointment or paste may be used. The umbilical region should be kept scrupulously clean and smeared with the mercurial ointment. The bed-clothing and linen should be sterilised. In severe cases, with extensive exfoliation, the infant should be exposed as little as possible and kept very warm. Recovery probably depends upon the development of immunity, and it is doubtful whether treatment affects the prognosis.

MULTIPLE ABSCESSES OF INFANTS

This condition, which is not a common one, is seen as a rule in marasmic children suffering from improper feeding, enteritis, bronchopneumonia, etc. It is apt to be associated with the infantile erythema of Jacquet. The abscesses begin as hard, deep nodules in the skin, particularly in situations liable to soiling, such as the buttocks and thighs, and to friction or pressure. Early lesions can be felt before they are visible, and the colour of the nodules remains unchanged until the abscess approaches the surface, when the overlying skin becomes red or bluish, and, unless previously incised, ruptures with the discharge of liquid pus.

In neglected infants ulcers or fistulæ may supervene, and secondary adenitis, with subsequent softening, may be a complication.

The nodules vary from a pea to a hen's egg in size, and the quantity of pus they contain is often astonishing. The diagnosis is easy, although the nodules have been mistaken for gummata, which are very rare in infants, and for cold tuberculous abscesses.

Ætiology. The abscesses were formerly thought to be pyæmic in nature, but it has been shown that they are due to infection with a staphylococcus (*S. aureus* or *albus*), *viâ* the sweat-ducts. The depth of the lesions is thus explained. With them may coexist small superficial intra-epidermic pustules which are formed at the orifices of the sweat-ducts.

Treatment. The most important part of the treatment is to attempt to raise the infant's resistance by attending to the underlying debilitated condition. Locally scrupulous cleanliness, the incision with a small knife of the abscesses, boric baths, and the copious use of a boro-talc powder are the only measures necessary. The infants should, if possible, be kept in bed out of doors.

SYCOSIS COCCOGENICA

By the term *sycosis* is meant a pustular folliculitis of the hairy parts ; two forms are recognised, one, *simple sycosis* or *sycosis coccogenica*, due to infection of the follicles with a staphylococcus, the other, *tinea sycosis*, due primarily to infection with a ringworm fungus, but later complicated by invasion with pyogenic organisms. The commonest sites of infection in coccogenic sycosis are the beard and moustache regions in men, but a similar folliculitis occurs on other hairy parts, such as the eyebrows, axillæ, pubis, and scalp. The lesions are follicular pustules and papules, which are pierced by the hairs. They may be discrete, but more commonly are confluent, occurring in irregular patches, or in severe cases involving the whole of the beard and moustache regions. The skin between the follicles is usually affected with a diffuse staphylococcal dermatitis (so-called " seborrhœic sycosis "). The degree of inflammation varies ; in some cases it is severe, so that the affected parts are red and swollen and covered with yellowish crusts, formed by the dried sero-purulent exudate ; in others there is no swelling, but either discrete pustules and papules, arranged singly or in confluent patches, or a diffuse scaly dermatitis dotted with yellow follicular pustules.

Contrary to what might be expected, the infection in sycosis is superficial, intra-epidermal and localised to the upper third or quarter of the follicles. Only very rarely does it spread to the deeper parts of a follicle and destroy the hair. It is for this reason that the hairs resist traction with forceps ; epilation is painful, and permanent cicatricial atrophy is rare in sycosis, except as the result of excessive radiotherapy. Sycosis begins as an attack of acute porofolliculitis, or gradually becomes established after several attacks. The essential difference between the two forms of folliculitis is that, whereas in simple porofolliculitis the epidermis is able to deal with the infection and the pustules occur singly and heal spontaneously, in sycosis the epidermis has lost its defensive power, and new pustules keep on forming in it beneath the older ones. It will be noted that the only regions affected in sycosis are those that bear large hairs, hence on the cheeks and upper lip it occurs only in males ; moreover, it is men in whom the hairs of the beard and moustache are particularly coarse that are most liable to the disease. Removal of the hairs from the follicles, either by epilation or the X-rays, leads to a temporary cessation of the pustulation, but recurrence takes place with their regrowth. It is clear, therefore, that the presence in the follicles of coarse hair is an important factor.

Morbid Anatomy. The elementary lesions of sycosis occur solely in the epidermis, and are essentially those of a porofolliculitis (*q.v.*), but they are confluent, occupy nearly all the follicles of the affected region, and are constantly

renewed. The chronicity of the affection is due to this incessant formation of new pustules, which are situated at the ostia and in the infundibula of the follicles; small miliary intra-epidermic abscesses develop beneath these pustules. Rarely the infection spreads downwards to the hair bulb, involving the whole depth of the follicle, a peribulbar abscess is produced, the hair is loosened and expelled, and the follicle sclerosed and destroyed. On extracting such a hair with forceps the epithelial sheath will be found infiltrated with pus, but this is very exceptional. The polymorphonuclear exudation is confined to the epidermis, and dermal abscesses are never found. Around the infected follicles, however, there is vascular dilatation in the dermis and infiltration of its upper portion with mononuclear cells. In cases of some months' duration plasma cells and giant cells appear, and the induration that characterises the nodular type of sycosis is due to the density of this cellular infiltration of the dermis. In long-standing cases may be seen epithelial down-growths, and a tendency to the formation of new follicles with rudimentary hairs.

Ætiology. The infecting organism is usually a *Staphylococcus aureus*, although the white and yellow varieties are sometimes responsible. The condition is never seen except in seborrhœic persons, and usually other seborrhœic manifestations, such as pityriasis, seborrhœic dermatitis, acne and boils, are or have been at times present. The most severe and resistant cases occur in those whose resistance to infection has been low from childhood, the subjects of chronic infective eczematous dermatitis of the scalp, ears and flexures, chronic blepharitis, rhinitis, and naso-pharyngeal catarrh. The condition may arise on the beard region after an attack of seborrhœic dermatitis or furunculosis, from direct infection in the barber's shop, and from the extension of the superficial staphylococcal folliculitis so common in seborrhœic persons with a stiff beard. It may also follow an attack of impetigo contagiosa, the secondarily infecting staphylococci invading the follicles. The possibility of this complication should always be borne in mind in cases of impetigo of the beard region in men. Sycosis of the moustache is nearly always secondary to an acute or chronic nasal catarrh; it may be unilateral at its commencement. As Sabouraud has pointed out, it not infrequently occurs in those who have suffered from childhood from a chronic staphylococcal blepharitis, virulent staphylococci passing down the nasal duct and invading the follicles of the upper lip when the moustache begins to grow.

Besredka's contention that resistance to staphylococcal infection is a function of the epidermis would seem to be illustrated by the special features of sycosis, the persistence of which is clearly dependent upon a loss of this defensive power, the reasons for which are not altogether understood. However (**12**), when an infection, as in sycosis, is limited to the epidermis, vaccines given by subcutaneous injection are useless, but when the epidermal barrier is passed and the dermis is itself infected, they may be expected to give good results. Rational treatment of a purely epidermal infection with banal organisms must obviously be designed to restore the antibacterial function of the skin to normal, and a study of those in whom sycosis occurs gives us a clue as to how this function may be lost. We can recognise two groups of cases—one occurring among the poorer classes, in which owing to unhygienic surroundings, lack of fresh air and sunlight, and a deficient dietary, the patients suffer from childhood from chronic infection of the skin and mucous membranes with pyogenic organisms, and in them the sycosis is merely a superadded complication consequent upon the adult growth of the moustache and beard; the other, occurring among the well-to-do, who develop seborrhœic manifestations owing to excess of food and drink and lack of outdoor exercise.

Treatment. *Local.* A consideration of the micropathology of sycosis suffices to explain why it is impossible to effect a cure by local antiseptic applications, since these cannot penetrate to the depth of the horny layer, much less to the infundibula of the follicles or the rete Malpighii. One may attempt to

limit the spread of infection by painting the surrounding skin with a 1 per cent. solution of iodine in spirit, or by the application of ointments or pastes containing sulphur, mercury, resorcin, etc., but the actual infected areas are best treated by painting them with an aqueous solution of ichthyol (25 to 75 per cent.) at night-time, which can be washed off in the morning, or with brilliant green (5 gr. to the ounce of 25 per cent. spirit). The effect of epilation has already been noted, and in chronic cases is advisable. By far the most rapid result is obtained by radiotherapy, and a single epilation dose usually produces apparent cure, but relapse is the rule when the hair regrows. Fractional doses of X-rays also have a beneficial effect, even though they do not cause the hair to fall. Epilation with forceps, though tedious and painful, has the advantage over radiotherapy that it may be continued indefinitely; it should be carried out not only on the affected area, but also beyond it to prevent extension. Local applications of ultra-violet light are undoubtedly of value, and probably act by stimulating the defensive mechanism of the skin; they may well be combined with total light baths.

General. If possible the patient should live an outdoor life, and take vigorous exercise in light clothing. Sun-bathing and the action of cool air on the skin of the whole body are more likely to effect a permanent cure than any other method of treatment. The dietary should be that advised for the seborrhœic state. Staphylococcal vaccines, given subcutaneously, are of little or no value. Injected *intradermally*, however, in doses of from 25 to 500 million their effect may be very striking, and good results have been obtained, even in long-standing cases. Besredka's staphylococcal antivirus (the filtrate of ten-day-old cultures which contain auto-inhibitory substances), applied on compresses to the affected areas at night time, is also claimed to have been successful in early cases.

SYCOSIS NUCHÆ

(*Acne Cheloid; Dermatitis Papillaris Capillitii*)

This condition is analogous to ordinary sycosis, and like it occurs exclusively in males who are seborrhœic. It is a perifollicular inflammation of the nucha, and is characterised by the formation of dense cheloid-like sclerosis of the connective tissue. On the affected area comedones, deep follicular pustules, and abscesses are seen. Sometimes bluish-red papillomatous vegetations arise, which bleed easily and discharge an offensive semipurulent secretion. These vegetations later become transformed into cheloid bands. Many of the hair-follicles are destroyed by the chronic inflammation, but some are spared, so that characteristic little tufts of hair are left projecting from the cheloid mass.

Ætiology. The condition, as has been said, is confined to males, many of whom suffer or have suffered from ordinary acne or sycosis. It is without doubt due to a chronic infection of the nuchal skin with a *Staphylococcus aureus*, and probably the dense nature of the connective tissue in this situation is responsible for the peculiarly indolent nature of the inflammatory process, and for the resulting cheloid-like formation.

Treatment. Apart from the general measures advised in sycosis, the only treatment that is really satisfactory is radiotherapy. Full pastille doses should be given at intervals of a month, or fractional doses at shorter intervals.

ACNE NECROTICA

(*Acne varioliformis. Acne frontalis.*)

This eruption is met with chiefly in persons over forty years of age, living a sedentary indoor life and eating to excess, but occasionally it occurs in adolescence. It is commoner in the male sex. The lesions are characteristic, both

clinically and microscopically. They commence as follicular papules, surrounded by a red halo of inflammation; at their apices develop vesiculo-pustules, which very rapidly dry up to form the characteristic crusts. These are biconvex, yellowish-brown in colour, and firmly embedded in the skin; on the scalp they are always centred by a hair; when they fall they leave pitted scars, the depth of which varies according to the severity of the case. Usually small, the lesions may occasionally attain the size of a threepenny bit, and the resulting scars are then very disfiguring. The sites of election are the forehead, along the margin of the hair, the temples, the scalp, the nose and naso-labial folds, and the midline of the back and chest. The eruption is essentially chronic, and progresses by the development of fresh crops of lesions, which are heralded by severe itching, burning, or even actual pain, the subjective symptoms being usually out of proportion to the objective signs.

Morbid Anatomy. Histologically the lesion is seen to result from necrosis at the orifice of a pilosebaceous follicle, involving the whole epidermis and a portion of the underlying dermis. This necrotic area forms the lenticular crust, in the centre of which are found the remains of the follicle, hair, and sebaceous gland. Lying in the infundibulum of the follicle are colonies of the microbacillus of acne, at the ostium and along the upper and lower borders of the crust are masses of the *Staphylococcus aureus*.

Ætiology. Acne necrotica would appear to be due to a superadded infection with a *S. aureus* of a follicle already infected with the acne bacillus. These two organisms are constantly present, and the necrotic nature of the lesions is due to the staphylococcus. The patients are always seborrhœic, and the eruption is commonest in fat, plethoric men past middle age. As with other seborrhœic conditions, an excessive carbohydrate dietary, alcoholism, and lack of outdoor exercise are important factors.

Treatment. Locally, frequent washing of the scalp and other affected areas, and the application at night time of an ointment containing sulphur and oil of cade, *e.g.* ℞. Olei cadini 10·0, Sulphur præcip. 1·0, Vaselini alb. lanolini āā 10·0, or sulphur alone, will usually suffice to clear the eruption temporarily, but relapse is the rule unless the diet and mode of life be changed. Sabouraud advises total abstention from bread, but the general treatment is that for the seborrhœic state (*q.v.*). In constantly relapsing cases an autogenous or stock staphylococcal vaccine, given intradermally as advised for sycosis, should be tried.

HIDRADENITIS

Frequently mistaken for furunculosis, this affection occurs almost exclusively in the axillæ and, more rarely, in the perinæum. The lesions consist of oval, inflammatory nodules, which are often extremely painful; they may involute without breaking down, but more commonly soften, burst and discharge a creamy pus, but, unlike a boil, no core. The inflammation is essentially indolent, and each nodule may last from ten days to a fortnight. Recurrence is very common, and in severe cases both axillæ in their entirety may be involved with multiple lesions.

Ætiology. The nodules, like those of the condition known as "multiple abscesses of infants," are due to staphylococcal infection of the sweat-glands, and not of the pilo-sebaceous follicles. The affection is commoner in women than in men, and occurs in seborrhœic persons who perspire freely. It is a not uncommon complication of generalised seborrhœic dermatitis, particularly when the axillæ are involved, or of infective eczematoid dermatitis.

Treatment. The measures already indicated for the treatment of the seborrhœic state and of staphylococcal infections should be instituted. Locally, the axillæ should be painted daily with R. Tinct. Iodi. mitis 1·0, Spirit methyl. ad 10·0, and a boro-salicylic dusting powder applied freely.

GRANULOMA PYOGENICUM

In this country two different types of lesion are referred to under this term:

(1) The condition was formerly called *Botryomycosis hominis*. It has been applied to small, pedunculated tumours of the skin similar to those which sometimes develop in horses in the wound left by castration. They were thought to be due to infection with a special fungus, the Botryomyces, but the mulberry-like masses, which were mistaken for parasitic elements, are really degenerated cells. The tumour varies in size from a pea to a nut. It is red in colour, round or slightly flattened vertically, and its surface is smooth or mamillated. It is not, as a rule, covered by epidermis, but rests on the dermis, from which it is separated by a groove, at the bottom of which, on drawing the tumour to one side, the pedicle can be seen. It is firm and elastic to the touch, and bleeds easily; sometimes it is covered with a yellowish crust. The lesions are seen most commonly on the hands and fingers, but may also occur on the face, feet, legs, lips, scalp and even the tongue. Unless removed they tend to persist indefinitely. Histologically they consist of embryonic connective tissue with large numbers of newly-formed, friable capillary blood vessels, such as are seen in an angeioma.

(2) A fungating warty patch, often of considerable size, resembling blastomycosis or lupus verrucosus. It begins as a pustular lesion, which spreads excentrically and develops soft vascular granulations. These later take on a verrucose appearance, and the fully developed patch is circular or irregular in shape, projects to a varying extent above the level of the surrounding skin, and is covered with crusts, between and beneath which can be seen the warty, vegetating, granulomatous surface. Pressure on the lesion causes droplets of pus to exude. The subjective symptoms are slight, and, unless treated, the course of the affection is indolent and chronic.

Ætiology. Both types of pyogenic granuloma tend to occur on exposed parts, and to complicate a preceding septic infection, particularly a suppurating abrasion or wound. On bacteriological examination a *Staphylococcus aureus* is usually obtained in pure culture, but the factors responsible for the vegetating character of the lesions are unknown. Irritation by caustics sometimes appears to provoke the appearance of the first type. It is important to distinguish the second from lupus verrucosus, blastomycosis, sporotrichosis, and trichophytosis.

Treatment. The first type of lesion should be snipped off with scissors, and the pedicle cauterised with a silver nitrate stick to prevent recurrence. The local application of ultra-violet light has also been found curative. The second type will usually yield to the constant application of antiseptic lotions, such as perchloride of mercury (1 in 3,000), or the eau d'Alibour. In some cases a full pastille dose of X-rays is advisable.

DERMATITIS INFECTIOSA ECZEMATOIDES

Under this title Engman, and later Fordyce and Sutton, have described a form of eczematoid dermatitis, which usually follows some localised infective lesion of the skin, such as a chronic patch of varicose dermatitis, occupational eczema, furunculosis or carbuncle, wounds, chronic otorrhœa, discharging sinuses, etc. It is not uncommonly seen after an attack of scabies with secondary infection, in chronic osteomyelitis with infection of the overlying skin, and after compound fractures. The eruption, as a rule, begins as eczematous patches around the original infective lesion, and then there appear *at a distance from this* more or less sharply circumscribed circular or oval patches, most commonly situated on the arms, thighs and legs. These patches are highly characteristic, and may be seen to arise from a single vesicle or vesico-pustule on an erythematous base; the inflammation spreads peripherally until a circinate patch is formed; the vesicles are large, and dry up to form discrete yellowish crusts.

Ætiology. The type of inflammation of the skin which we call *eczema*

is an indication of epidermal sensitisation, and in dermatitis infectiosa eczematoides the sensitising agent is a staphylococcus, usually the *S. aureus*. Sensitisation takes place owing to the existence of some focus of staphylococcal infection in the skin. Positive cutaneous reactions to the staphylococcus are often obtained, and Sutton has pointed out that in about 25 per cent. of cases urticarial lesions may accompany the eruption, thus indicating that dermal, as well as epidermal, sensitisation has occurred. Eyre has shown that specific agglutinins to the infecting staphylococcus are often present in the blood.

Treatment. It is essential first to treat the original focus of infection, to which the sensitisation of the skin is due. When this is cured the further outbreak of eczematous patches sometimes, but not always, ceases. Desensitisation should, in persistent cases, be attempted by increasing doses of an autogenous staphylococcal vaccine. In some cases intravenous or intramuscular injections of peptone are successful. Locally the eczematous patches should be covered with a paste containing tar and ammoniated mercury, *e.g.* ℞ Liq. picis carbonis m. xxx to dm. i, Hydrarg. ammoniat. gr. v, Past. Zinci Comp. B.P. ad oz. i ; they may be painted, previous to the application of the paste, with a 2 per cent. solution of silver nitrate in Spt. ætheris nitrosi, and in some cases a crude coal tar paste is the most effective application. Most patients who develop the condition are seborrhœic, and the administration of alkalis, as Sutton has noted, is often valuable.

ACRODERMATITIS CONTINUA

(*Dermatitis repens*)

In 1888, Radcliffe Crocker (**13**) described under the term *Dermatitis repens* an eruption which he defined as " a spreading dermatitis, usually following injuries, and probably neuritic, commencing almost exclusively in the upper extremities."

Symptoms. Crocker's description of the localised eruption was as follows :—

" In all cases in which inquiry has been made, an injury, often a trivial one, has been the exciting cause. Vesicles or a bulla have appeared at the site of the injury, and these have ruptured, and the elevated epidermis has been thrown off, leaving a bright red surface, oozing a clear or slightly turbid fluid. The border of the denuded area is bounded by a collar of the epidermis, which is raised up by subjacent fluid, clear or turbid, and is sodden and irregular. Sometimes extension takes place by the continued detachment of the epidermis by further exudation, or there may be fresh vesicles or small bullæ just beyond the border, which break down and add a newly-denuded area to the original adjacent one."

One of the most characteristic features of the condition is involvement of *the nails*, which are affected exactly as in ordinary whitlow. The eruption may be confined to one hand or foot, but both hands or all four extremities are involved in some cases. The subjective symptoms are moderate local itching, and sometimes pain, which may be intense. There is seldom any secondary lymphangitis, and constitutional disturbance is slight or nil. The course is essentially slow and chronic, and at one time the disease was considered incurable. Finally there may be shrinking of the affected digits, with disappearance of the nails, and their reduction to little conical and sclerosed stumps. X-ray examination may reveal, even in cases of moderate severity, osteitis and absorption of the underlying bones, particularly of the terminal phalanges.

In the generalised form of the disease, apart from the characteristic eruption of *Dermatitis repens* on the hands and feet and the involvement of the nails, pustular lesions appear on the trunk, limbs and scalp. These extend peripherally, drying up in their central portions to form crusted patches often of considerable size. The crusts may resemble at first sight those of chronic psoriasis, but they consist of the exfoliated horny layer and dried sero-pus, and beneath them liquid

pus is exuded from a moist oozing surface. The oral, conjunctival and urethral mucous membranes may all be involved in generalised cases, as in a male patient observed by the writer. The tongue is affected by a superficial glossitis, with white patches due to the formation of a diphtheroid membrane ; recurrent acute attacks, coinciding with exacerbations of the eruption on the skin, occur, and may lead to furrowing as in *lingua plicata*.

Morbid Anatomy. The essential lesion is caused by an infiltration of the upper Malpighian layers by polymorphonuclear leucocytes, with the result that an abscess is formed just beneath the horny layer, extending downwards to the summit of the underlying papilla. Resolution takes place by the desiccation of the abscess, and its inclusion and exfoliation by parakeratotic horny cells. Histologically, therefore, *Acrodermatitis continua* may be compared to psoriasis, but in the latter the polymorphonuclear infiltration does not form true abscesses, except in the pustular variety of the disease.

Ætiology. From the investigation both of the localised and generalised forms of the disease, it would appear that the primary cause is an infection with *S. aureus* (**14**).

Prognosis. Both forms of the eruption are essentially chronic and resistant to treatment. In Stowers's case the condition lasted forty-five years and persisted till death. In Strandberg's three cases it had been present fourteen, thirteen and five years respectively. In one observed by the writer the duration was nine months from the onset to the final recovery ; in another the patient had been affected for twelve years with periodical remissions. The view, however, that the disease is incurable is erroneous.

Treatment. The methods of treatment that have been successfully employed by the writer are : (1) Autogenous vaccine therapy with the staphylococcus isolated, persisted with over a long period in suitable increasing doses. (2) The local application to the lesions of an autogenous antivirus, and various antiseptics, combined with baths to which cyllin or monsol is added. (3) Total ultra-violet light baths, and as far as possible an out-of-door life. It is probable that *intradermal* rather than subcutaneous injections of the vaccine would, as in staphylococcal sycosis, be more effective.

THE SEBORRHŒIC STATE AND ASSOCIATED INFECTIONS

Ætiology. As already pointed out, there are three micro-organisms that are so commonly present in the skin of civilised man that they may be considered as its normal habitants, viz. the pityrosporon of Malassez, the microbacillus of acne, and the *S. albus*. On absolutely healthy skin they are present merely as saprophytes ; when, however, conditions are favourable, they take on active growth, and produce reactions in the skin, which vary in nature according to the organism responsible. It is important to note that, when it occurs, active growth of all three organisms usually takes place simultaneously, although one or other may predominate ; consequently it may be concluded that the conditions that favour the changes from saprophytism to parasitism are the same for all three.

The most important predisposing factor responsible for this change is the morbid state of the skin known as *Seborrhœa*, by which is meant an excessive and altered secretion from the sebaceous glands, and a change in the composition of the fat in the horny layer. The normal fat of the skin is composed of various neutral fats, mixed with fatty acids, which are in combination, not with the trihydroxy-alcohol glycerol, but with the monatomic alcohol cholesterol. These cholesterol fats are not easily decomposed by bacterial growth, and are not a suitable culture medium. It is probable that the *essential* factor that favours the active growth of the above three organisms, and consequently the various

seborrhœic infections, is the alteration in the secretion and composition of the cutaneous fat that obtains in seborrhœa, but the factors predisposing to this are complex. They may be briefly reviewed as follows :—

Heredity and Predisposition. There is unquestionably in many cases an hereditary tendency to seborrhœa and its complications. Seborrhœic families are common, and conversely some appear to be comparatively immune. Heredity is certainly an important factor in calvities—the so-called seborrhœic alopecia of men. There is also a congenital predisposition to the seborrhœic state, which may sometimes be detected in infancy.

Age and Sexual Evolution. In a person with a congenital predisposition the various seborrhœic manifestations follow a certain evolution in relationship to age. The true milk-crust is by many considered the earliest sign of the seborrhœic tendency. The infant's head early becomes infected with the pityrosporon, which may cause the seborrhœic variety of infantile eczema. This infection persists as dry dandruff of the scalp until puberty, at which time the sebaceous glands awaken into activity. The scalp and face become greasy, and the simple infection of the former with the pityrosporon is complicated by the active growth of the *S. albus*, resulting in the so-called *Pityriasis steatoides*. The acne bacillus now grows actively in the infundibula of the pilo-sebaceous follicles, and the comedones and pustules of juvenile acne appear. This continues until the age of twenty-five or longer, and is often associated with or succeeded by seborrhœic dermatitis. At about eighteen years, or later, begins the loss of hair on the vertex and temples, which progresses towards the calvities of early middle life. In the third or fourth decade the acne of adolescence is succeeded by rosacea, which in women is often accompanied by hypertrichosis ; at this time, too, appear the so-called seborrhœic warts, which persist till death.

Influence of Sex. There is an intimate relationship between the pilo-sebaceous system and the sexual glands, and also between the growth of the hair and the activity of the sebaceous glands. Virility tends to a loss of hair on the scalp, with its increased luxuriance on the face and body : feminism to a converse distribution.

Eunuchs never develop calvities, and women at the time of the menopause are apt to suffer a considerable loss of hair and to develop a rudimentary beard and moustache. Seborrhœa in both sexes is usually associated with a tendency to a fall of hair on the scalp and growth of coarse hair on the face and body. In cases of suprarenal tumour in women, apart from other signs of virilism, the pilo-sebaceous system undergoes changes characteristic of the male, and the growth of a beard and moustache is accompanied by calvities.

Diet and Mode of Life. If it is admitted that the seborrhœic state is associated with a faulty metabolism of fat and fat-forming foods, it is obvious that diet, or rather the correlation between diet and the expenditure of physical energy, is a factor of great importance. Even those who have no inborn predisposition, and who, while living the active outdoor life of adolescence and early adult life, remain free from seborrhœic symptoms, may develop them for the first time when they abandon their games, adopt a sedentary occupation, and continue to eat as much or more than previously. Clinical observations show clearly that, as regards diet, carbohydrates, particularly cane sugar and soft starchy foods, which are liable to undergo bacterial fermentation with fatty-acid production, certain fats, and alcohol, are, when taken in excess, most likely to provoke seborrhœa and its complications. Sabouraud has emphasised the beneficial effect upon certain seborrhœic eruptions, *e.g.* acne necrotica, rosacea, of complete abstention from ordinary bread, which is often consumed mechanically at meals otherwise adequate or excessive. Other soft farinaceous foods, particularly if cooked with milk, are equally harmful.

With regard to fats, it has been shown that the sebaceous secretion may abnormally have the same chemical characteristics as the fat ingested, and that this is due to the ability of the sebaceous glands to fix directly fatty particles

circulating in the blood. This extraneous fat, like other depôt fat, is coloured by sudan-red given with food, whereas the normal sebum, which is elaborated from the fatty-acids in the blood by a process of cellular acitvity, *i.e.* is a true secretion, is not. The normal function, therefore, of the sebaceous glands is adipogenesis, the manufactured fat having a special composition of its own; under certain conditions, *e.g.* in animals after hyperalimentation, they take on the function of adipopexy, in which case the fat taken up directly from the blood may have the characters of that ingested. Presumably, therefore, the composition of the sebum may be altered by an excessive intake of fat or fat-forming foods, or by the ingestion of special forms of fat. Pig fat, cheese, and chocolate in some cases of acne invariably aggravate the eruption; milk fat also, which is particularly liable to bacterial decomposition, when taken in excess appears to increase a tendency to seborrhœa. Alcoholic liquors have a similar effect, partly, no doubt, because alcohol is a a fat-sparer and a vasodilator, and partly owing to the sugar they contain. It is clear, however, that the question of diet must be considered in relationship to the amount of exercise taken, and the mode of life (see section on treatment).

Apart from these factors, it should be noted that the secretion of sebum is, like that of the sweat, saliva, and tears, under the control of the autonomic nervous system. In encephalitis lethargica, and in other cases manifesting the Parkinsonian syndrome, excessive secretion of sebum, giving rise to the "seborrhœic facies," usually associated with sialorrhœa, may be a striking symptom, and would appear to depend upon lesions in the neighbourhood of the third ventricle involving vegetative nerve centres (**15**).

The Seborrhœic Triad of Organism. The three organisms, to the active growth of which in the skin the seborrhœic state predisposes, are, as has been said, the pityrosporon of Malassez, the acne bacillus, and the *Staphylococcus albus*. *The pityrosporon* (sometimes called the "spore of Malassez, and, erroneously, the "bottle-bacillus") is now generally accepted as the cause of simple dandruff, or *pityriasis simplex*, in the horny scales of which it is found in a state of active growth. It is a pleomorphic organism, and simple spherical or sausage-shaped forms are seen mingled with the commoner and characteristic flask-shaped variety. It was pointed out (**16**) that, whereas this organism is found alone in pityriasis simplex, growing between the superficial layers of the stratum corneum exactly as does the *Microsporon furfur* in pityriasis or tinea versicolor, in pityriasis steatoides, and in the group of eruptions variously known as seborrhœic dermatitis or eczema, seborrhœides, *eczématides* (Darier), *S. albus* is also seen with it in a state of active multiplication. It was therefore held that these conditions were due to a symbiotic infection with both organisms. Attempts to obtain the pityrosporon on artificial media in pure culture have generally failed, but Garner has claimed to have succeeded, using maltose agar and acid glycerine agar. MacLeod and Dowling (**17**) determined the sugar-reactions of his cultures, and performed inoculation experiments with it. They conclude that the organism is one of the fungi imperfecti, belongs to the class *Oösporaceæ*, and is nearly related to the monilia group. By inoculation of cultures they were able to produce typical figurate seborrhœic dermatitis, indistinguishable both in evolution and appearances from the natural eruption. Inoculation on normal non-seborrhœic skins produced a group of follicular papules within twenty-four hours, which lasted about ten days and then disappeared; in some seborrhœic subjects, particularly those with active seborrhœic dermatitis present, a more acute reaction developed, and a widespread figurate patch sometimes resulted. They also found that intradermal injections of the organism in persons with seborrhœic dermatitis produced both local and focal reactions. They therefore regard seborrhœic dermatitis as being primarily due to the pityrosporon, and the *S. albus* as a secondary invader. The fact remains, however, that the latter is always found in a state of active growth in this condition.

The acne bacillus (or microbacillus of seborrhœa) in seborrhœic persons flourishes in the infundibulum or upper third of the pilosebaceous follicle, and if the so-called "seborrhœic cocoon" be expressed from the follicle, squeezed flat on a slide, and suitably stained, myriads of acne bacilli will be seen obviously in a state of active growth. As a result of infection of the follicles with this organism there may arise in certain situations the polymorphic lesions of the common acne juvenilis—comedones or "blackheads," acne papules, pustules, etc. Sabouraud maintains that the true acne pustule is due to the acne bacillus, and not to a secondary invasion with *S. albus*, although staphylococcal lesions may be and often are present in acne. This view has been recently confirmed by work on the staphylococci in acne vulgaris (**18**).

The characters and *rôle* of *S. albus* have already been referred to (p. 841).

It should be noted that each of these three organisms has its own localisation or site of election in the skin, and each, when it takes on active growth, excites a special type of cell-response to invasion. Thus the pityrosporon, like a ringworm fungus, *e.g.* the microsporon furfur, grows in between the layers of the stratum corneum, which hypertrophies, and is shed in visible flakes or pellicules ("dandruff" or "scurf"), such exfoliation, no doubt, being an attempt to cast off the parasite; on the scalp and other hairy parts, the pityrosporon, like certain ringworm fungi, may excite little or no inflammatory response in the cutis, but on the glabrous skin both it and a ringworm fungus provoke definite clinical and histological signs of inflammation. The acne bacillus flourishes in myriads in the infundibular portion of the pilosebaceous follicles, and there may, like the pityrosporon, provoke both a non-inflammatory and inflammatory defence-reaction—viz., the comedo and the acne pustule. The comedo may be regarded as a cyst, formed of horny cells, and designed to enclose the mass of acne bacilli like a foreign body. The true acne pustule represents the inflammatory defence-reaction to the bacillus, although it has commonly been held to result from secondary infection with a *Staphylococcus albus*. Sabouraud has clearly shown that the acne bacillus alone is responsible, and he points out that the leucocytic reaction is denser than in staphylococcal infection, producing thick caseous pus, unlike the fluid creamy "laudable pus" of the latter. The site of election for staphylococci is the ostium of the pilosebaceous-follicle, and the migration of polymorphonuclear leucocytes is the normal defence-reaction in response to staphylococcal infection.

Symptoms. *Cutaneous.* The skin of a person in perfect health, who lives an athletic outdoor life, is smooth, supple and clear. The horny layer is thin and translucent, and is cast off in invisible flakes, the pilosebaceous orifices are hardly visible, and the secretion of sebum and sweat (except in heat, strong sunlight and after exercise) is imperceptible; the hair is sleek and not greasy, and there is no evidence whatever in the skin of active bacterial growth.

In the seborrhœic person, on the other hand, the skin as a whole appears thickened, coarse and dirty, particularly in dark-complexioned persons; the horny layer is improperly formed, and hypertrophied; the pilosebaceous orifices are enlarged and patulous, and either exude visible droplets of oily sebum or are filled with solid plugs—the so-called seborrhœic cocoons—containing countless acne bacilli; there is often visible hyperidrosis in certain situations; the scalp after puberty is greasy, covered with adherent dandruff, which swarms with the pityrosporon and the *S. albus*, and the hair dank and lifeless. To this picture must be added the infective complications—the comedones, pustules, and nodules of acne, the various forms of seborrhœic dermatitis, the superficial pustules due to the *S. albus*, the deeper folliculitis of sycosis and boils due to the *S. aureus*. In middle life rosacea, which sooner or later becomes complicated by a superadded infection of the flushed area with the seborrhœic organisms, is common. It should be noted, however, that clinically can be recognised two types of seborrhœic person. The one, usually fair-complexioned, is flushed, robust,

active, and in later life often plethoric; the other, usually dark, is pallid, coarse-skinned, pigmented and indolent. In the latter a history of tuberculosis of glands, bone, or peritoneum in childhood is often obtained, and many develop phthisis in adult life; it is in them that the deep nodular form of acne, with deep and often cheloidal scarring, is most commonly seen.

Mucous Membranes. In the first type of seborrhœic the vermilion borders of the lips are usually bright red, and covered with a yellowish superficial crust; the tongue is firm and red, and the papillæ prominent; gingivitis, representing doubtless the same lowered resistance to infection that characterises the skin, is common, and the earlier the onset of the seborrhœic state, the sooner does it occur. In the other type of seborrhœic person, the lips may be pale or bluish, the tongue pale and indented, and its papillæ hardly visible. Accompanying the gingivitis there is often a marked tendency to dental caries.

Chronic nasopharyngeal catarrh, with frequent exacerbations, is almost invariably present in severe cases of the seborrhœic state. It was a striking symptom among those met with in France during the war. In chronic seborrhœics, with symptoms dating from childhood, this catarrh is usually associated with the adenoid facies and marked hypertrophy of the lymphoid tissue; on the other hand, it may develop as an entirely new symptom, in conjunction with infection of the skin, in those who became seborrhœic as a result of adopting a sedentary existence in middle life.

The Digestive System. True flatulence, distinct from aerophagy, is a common symptom, due apparently to fermentation of carbohydrates, since it is usually relieved by exclusion of soft carbohydrate foods from the dietary.

The Urine in the seborrhœic state has been studied by several observers. The alkaline tolerance is, as a rule, markedly raised, so that very large doses of alkali may be required to render the urine alkaline. In some cases, usually of long standing, the ammonia-ratio and acid-ratio are high. Observations on the hydrogen ion concentration of the urine in the seborrhœic state have shown that the *p*H value in normal controls (from which seborrhœic persons were carefully excluded) varied from 6·4 to 6·8, whereas in patients with seborrhœic manifestations it varied from 4·8 to 5·8. Striking benefit accrues in these cases from the administration of alkali in sufficient quantity to restore the *p*H value to normal. A point of great interest is that the urine of a patient, even with severe seborrhœic manifestations, may be found to be slightly acid or even neutral, but that, when alkali is administered, its acidity increases progressively up to a certain point before becoming alkaline.

Treatment. The treatment of seborrhœic patients naturally varies according to the individual case, but certain general principles may be outlined. The *diet* must be regulated according to the climatic conditions and the amount of physical exercise taken. Starchy foods must be taken in a form that requires thorough mastication, and ordinary white bread, milk puddings, and other soft farinaceous foods should be forbidden. Concentrated sweetstuffs, particularly cane-sugar and chocolate, pig-fat, excess of milk-fat, alcoholic liquors, and in some cases cheese, usually aggravate seborrhœic conditions, particularly in those living a sedentary life. Raw and cooked fruits and vegetables, a moderate amount of meat, fish, eggs, milk and butter, together with crisp farinaceous foods, should form the staple dietary.

Clothing and Exercise. Excessive clothing is probably an important factor predisposing to the seborrhœic state, since it robs the skin of its natural stimulation by cool air, which activates the thyroid-adrenal-sympathetic system; it also undoubtedly favours the growth of the seborrhœic organisms. The effect of total air and sun baths upon seborrhœic skins is very striking. The patient should be gradually trained to accustom himself to light porous clothing, and should, if possible, take vigorous outdoor exercise regularly in running costume.

Bathing. A daily hot bath, followed by cold douching, is advisable, and in severe cases hot sulphur baths taken at bedtime, at first every night, and later twice a week, may be ordered. When Spa treatment is available, alternate hot and cold douching ("Scotch douche") is of great value.

Alkalies. In those with increased urinary acidity an initial course of alkaline saline aperients should be given, and later a single early morning dose of alkali in a tumbler of water taken as a routine.

PITYRIASIS SIMPLEX

The term *pityriasis* has, unfortunately, been applied to several distinct affections of the skin. Derived from πίτυρον, bran, it merely signifies scaliness. *Pityriasis versicolor* is due to infection of the horny layer with a fungus, the *microsporon furfur*. *P. rosea* is a specific disease due to infection with an organism hitherto undiscovered; *P. rubra pilaris* is also a specific entity of unknown causation, and *P. rubra* is an erythrodermia.

Pityriasis simplex is a non-inflammatory, desquamative affection of the horny layer, commonly known as *dandruff* or *scurf*. In its simple form it affects chiefly the hairy regions, particularly the scalp (*P. capitis*), but, as has been pointed out, the causal organism is concerned with staphylococci in the production of the inflammatory condition known as seborrhœic dermatitis (*P. circinata*). The earliest stages of the affection are seen in young children, on whose scalps it begins, usually on the vertex, as little patches of dry scurf around the hair follicles. It gradually spreads as circular scaly areas, not unlike ringworm, until it becomes diffuse. From about the age of puberty onwards, when there is likely to be concomitant seborrhœa, the scales become greasy.

The condition is due to infection of the horny layer with the pityrosporon, which has already been described. There is no doubt that infection with this organism is spread by direct and indirect contact. When it occurs in babies, in whom pityriasis simplex of the scalp may be the starting point of one form of "infantile eczema," examination of the scalp of the mother or nurse will usually reveal a heavy infection, and the indiscriminate interchange of hair-brushes is doubtless a potent cause of indirect spread.

Treatment. The general treatment of the seborrhœic state (*q.v.*) is indicated, as it is extremely difficult to eradicate the infection by local measures alone. The scalp should be washed frequently, once a week in women, twice or oftener in men. At the beginning of treatment, soap spirit (spiritus saponatus, B.P.C.), or ether soap may be employed, but they should not be persisted with. Certain proprietary shampoos, containing tar, are the best and pleasantest for regular use. In mild cases the thorough daily application of a hair-lotion is sufficient, *e.g.* ℞. Resorcin, Acidi salicylici āā gr. x; Hydrarg. perchloridi gr. 1/6; Ol. lavand. m. ii (Ol. ricini q.s.); Acetoni dm. i; Spirit vini meth. indus. ad oz. i, the resorcin being omitted in persons with grey or fair hair. The lotion may be shaken on to the scalp through a sprinkler-cork and then well brushed in, or applied with a spray. In severe cases, particularly if there is much seborrhœa, the additional use of a pomade is essential, *e.g.* ℞ Sulphur præcip., Acidi salicylici āā gr. xx; Vaselin alb. dm. ii; Ol. cocois nuciferæ ad oz. i; Perfume q.s.; this should be thoroughly rubbed into the scalp on the nights previous to shampooing, and the above lotion (without the perchloride of mercury) used daily. It cannot be too strongly emphasised that the popular idea that the scalp should be washed only occasionally is erroneous, and is responsible very largely for the prevalence of dandruff. Provided that strongly alkaline and spirituous shampoos (which render the hair brittle, and in women, combined with the deleterious action of dyes and waving, produce the condition known as trichorrexis nodosa) are not employed, the head may be washed as often as desired.

COMEDO

(*Blackhead*)

The *comedo* is one of the lesions of acne vulgaris (*q.v.*). It is a small, horny, cocoon-like mass, embedded in the mouth of a pilo-sebaceous follicle, and consists of concentric sheaths of horny cells, surrounding a partitioned cavity, in which lie masses of the acne bacillus, inspissated sebum, and the *débris* of a dead lanugo hair. The summit of the comedo is coloured dark-brown or black, not owing to adherent dirt, but to an oxidation product of keratin (ultra-marine); the lower part of the comedo is of a yellow colour. Sometimes "double" or "multiple comedones" are seen, *i.e.* two or more closely approximated comedones communicating at the base. The comedo is a retention cyst, and is due to hyperkeratosis at the mouth of a follicle, provoked doubtless by the irritation, mechanical or toxic, of the acne bacilli growing in the infundibulum. *The acne bacillus may, therefore, be considered as the cause of the comedo,* and the essential predisposing factor to the formation of true comedones is seborrhœa, which favours the active growth of this bacillus.

Apart, however, from the comedones of ordinary acne, various external irritants are capable of inducing comedo-formation, which may be followed by the development of pustules. The commonest of these is camphorated oil, which gives rise to the so-called "grouped comedo" of infants and children, whose chests have been assiduously rubbed for bronchitis. The suppuration in camphorated oil acne may be severe and lead to extensive scarring. Turpentine liniment sometimes produces the same condition, and in adults various tars, particularly oil of cade, and chlorine vapours may respectively be responsible ("tar-acne," "chlor-acne").

The **Treatment** of comedo is dealt with under Acne vulgaris.

ACNE VULGARIS

The term *acne* (according to Littré, altered by a copyist from ἀκμή, a point) has been applied, since Willan and Bateman first introduced it, to a number of distinct eruptions in which the pilo-sebaceous follicles are affected. It is now less widely used, being as a rule reserved, apart from *acne necrotica seu varioliformis,* for the common disease *acne vulgaris*—polymorphic or juvenile acne.

The epithet "polymorphic" indicates that in acne there is not a single characteristic lesion, but rather a number of different forms of eruptive elements, some of which predominate in one case, others in another. The essential predisposing factor in the development of acne is seborrhœa, and the earliest lesion is usually the *comedo* (*q.v.*), a retention cyst, the formation of which is provoked by the active growth of the *acne bacillus* in the pilo-sebaceous follicle. In some cases comedones in large numbers are present alone—*acne punctata;* in others reddish papules, usually formed around comedones, occur intermingled with simple comedones—*acne papulosa;* in others, again, the infection is more acute, the papules are bright red and acuminate, suppuration takes place at their summits, and the pus produced either exudes or dries up to form crusts, under which the papule involutes, leaving a minute scar—*acne pustulosa;* in the more severe cases large, indurated, deep-seated nodules are seen, some of which undergo a slow transformation into indolent pustules, from which a quantity of pus may be evacuated, and which on healing leave scars of considerable size and depth—*acne indurata.* Sometimes bluish-red, fluctuating abscesses are formed, which may involve the hypoderm. The so-called "butyric cysts" result from degeneration of large comedones, and contain a semi-fluid, cheesy substance, having a peculiarly nauseous smell. Mucoid cysts, due to cystic degeneration of long obstructed sebaceous glands, are more rarely seen.

As has been indicated, these different types of lesions coexist in the same patient, and all degrees of severity are met with, from a few comedones and occasional papulo-pustules to the worst form of acne indurata with large, painful nodules and abscesses, and extensive deep scarring. The distribution of acne is more or less constant, the eruption occurring almost exclusively on the face and back, less commonly on the front of the chest and over the deltoids; on the back, it involves chiefly the scapular regions and only rarely descends below the waist line.

Ætiology. The various lesions which together constitute acne vulgaris occur exclusively in seborrhœic subjects, in whose sebaceous follicles the acne bacillus grows in profusion. The disease usually first makes its appearance at about the age of puberty, when there is a great increase in the development and activity of the sebaceous glands. It may, however, occur in mild form several years before puberty. It reaches its acme of severity, as a rule, between the ages of sixteen and twenty-five, and then tends to decline, being succeeded by other manifestations of the seborrhœic state, such as calvities, furunculosis, sycosis, and seborrhœic dermatitis. In some cases, however, it may persist till late in middle life, and it is by no means uncommon to find comedones and acne papulo-pustules even in the aged. Apart from the influence of sexual maturity, the predisposing causes of acne are those of the seborrhœic state, and of particular importance are an *unsuitable dietary*, above all an excess of sweet and starchy foods and certain forms of fat (as Kenneth Wills has emphasised, pig-fat is especially injurious), *lack of fresh air, sunshine and exercise*, and *chronic constipation* with intestinal toxæmia. The worst examples of the disease are usually seen in thick-skinned persons of the scrofulous type, with the symptoms and signs of intestinal autointoxication. Many of such patients have suffered from tuberculosis of glands, peritoneum, bones or joints, and it is in these that deep scarring is most likely to occur.

Treatment. *Internal.* The internal treatment of acne vulgaris must depend on the symptoms presented by each individual patient. Thus in some cases there is anæmia, hypochlorhydria, chronic constipation, and an excess of indican in the urine; for these, morning saline aperients, pills containing iron and aloes, and dilute hydrochloric acid in doses of 20 to 40 minims after meals are indicated, In full-blooded patients, on the other hand, an alkaline mixture containing sodium bicarbonate, potassium citrate, and magnesia taken before meals is often beneficial. As regards the diet, it is usually important to restrict the amount of carbohydrate and fat, and sweets, cakes, pastries, puddings, jam and marmalade, pig-fat, chocolate, and cheese should be forbidden altogether; plenty of fresh fruit and green vegetables, and lean meat, fish, and poultry should be taken. Avoidance of excess of tea and coffee is also essential, and, whereas beer and stout in moderation are probably beneficial, wines and spirits certainly do harm. Vaccine therapy in acne is not so successful as in furunculosis, but may be of value in the pustular form. An active preparation of yeast, calcium sulphide gr. i, t.d.s., p.c., or collosol sulphur dm. ii, t.d.s., p.c., ex aqua, are worthy of trial. In certain cases with thick, sluggish skins and a feeble peripheral circulation thyroid is of very great value, and in females with irregular or scanty menstruation an active ovarian preparation should be tried.

Local. The object of the local treatment of acne vulgaris is to render the skin dry by reducing the activity of the sebaceous glands. If this be done, the micro-organisms responsible for the lesions will tend to lose their virulence and to die out. By far the most effectual method of accomplishing this object is by means of the X-rays, given preferably in fractional doses. Their employment, of course, requires great care, as over-dosage will lead to permanent telangiectatic atrophy of the skin. Next to the use of X-rays the quickest method is to produce exfoliation of the skin of the affected parts by means of strong pastes containing resorcin and sulphur, *e.g.* ℞ Resorcin, Camphor, āā 10·0, Sapo. moll. virid. 15·0, Sulph. præcip. 30·0, Cretæ præpt. 5·0, Paraff. moll. flav. 10·0, Adipis. lan.

anhyd. 20·0. The paste should be applied at night-time only, unless the patient can remain indoors; after a few days the skin will become red and sore, and will begin to peel; a soothing lotion or cream may then be substituted until exfoliation is complete, when the procedure may be repeated. By the persistent use of this method of exfoliation excellent results are obtainable even in the worst cases, and it is of great value in the treatment of severe acne of the back. Milder measures consist in applying lotions and powders or a weaker paste containing sulphur, resorcin, salicylic acid, or mercury. One of the following lotions may be applied thoroughly twice daily, after washing with a soap containing sulphur and salicylic acid (2 to 10 per cent. of each) and expressing the comedones and pustules: (1) ℞ Potass. sulphidi ʒj, Zinc sulph. ʒj, Aq. rosæ ad ʒiv; (2) ℞ Resorcin gr. x to xx, Boracis purif. gr. x, Zinc oxid., Calaminæ, āā gr. xv, Glycerini ℥xx, Eau de Cologne ℥xxx, Aq. calcis ad ʒj. The thorough application of a medicated soap containing sulphur and salicylic acid, the lather being allowed to remain on for several minutes, may alone be sufficient to cure mild cases. A suitable face powder consists of equal parts of talc and zinc oxide containing from 2 to 5 per cent. of sulphur. For the successful treatment of acne it is essential that the rules for diet laid down should be rigorously adhered to, that the patient should have plenty of daily exercise out of doors, that constipation should be avoided, and that the skin be kept dry and comedones and pustules systematically evacuated. Seborrhœa and pityriasis of the scalp, which almost constantly accompany acne, must be treated by frequent shampooing and the use of a hair lotion containing hydrarg. perchlor., salicylic acid and (except in fair- or grey-haired persons) resorcin.

Heliotherapy or total ultra-violet light baths give more permanent results, if persisted with in suitable dosage, than any other form of local treatment.

SEBORRHŒIC DERMATITIS

The term "seborrhœic dermatitis" includes a group of eruptions which have received a variety of names from different observers; for example, *lichen circumscriptus* (Willan and Bateman), *lichen annulatus serpiginosus* (Erasmus Wilson), *pityriasis circinata* (Bazin), *seborrhœa corporis* (Duhring), *eczema seborrhœicum* (Unna), seborrhœides (Audry, Brocq), "flannel-rash," etc. Darier has proposed for them the term "*eczématides*," thus indicating their close clinical and histological relationship to eczema.

It is possible to recognise three main types of seborrhœic dermatitis (**19**): (1) The figurate type (*pityriasis circinata*, figurate medio-thoracic dermatosis of Brocq, *seborrhœa corporis* of Duhring, *pityriasis steatoides* of Sabouraud, "flannel-rash"); (2) the pityriasiform type; (3) the psoriasiform type. But it must be admitted that these distinctions are artificial, since they depend partly on the particular site involved, and they may all co-exist in the same patient.

1. *The Figurate Type.* This is seen most typically in the presternal and interscapular regions, whence it may spread laterally, and on the scalp, from which it may extend to the forehead (*corona seborrhœica*), the temples, and behind the ears. Its evolution can best be studied on the trunk. It will be observed that the inflammatory process begins at the mouths of the pilo-sebaceous follicles, so that the eruption is primarily follicular; the interfollicular areas are then involved, with the formation of petaloid patches, which by coalescence become figurate. These patches are of a pinkish or bright red colour at the spreading margins, which are slightly raised, yellowish or fawn-coloured in the centre. They are covered with greasy scales. The eruption may cause considerable itching, or may pass unnoticed and be present for years. It is very common in seborrhœic persons, particularly in those who wear flannel next the skin or excessive underclothing, and often co-exists with other seborrhœic eruptions, such as acne rosacea, sycosis, furunculosis, etc.

2. *The Pityriasiform Type.* This type represents a more diffuse form of seborrhœic inflammation of the skin. It occurs as oval, round, or irregular patches, slightly scaly, dry or greasy, according to their situation, and pink or pinkish-yellow in colour. They occur on and around the scalp, the neck, the upper portion of the trunk, and in the joint flexures, such as the axillæ, antecubital fossæ, popliteal spaces, and groins, and in the inter-natal cleft. They may also be present on the extensor surfaces of the limbs in persons with dry skins, the vulnerability of the horny layer doubtless favouring infection. Sometimes acute outbreaks of this form of seborrhœic dermatitis occur on the trunk, and the eruption may closely resemble pityriasis rosea, but the presence of the " bottle bacillus " in a state of active growth in the scales of the former suffices to distinguish between them. Secondary eczematisation may take place, particularly on the scalp, ears, neck, and joint-flexures, so that the eruption becomes red, vesicular and moist from serous exudation.

3. *The Psoriasiform Type.* In this form the inflammation is deeper and more intense than in the preceding varieties. The patches are more infiltrated, of a darker red, and covered with thicker more or less adherent scales. They may resemble psoriasis very closely; in fact, in some cases it may be impossible to make a differential diagnosis without a careful microscopical examination. The eruption may occur as a single chronic patch, or may extend widely and form confluent areas of considerable size. Itching is, as a rule, a prominent symptom, and may be intense; from constant scratching and rubbing lichenification may result.

Morbid Anatomy. Although the different types of seborrhœic dermatitis vary considerably in their histological appearances, the essential lesions are much the same, and consist of small areas of *spongiosis*, *parakeratosis*, *crusts* formed by dried serum enclosing leucocytes, *acanthosis*, and œdema with perivascular cell-infiltration of the dermis. The histological changes, therefore, are of the eczematoid type, but the spongiosis is less marked, and both it and the parakeratosis are more discrete than in true eczema. The psoriasiform variety of seborrhœic dermatitis simulates psoriasis histologically as well as clinically, but researches (**20**) have shown that the histological differences are such that the two can be distinguished with certainty. The more important are that in the former the superficial layers consist not only of nucleated horny cells, but also of the crusts above referred to; the parakeratosis is often discontinuous; in the papillary body of the epidermis are found small areas of spongiosis, enclosing mononuclear leucocytes, and not polymorphonuclears as in psoriasis. It is these areas that become the crusts when they reach the stratum corneum. By special staining methods it can also be demonstrated that, whereas the lesions of psoriasis are remarkably amicrobial, those of seborrhœic dermatitis reveal very active microbial growth.

Ætiology. Seborrhœic dermatitis may be regarded as a diffuse catarrh of the skin due to microbial infection—in other words, an infective epidermodermatitis. It is characterised by the presence in the lesions of the pityrosporon and staphylococci in a state of active growth. It thus differs essentially from psoriasis, and from pityriasis rosea, in which the pityrosporon is absent. Dowling considers that all forms of seborrhœic dermatitis are primarily due to infection with the pityrosporon, which may be true, but it is probable that the differences that characterise the clinical varieties of the eruption depend chiefly on the type and virulence of the infecting staphylococcus. The seborrhœic state is the principal predisposing factor to the active growth of these organisms, and, as has been suggested, it is probably the alteration in the composition of the fat of the horny layer and sebaceous glands that favour their growth; for this reason the distribution of seborrhœic dermatitis usually corresponds to the areas in which the sebaceous glands are largest and most active. Needless to say, lack of personal cleanliness and the wearing of excessive clothing are additional predisposing causes.

Treatment. The internal treatment is that of the seborrhœic state, and the local measures to be adopted will depend on the type and severity of the inflammatory process. The figurate variety, that is seen so frequently on the back and chest, is rapidly cured by applications of sulphur, *e.g.* ℞ Sulphur præcip. gr. x to xx, Resorcin gr. x, Past. Zinci Comp. B.P.C. ad oz. i. For the diffuse pityriasiform patches, which occur chiefly in the joint-flexures, behind the ears, and on the neck, sulphur is apt to be too irritating, and ichthyol and tar in an ointment or paste are more suitable, *e.g.* ℞ Ichthyol gr. v, Liq. Picis Carbonis gr. xxx to dm. i, Past. Zinci Comp. B.P.C. ad oz. i. In the psoriasiform type more active preparations are necessary, such as oil of cade, the crude coal-tar paste recommended for chronic patches of eczema, and even chrysarobin. The X-rays are of great value, but the dosage must be carefully controlled.

In all cases of seborrhœic dermatitis it is essential to treat the scalp, which is so often the original source of infection. In men it should be shampooed with a tar soap twice or thrice a week, and on the nights before shampooing the following pomade should be well rubbed in: ℞ Sulphur præcip. gr. xv to xxx, Acidi Salicylici gr. x to xx, Vaselin alb. dm. ii, Ol. cocois nuciferæ ad oz. i, Perfume q.s. Every morning the following lotion may be used: ℞ Resorcin gr. x (to be omitted in persons with fair or grey hair), Acidi Salicylici gr. x, Hydrarg. perchloridi gr. $\frac{1}{6}$, Ol. Lavandulæ m. ii, Ol. ricini m. x, Spt. vini meth. indust. ad oz. i. In women the hair should be shampooed once or twice a week, and the pomade rubbed in the previous evening; the above lotion should be used daily, the castor oil being omitted from the prescription; but care should be taken to avoid irritation of the face and neck by the sulphur in the pomade, and a bathing-cap should be worn during the nights on which it is applied.

In cases of very acute seborrhœic dermatitis, or when eczematisation has occurred, soothing applications should be used, such as calamine liniment or an ichthyol cream, *e.g.* ℞ Ichthyol gr. v, Ol. Olivæ, Zinci Oxidi āā oz. ss. Adip. lanæ anhyd. dm. i, Aq. Calcis dm. iii, and olive oil should be employed to clean the affected parts morning and evening.

Bacterial Diseases. II. Bacillary.

Comedo	*B. acnes* (p. 860)
Leprosy	*B. leprœ* (p. 1016)
Glanders	*B. mallei* (p. 91)
Anthrax	*B. anthracis* (p. 92)
Diphtheria	*B. diphtheriæ* (p. 63)
Tuberculosis	*B. tuberculosis* (p. 83)
Soft sore	Strepto-bacillus of Ducrey-Unna (p. 875)
Rhinoscleroma	Bacillus of Frisch (p. 877)
Erysipeloid	Bacillus of swine erysipelas (p. 877)

TUBERCULOSIS

Active cutaneous tuberculosis of the skin may be classified as follows:—(1) Tuberculous chancre; (2) Tuberculous ulcer; (3) Tuberculous gumma; (4) Lupus verrucosus; (5) Lupus vulgaris. The two last and the tuberculides and sarcoids will be described.

LUPUS VULGARIS

This, the most familiar form of tuberculosis of the skin, is happily becoming much less common, and it is comparatively rare now to see the terrible mutilations that the disease is capable of producing. The primary lesion of lupus is a characteristic miliary nodule, embedded in the skin, and representing histologically

a minute infective granuloma ; it may conveniently be called a *lupoma*. In size it ranges from that of a pin's head to that of a large pea ; in colour it varies from yellowish- to brownish-red, with sometimes a bluish tinge ; it may form a raised papule or nodule on the surface of the skin, or may not project at all ; it has a translucent look and is soft in consistency, being easily pierced by a sharpened match. A patch of lupus may begin by the appearance of a single nodule of this kind, which gradually enlarges, while near it others are formed, or by two, three or more arising simultaneously. The patch spreads by the enlargement of individual nodules and the formation of new ones, and there is a tendency for these isolated lesions gradually to coalesce. Under vitropressure lupus nodules present a very characteristic appearance. They look, as Hutchinson aptly said, like specks of apple-jelly embedded in the skin, and their translucency is due to the local disappearance of the elastic and connective-tissue network.

If left untreated a patch of lupus tends to undergo one of two changes. In some cases spontaneous cicatrisation takes place in the centre, while the patch tends slowly to extend at the borders by the formation of fresh nodules. But in the central, soft, white scar a few nodules persist or reappear, and this characteristic feature is of importance in the differential diagnosis between lupus and the serpiginous syphilides. In other cases the overlying epidermis is destroyed, so that there is ulceration with secondary pyogenic infection and the formation of impetiginous crusts.

There is very considerable variety in the clinical appearances of the disease according to the predominance of one or other of the above processes. Thus in some cases the nodules are small and superficial, and the patch is red, scaly, and projects hardly or not at all above the level of the surrounding skin. This type (*L. erythematoides*) is often mistaken for lupus erythematosus ; on vitropressure the characteristic apple-jelly nodules may be seen, but sometimes are only recognisable on microscopical examination. In other cases the nodules are large, confluent and raised to form a tumour (*L. tumidus* or *hypertrophicus*). Sometimes, probably as the result of secondary pyogenic infection, an ulcerating patch develops papillomatous vegetations, soft at first and later becoming warty, thus resembling lupus verrucosus (*q.v.*) (*L. papillomatosus*). Patches which ulcerate at the margin, while undergoing spontaneous cicatrisation in the centre, imitate ulcerating syphilides (*L. serpiginosus*). Formerly the non-ulcerating forms of lupus were termed *L. non-exedens*, the ulcerating *L. exedens*, but this distinction is somewhat artificial. The most malignant type of ulcerating lupus—*L. vorax seu phagedœnicus*—is fortunately rare ; it may rapidly produce the most frightful destruction and deformity.

The course of lupus is essentially chronic and its spread insidious. Although spontaneous involution with scarring commonly occurs, the disease extends peripherally, fresh nodules arise in the scarred area, and, except in *lupus disseminatus*, it is exceedingly rare for a natural cure to result.

Distribution. Lupus affects both the skin and mucous membranes. It may spread from the skin to the mucous membranes, but, as Audry insists, it is probable that the reverse is true far more commonly than was originally supposed. On the skin, the face is the commonest site (78 per cent. according to Sequeira). Emlyn Jones found that the disease started about the nose in 28 per cent., and in other parts of the face, including the auricles, in 48·4 per cent. In 1·8 per cent. the lips, in over 13 per cent. the neck, and in 8·5 per cent. the trunk or extremities were the primary sites. It is rarely seen on the scalp, forehead, upper eyelids, genitals, axillæ, or on the palms and soles.

The *mucous membranes* are affected in a large percentage of cases (43·25 per cent. among Sequeira's cases, 80 per cent. in Christiansen's series at the Finsen Institute). The nose, mouth, palate, pharynx, larynx, tongue, nasal duct, lachrymal sac, conjunctiva, and middle ear may be involved. The nose is by far the commonest site, and is frequently the primary source of involvement of

the skin. Sometimes the infection spreads up the nasal duct to the lower eyelid and conjunctiva, or from a primary tuberculous lesion of the conjunctiva it may spread downwards and invade the nasal mucous membrane, and thence the skin. On the palate, pharynx, and in the mouth lupus appears as a pinkish-red, mamillated patch, with here and there small ulcers, which may extend until the whole area is ulcerated and crusted. On the gums it produces swollen, red, fleshy granulations, and the teeth often become loose. On the tongue, a rare site, a papillomatous patch is the rule, but ulceration may occur.

Ætiology. The disease is due to the actual growth in the skin or m[illegible]us membrane of the tubercle bacillus, which may be either of a human or b[illegible] strain, the proportion varying in different countries. From the researc[illegible] Griffith and others it is evident that in most cases the strain, whether hum[illegible] bovine, is of low virulence. Although lupus may begin at any age, in more [illegible] half the cases it appears before the tenth, and in over 80 per cent. before twentieth year. It is more than twice as common in females than males, [illegible] occurs far more in Northern Europe than in the South, partly, no doubt, bec[illegible] of the lack of sunlight, and is comparatively rare in the Colonies, the tro[illegible] and in America. It affects, as a rule, scrofulous persons, who have been infec[illegible] with tubercle in early life, and a strong family history of tuberculosis is often obtainable. It is almost invariably associated with tubercular adenitis, and sometimes with tuberculosis of bones, joints, or the peritoneum. As Besnier pointed out, phthisical persons do not develop lupus, whereas patients with lupus frequently become phthisical.

As regards the actual mode of infection of the skin, this may occur (1) directly from without; (2) by extension from deeper tubercular foci or from mucous membranes; (3) through the blood-stream. The first method is probably common, and doubtless accounts for the frequency of the disease in or around the nose, the organism being carried by dust or by the fingers; cases in which it has started in vaccination or tattoo marks, or after piercing the ears for ear-rings, have been recorded.

The second method is instanced by the occurrence of lupus in the skin over tuberculous glands, which have broken down or been excised, and by the spread of infection from the nasal mucous membrane, or *viâ* the nasal duct from the conjunctiva. The third method accounts for the multiple disseminated patches of lupus that appear most commonly after measles or whooping-cough, and it is probable that infection of the skin through the blood-stream is commoner than is usually believed.

Morbid Anatomy. The epidermis is usually atrophied, and beneath lies a mass of tubercular tissue, consisting of lymphocytes, epithelioid and plasma-cells, and here and there typical giant cell systems. There is destruction of the elastic and connective tissue, and of the blood vessels, and the newly-formed tissue undergoes degeneration without actual caseation. The histological picture, of course, varies according to the type of the disease, and the presence or absence of ulceration and secondary infection. Tubercle bacilli may be demonstrated, but, as a rule, only after prolonged search through serial sections.

Diagnosis. The conditions for which lupus is likely to be mistaken are tertiary syphilis, rodent ulcer, nodular leprosy, lupoid sycosis, certain forms of sarcoid, and lupus erythematosus; it is not uncommonly from carelessness confused with impetigo, impetiginised eczema and psoriasis.

From a tertiary syphilide it may be distinguished by the age of onset, by the length of history (since, with the exception of lupus vorax, lupus takes many years to produce lesions of the same extent as a syphilide of a few weeks or months standing), by the soft consistency of its nodules and their apple-jelly appearance on vitropressure, and by the presence of nodules in the central scar. Necrosis of bone is never caused by lupus. The Wassermann reaction should always be done, even if the diagnosis of lupus is certain, since there appear to be mixed cases—

usually lupus in a patient with congenital syphilis—in which antisyphilitic treatment leads to striking improvement.

From lupus erythematosus the diagnosis may be difficult in certain cases. The chief points of distinction are the symmetrical distribution of lupus erythematosus (although by gradual spread lupus vulgaris may produce a bilaterally symmetrical patch over the nose and cheeks); the involvement of the scalp, edges of the ears, and fingers; the absence of ulceration and non-involvement of cartilage; and the different appearances on vitropressure.

. small nodular sarcoid may imitate lupus very closely, but the nodules
rder, the histology is characteristic, and guinea-pig inoculations are always
ve.
e age of onset, the hard, pearly, nodular edge, and the clean-cut ulceration
nguish rodent ulcer from lupus.

omplications. Apart from the disfigurement and mutilation that the
se may cause, the chief complications that occur are erysipelas and squamous-
d carcinoma. An attack of erysipelas may have a beneficial and even cura-
effect, as in the cases described by Hallopeau and Sequeira. Although carcinoma is a rare complication of lupus, particularly in women, its incidence has greatly increased since the introduction of the X-rays, the long-continued application of which is entirely unjustifiable in this disease.

Treatment. It must be remembered that the vast majority of patients with lupus have other tuberculous foci apart from the skin, and that a considerable proportion die from visceral tuberculosis. For this reason general treatment directed towards raising the patient's resistance in every possible way should be instituted. Heliotherapy, as carried out by Rollier at Leysin, is the method of choice, and is undoubtedly superior to any other known therapeutic measure. In England and countries which obtain relatively little sunshine, excellent results are achieved with the carbon-arc and mercury-vapour lamps. The introduction of this treatment has revolutionised the therapy of lupus and other forms of chronic tuberculosis, and has rendered unnecessary many of the local measures that were formerly employed. In addition, the internal administration of iodine and cod-liver oil is of great value. The former should be given in the form of a 10 per cent. solution in rectified spirit, of which 5 drops in milk may be taken at first twice daily, the dose being gradually increased up to as much as 60 drops *per diem* if well tolerated. Injections of tuberculin, if given prudently over a long period, are undoubtedly beneficial. Remarkable improvement is also sometimes obtained with intramuscular injections of calomel, but the results are inconstant.

Diet. In recent years, the dietetic treatment of lupus vulgaris and other tuberculous conditions of the skin, as advocated by Gerson and modified by Sauerbruch and Hermannsdorfer, has found increasing favour. The essentials of the dietary are: (1) the almost complete exclusion of sodium chloride, a compound rich in calcium but poor in sodium being used as a substitute (*e.g.*, Selarom); (2) liberal quantities of uncooked fresh vegetables, as salads with added fruit-juices, and extracts prepared by pressing uncooked vegetables; (3) the cooking of vegetables in their own juices with little water; (4) moderate restriction of meats; (5) restricted water-intake, but liberal amounts of the juices of fresh fruits and vegetables; (6) the administration of mineral compounds containing the lactate and phosphate of calcium, double salts of calcium and magnesium, strontium, aluminium, and silica, and cod-liver oil, thrice daily; (7) a high fat- and protein-intake, but a marked restriction of carbohydrates.

Local Treatment. Before employing any local measures for the destruction of the lupus tissue, it is advisable, in view of the remarkable results now being obtained by heliotherapy or the artificial light baths, to observe to what extent spontaneous healing will take place under such treatment, combined with the internal administration of iodine and cod-liver oil. From the cosmetic point of

view local phototherapy with the Finsen arc lamp undoubtedly gives the best results, the resulting scars being smooth and supple. The method is, however, very tedious and expensive. The modification of the Finsen Lamp, designed by Svend Lomholt, is a great improvement on the original one, and 80 per cent. of permanent cures have been obtained with it. The number of applications required is far fewer, the cosmetic results are excellent, and it can be used on the mucous membranes. The use of the X-rays should, as is now generally admitted, be reserved for the ulcerating, vegetating or papillomatous types of the disease. It may be combined with the application of the galvano-cautery, or with periodical scarification. Large doses of X-rays, or their continued use over long periods, are entirely unjustifiable owing to the risk of a subsequent radiodermatitis, with ultimate epitheliomatous degeneration of the scar. The thermo-cautery and galvano-cautery are useful adjuncts to treatment, and are of particular value in lupus of the mucous membranes. Recently, diathermy has been employed with excellent effect. Scarification, if correctly performed, gives scars hardly less satisfactory than those obtained with the Finsen lamp, but it is a tedious and painful method; it is, however, the method of choice for rapidly extending, vegetating lupus (*L. vorax*), and for the treatment of nodules embedded in scars. In France the filiforme douche is being used with good results for the destruction of lupus tissue. Various caustics, such as arsenious acid, pyrogallic acid, trichloracetic acid, the liquid acid nitrate of mercury, and a combination of salicylic acid and creosote in plaster form have a selective action on lupus tissue, but cause considerable pain, particularly arsenious acid. Adamson's method of employing the liquid acid nitrate of mercury is simple and gives excellent results. It is carried out as follows:—The lupus nodules are gently rubbed for from one to two minutes with a piece of cotton wool, twisted round the closed ends of a finely pointed pair of forceps, and moistened with the liquid. No subsequent dressing is necessary, although it is perhaps advisable to keep the treated surface covered with a piece of clean lint or gauze. A good deal of inflammatory reaction ensues, and a scab forms, which becomes detached in course of time, leaving a smooth pink surface. The subsequent scar compares favourably with that obtained by any other method, except, perhaps, the Finsen light. The method is rather painful, but an anæsthetic is not usually required. A considerable area can be treated at one sitting, and the applications can be repeated until all the active lupus tissue has been destroyed. In cases in which the nodules are large and deep, they may first be scraped under anæsthesia, and then treated with the acid nitrate of mercury or zinc chloride.

LUPUS VERRUCOSUS

(*Verruca necrogenica*)

This variety of tuberculosis of the skin is caused by direct inoculation of tubercle bacilli. It may arise in phthisical or other patients suffering from "open" tuberculosis as a result of auto-inoculation. More commonly it is met with in medical men, nurses, or students in contact with tuberculous patients, or in pathologists, *post-mortem* attendants, veterinary surgeons, butchers, and others who handle human or animal cadavers infected with tubercle. The lesions contain considerable numbers of tubercle bacilli, far more than those of lupus vulgaris, but less than tuberculous ulcers. They are met with usually on the hands, particularly on the thumb, but they also occur on the elbows, knees, feet, buttocks, peri-anal region, neck, and even on the face. The earliest lesion is a small erythematous nodule, from which, later, a bead of pus can be expressed; it gradually enlarges to form a warty plaque, surrounded by a bluish halo of erythema. In a fully-developed patch three zones can be recognised: at the periphery an erythematous area, within this a number of papillomatous nodules of a bluish-violet colour covered with adherent crusts, and in the centre

either a depressed scar or brownish warty projections, separated by fissures. A small quantity of pus, in which tubercle bacilli may be found, exudes from the surface, and the base of the plaque is indurated. The lymphatic glands are infected early, and the viscera may become involved.

Treatment. The method of choice is excision of the affected area of skin as soon as the diagnosis is established, or total destruction of the lesion with the actual cautery or by diathermy. Sequeira recommends removal of the warty surface with pyrogallic or salicylic acid, followed by the application of X-rays.

THE TUBERCULIDES

In 1896, Darier introduced the term "tuberculides" to designate a group of eruptions which occur in persons having a manifest tuberculous infection, and which, although differing from each other in their clinical appearances, are frequently co-existent in the same patient, thus indicating their relationship and common origin.

Classification. A. CUTANEOUS TUBERCULIDES, in which the lesions are dermo-epidermic.

(1) *Lichenoid Tuberculide.* Lichen scrofulosorum.
(2) *Eczematoid Tuberculide.* Dermatitis scrofulosa—a variety of the above.
(3) *Papulo-necrotic Tuberculides.* Folliclis. Acnitis.
(4) *Acneiform Tuberculide.* Acne cachecticorum—a variety of the papulo-necrotic type.
(5) *Lupoid Tuberculide.* Papular sarcoid of Boeck, or disseminated miliary lupoid, with which acnitis may be associated.
(6) *Erythemato-atrophic Tuberculides.* Lupus erythematosus in certain cases.
(7) *Rosaceous Tuberculide.*

B. SUBCUTANEOUS TUBERCULIDES.
Erythema induratum scrofulosorum (Bazin's Disease).
Erythema nodosum (in some cases).
Subcutaneous sarcoid of Darier-Roussy.

Ætiology of the Tuberculides. The tuberculides result from the embolism in a blood vessel either of the skin or subcutaneous tissue of tubercle bacilli, carried in the blood-stream from some local tuberculous lesion. They occur in persons who have been usually, if not always, sensitised to tubercle by an infection in early life, and whose resistance to the infection is, as a rule, good. The actual lesions represent inflammatory reactions produced by the interaction of the antibodies present in the sensitised tissues and the bacilli, this reaction bringing about destruction of the latter, so that the lesions heal with or without scar formation. It is obvious that for their occurrence the presence of antibodies is essential, and this probably explains why disseminated patches of true lupus may follow an attack of measles in a tuberculous person, since measles causes a temporary disappearance of tuberculous antibodies, so that the bacilli survive and multiply. An important factor in the genesis of tuberculides is circulatory stasis; the papulo-necrotic variety is seen in scrofulous persons with a chilblain-circulation, the sites of election being those in which the blood flow is most stagnant, and erythema induratum occurs almost exclusively in young females with cyanotic, œdematous-looking legs. As might be expected, owing to the rapid destruction of the bacilli, it is only rarely that they are demonstrable in tuberculide lesions. They have, however, been found in lichen scrofulosorum and erythema induratum. Inoculation of guinea-pigs with tissue from the lesions has more often given positive results. Injections of tuberculin not only give rise

to focal cutaneous reactions, but may provoke an outbreak in a tuberculous person of tuberculides not previously present. Moreover, minute doses of tuberculin, given at suitable intervals, have a striking curative effect in erythema induratum and the papulo-necrotic tuberculides.

Treatment of the Tuberculides. The general treatment of patients with tuberculides is the same as that already outlined for lupus vulgaris (*q.v.*). Injections of small doses of tuberculin intradermically, in combination with intravenous injections of novarsenobillon, are strongly recommended by Darier. The writer has obtained good results in folliclis and erythema induratum with injections of gold compounds, such as are employed in lupus erythematosus (*q.v.*), iodine and cod-liver oil internally, and total ultra-violet light baths. In erythema induratum, complete rest in bed, particularly in cases with ulceration, should be enjoined until the lesions have healed.

Lichen Scrofulosorum. This, the lichenoid type of tuberculide, is comparable to the lichenoid trichophytide, and to the papulo-follicular eruption, first described by Whitfield, in association with severe streptococcal impetigo (lichenoid streptococcide).

The eruption consists of two types of lesion—plane papules resembling somewhat those of lichen planus, and follicular papules, which vary considerably in appearance. The former are small, flat, polygonal, and yellowish or reddish in colour. They may be smooth and glistening, or covered by a small scale. The follicular papules may exist alone, but are more commonly seen in association with the plane variety. They are formed around the pilosebaceous follicles, are conical or acuminate in form, reddish in colour, and occasionally capped by a horny spine (one form of lichen spinulosus, cp. the lichenoid trichophytide). Sometimes vesico-pustules may form at their summits (cp. vesiculo-pustular trichophytides).

The various types of lesion are arranged in roundish groups, or circles, or segments of circles. They are distributed chiefly on the trunk, particularly on the flanks, more rarely on the limbs, and occasionally on the face. Itching is slight or absent. The eruption progresses by the appearance of fresh crops of papules from time to time, so that it may last for months.

Morbid Anatomy. The lesions are formed by a tuberculoid infiltration of the dermis with epithelioid and giant cells: there is little or no tendency to caseous degeneration. The infiltration is situated either in the papillary layer, or around a pilosebaceous follicle, according to the type of papule examined.

Ætiology. The eruption is, with the eczematoid variety, the simplest and most superficial of the tuberculides. It would appear to represent, with phlyctenular ophthalmic lesions, the first manifestation of tuberculous bacillæmia after the barrier afforded by the lymphatic glands is broken; hence its usual incidence in childhood. Boeck and Bruusgaard have described it as occurring in a child of sixteen months six weeks after the healing of a digital tuberculous chancre, and immediately after a phlyctenular keratitis; in another case, a girl of one year, with a vulvar tuberculous chancre and inguinal adenitis, keratitis developed before the healing of the chancre, and three months later an eruption of lichen scrofulosorum.

Tubercle bacilli have actually been demonstrated in microscopical sections of the papules, and positive inoculations have been obtained in a guinea-pig. Local, focal, and general reactions result from injection of tuberculin, and the eruption may be provoked by such injections in tuberculous persons. Adamson and Brocq have observed the development of follicular papules around the site of an intradermal injection of tuberculin. Cases have been recorded in which lichen scrofulosorum cleared up spontaneously after surgical removal of tuberculous glands.

Eczematoid Tuberculide. Boeck many years ago described, as attenuated forms of lichen scrofulosorum, a "disseminated papulo-squamous tuberculide"

and an " eczema scrofulosorum." Jadassohn has also indicated a scaly form of the eruption, in which somewhat infiltrated patches, reddish-brown in colour, and resembling those of psoriasis or seborrhœic dermatitis, are seen. Schaumann and others have seen such patches associated with typical lichen scrofulosorum, and on section the former found a tuberculoid structure with giant-cells, but without necrosis.

There has been described (**21**) a series of cases of an eczematoid dermatitis, occurring almost exclusively in children and adolescents, as scaly patches of a characteristic fawn or pale brown colour, usually dry, but sometimes oozing—probably as a result of scratching or rubbing—and situated chiefly on the extensor surfaces of the limbs, the trunk, and on the face, particularly on the temples and forehead below the margin of the hair. In about 80 per cent. of the cases definite signs of active tuberculosis were demonstrated. The writer named the eruption dermatitis scrofulosa. Later a further series of these cases was described (**22**) and it was shown (1) that exactly similar patches may arise *de novo*, and persist for some time in tuberculous children at the sites where Pirquet's cuti-test with tuberculin has been done, and (2) that in children with dermatitis scrofulosa patches, identical in appearance and histological structure with those already present, may be produced by applying tuberculin to the skin. Cases of undoubted lichen scrofulosorum were also observed, in which patches of dermatitis scrofulosa were co-existent, and the view was put forward that the latter is an eczematoid variety of the former.

The probable explanation of this eczematoid form of tuberculide is that it results from *epidermal* sensitisation to tuberculin, since every eczematous reaction is dependent upon sensitisation of the cells of the rete Malpighii. The experimental production of patches of dermatitis scrofulosa by the application of tuberculin to the skin, above referred to, is in favour of this view.

Diagnosis. The eruptions with which dermatitis scrofulosa is most likely to be confused are the dry scaly form of streptococcal impetigo, the scaly patches that result from the use of strongly alkaline soaps, and those due to infection with the pityrosporon. None of these have the same fawn or reddish-brown colour, nor is there in them the same degree of infiltration that characterises dermatitis scrofulosa.

Papulo-Necrotic Tuberculide. This form of tuberculide is not uncommon, and is seen chiefly in adolescents and young adults with a poor peripheral circulation and tuberculosis of the glands, bones, joints, or peritoneum. The elementary lesion is a small firm papule, surrounded by a reddish border, and embedded in the dermis. The central portion becomes bluish in colour, and there forms beneath its epidermis a vesiculo-pustule, which, on being opened, exudes a sero-purulent fluid and exposes a small necrotic cavity. When untouched, the pustule dries up to form a crust, which covers the central necrotic area; when this falls, a pitted scar is left, surrounded by a narrow zone of pigmentation.

The distribution of the lesions to a great extent corresponds to the sites of maximum vascular stasis, and they are found principally on the hands and feet, the elbows and knees, the extensor surfaces of the forearms, the ears, and the rosaceous area of the face. They appear in crops, particularly in winter, when the peripheral circulation is most sluggish, and may continue to do so for months or years. As with erythema induratum, however, the eruption tends to disappear spontaneously, even without treatment, as the patient approaches middle age.

Morbid Anatomy. The lesions presumably result from embolism of tubercle bacilli in a small dermic vessel, as a result of which an area of necrosis is formed in the connective tissue; this becomes surrounded by a zone of inflammation, which may have a definitely tubercular structure, epithelioid and giant-cells being found in irregular groups. The site of necrosis varies, being very superficial in so-called acne cachecticorum.

Ætiology. Like lichen scrofulosorum, the papulo-necrotic tuberculides may be the first manifestation of bacillæmia. Bruusgaard observed a case, a boy of seventeen months, in which they appeared shortly after the healing of a tuberculous chancre of the chin. From the tuberculides a guinea-pig was successfully inoculated, and a bacillus of the human type was cultivated.

***Lupus Miliaris Faciei* (*Papular Sarcoid of Boeck*).** This eruption, which Schaumann rightly distinguishes from the true sarcoids that form part of his benign granuloma, is best classified among the tuberculides; in some respects it appears to provide a transition between these and the active tuberculous dermatoses, such as lupus vulgaris. Schaumann considers that it should include the follicular disseminated lupus of Tilbury Fox, the acne agminata of Crocker, and the acnitis of Barthélemy.

It consists of hemispherical papules, of the size of a millet-seed to that of a pea, reddish-blue or brownish in colour, and moderately firm to the touch. They are arranged symmetrically on the face, particularly over the rosaceous area, on the neck, and less commonly on the wrists, extensor surfaces of the upper limbs, shoulders and back, scalp and lower limbs. They may appear quite suddenly, and continue to form crops over a long period of time: they may be absorbed, leaving scarcely perceptible cicatrices, or undergo visible necrosis, with superficial suppuration, and subsequent pitted scarring (acnitis). Some would separate the latter form from the non-ulcerative type of eruption, but the two may, as Schaumann points out, coexist, and histologically one may find evidence of necrosis both in the lupoid papules, and in those with suppuration.

Morbid Anatomy. Histologically the papules are found to consist of masses of epithelioid cells, with or without giant cells, mingled with numerous lymphocytes. Central caseation is often seen.

Ætiology. The eruption may appear in advanced cases of phthisis, but more commonly the clinical evidence of tuberculosis in those affected is not striking, particularly in the purely lupoid form, which is seen chiefly in women of middle age. Radiographic examination of the chest usually reveals evidence of old hilus phthisis, with calcification of the bronchial glands, and sometimes of a former apical lesion, but, according to Schaumann, the lungs never show the shadows seen in benign lymphogranuloma. Tubercle bacilli have been found in the lesions by several observers, and others have obtained positive animal inoculations. The intradermal tuberculin test is always positive, according to Schaumann.

Rosaceous Tuberculide. This variety of tuberculide differs from the above in that the rosaceous element (flushing, telangiectasia, and scaliness) is more apparent, the lesions are smaller and more superficial, and there is less tendency to scarring. Histologically, although their structure is tuberculoid, the classic tubercle with central caseation is not found.

The condition was first described by Lewandowsky, and many cases have since been reported (**23**). The lesions consist of minute papules, sometimes but not always follicular, and irregularly distributed; although usually discrete, they may be grouped in small patches. Their colour varies from bright red to brownish yellow. On vitropressure they resemble lupoid nodules, unlike the papules of true rosacea. Some of them may become pustular, but the pustules are small and superficial. The degree of rosaceous flushing and of telangiectasia varies.

The lesions persist for a considerable time and then slowly undergo involution, either leaving no visible trace or a small pitted scar. The diagnosis from papulopustular rosacea is sometimes difficult, the main points being the lupoid appearance of the papules both with and without vitropressure; the involvement of the lateral parts of the forehead and cheeks and of the neck; oily seborrhœa, usually present in rosacea, is as a rule absent or slight, and the tendency to pustulation is much less, the pustules, when present, being small and superficial; the

histological structure of the lesions; the sensitiveness of the skin to tuberculin (intradermal and Moro tests), but in some cases this is slight.

Morbid Anatomy. In chronic indurated papules of ordinary rosacea a tuberculoid structure with occasional giant-cells is sometimes found as a reaction to broken-down follicles and sebaceous glands. In rosaceous tuberculide even minute and recent papules reveal circumscribed tuberculoid infiltrates, lying just below the epidermis, with giant-cells here and there. They may be perifollicular or around a sweat-duct, but are often independent of the glandular appendages, unlike those of rosacea.

Treatment. Apart from the general treatment already indicated for tuberculous conditions of the skin, injections of gold compounds have been found by the writer and others to be of great value.

Erythema Induratum (*Bazin's Disease*). Under the term erythema induratum two types of indolent subcutaneous nodules are included, the one tuberculous the other not. The former is commonly known in this country as Bazin's Disease, and is seen almost exclusively in young girls with fat, cyanotic, œdematous legs, in which there is vascular stasis, most evident on the postero-external surface of the lowest third ("erythrocyanosis crurum puellaris"). Since the nodules are of embolic origin, they occur most commonly on this area. They appear as deeply indurated, reddish or violet plaques of varying size, which may slowly resolve, or rupture, exuding an oily fluid, the product of fat-necrosis; in the latter case indolent ulcers result, which become secondarily infected with pyogenic organisms. As might be expected, the occurrence of fresh nodules is predisposed to by long periods of standing, which increase the vascular stasis, and their resolution is hastened by rest in bed.

Morbid Anatomy. It is probable, as Schaumann suggests, that in erythema induratum, and the subcutaneous variety of sarcoid, the tubercle bacilli come to rest in one of the vasa vasorum of a subcutaneous vein, with the result that there occurs a thrombo-phlebitis. Around the embolised vessel there may be a tuberculoid infiltration in the wall of the vein. As in erythema nodosum there is extensive necrosis of the subcutaneous fat, the products of which are absorbed by histiocytes and giant-cells.

Ætiology. This variety of erythema induratum is probably always of tuberculous origin. Numerous successful animal inoculations with material from the nodules have been made. Strongly positive cutaneous and intradermal tests are obtained with tuberculin, and marked focal reactions occur if it be injected. Like lichen scrofulosorum, the eruption may arise for the first time in a tuberculous person after a therapeutic injection of tuberculin. Not uncommonly papulo-necrotic tuberculides and erythema induratum coexist in the same patient.

Subcutaneous Sarcoid of Darier-Roussy. This variety of tuberculide is very closely allied to the tuberculous form of erythema induratum. The lesions consist of indolent hypodermic nodules, varying in size from that of a pea to that of a walnut, or may be even larger. They may become more or less confluent and form nodular plaques. The overlying skin is of normal colour or bluish, and in places adherent. They occur in adults of both sexes, rarely in children. The sites of election are the scapular region, the sides of the chest, the flanks, and the thighs; but they may also be met with on the arms and legs, and even the scalp. Unlike erythema induratum and tuberculous gummata, they never undergo necrosis with ulceration.

Morbid Anatomy. The histological appearances resemble those of erythema induratum, but the tuberculous structure is more apparent. Typical giant-cell systems are found, in combination with fat necrosis.

Ætiology. Successful animal inoculations have been made with the tissue from the nodules, and positive local and focal reactions obtained with tuberculin.

SARCOIDS

A very important group of eruptions may be conveniently classified under the term *sarcoid*, but considerable confusion still exists concerning them. In the following account the views of Schaumann (**24**), to whom we owe the conception of a *benign lymphogranuloma*, will be largely adhered to, although further research may demand their modification.

The types of eruption to which the term sarcoid has been applied are as follows :

(1) *Multiple benign papular sarcoid of Boeck*, by many now called disseminated miliary lupoid.
(2) The large nodular benign sarcoid of Boeck.
(3) The hypodermic sarcoid of Darier-Roussy.
(4) Lupus pernio.

According to Schaumann, the small papular and the hypodermic varieties should be classed among the tuberculides (*q.v.*), whereas the large nodular cutaneous sarcoid and lupus pernio should be regarded as part of his benign lymphogranuloma, and grouped with the tubercular form of lupus erythematosus, and the malignant lymphogranuloma of Sternberg (Hodgkin's disease) as para-tuberculosis.

Lupus Pernio and Nodular Benign Sarcoid (*Benign Lymphogranuloma*). Thanks to Schaumann's researches, it is now recognised that these are the cutaneous lesions of a widespread and chronic form of granuloma, which involves, apart from the skin and subcutaneous tissue, the lymphatic glands, the tonsils, the bones of the extremities, the lungs, the spleen and the liver. Severe cases of the disease are rare. In them may be seen lupus pernio of the face, ears, and extremities, combined with multiple sarcoid lesions, varying from superficial lupoid nodules to large subcutaneous tumours, and radiograms of the bones of the hands and feet and of the lungs may reveal extensive involvement. On the other hand, milder cases, with a few scattered sarcoid nodules of moderate size and without lupus pernio or evidence of affection of the bones and lungs, are not uncommon.

Lupus Pernio. This term is given to a diffuse symmetrical infiltration involving the nose, malar regions, pinnæ, the backs of the hands, the fingers, and more rarely the toes. The consistency of the swellings is doughy, the colour bluish-grey, sometimes with a reddish tinge. The fingers become fusiform in shape, and there may be deformity from destruction of the underlying bones (spina ventosa). Sometimes there is ulceration, with subsequent scarring.

Nodular Sarcoid. The most superficial nodules are yellowish-red in colour, grouped, and resemble very closely those of lupus vulgaris, but are harder. Others vary in size from that of a pea to that of a walnut, may be rose-coloured or greyish, and often have a characteristic translucent appearance. The largest lesions form dermic or hypodermic swellings, sometimes as large as a hen's egg, bluish-grey in colour, like lupus pernio, and situated chiefly on the arms, legs, trunk, and malar regions of the face. Resolution may occur, leaving the overlying skin flaccid, or there may be ulceration and crusting of the surface.

There is also a rare variety of sarcoid which merits separate description. It is seen most commonly in women, and the lesions are found principally on the scalp, forehead, temples, ears and neck. The elementary lesion is a raised nodule, resembling in colour and appearance very closely that of lupus vulgaris ; the nodules tend to arise in groups, and to spread peripherally, while undergoing resolution with scarring in the centre. In this way complete or incomplete rings are formed enclosing a depressed cicatricial centre. The borders are constituted by the reddish-yellow sarcoid infiltration. The condition is apt to be mistaken for the multiple superficial form of basal-celled carcinoma, but the " apple-jelly " colour of the edges should prevent confusion. Numbers of these lesions,

varying in their stage of evolution from single circular or oval nodules to discrete or confluent rings of considerable extent, may be found in the above situations. They leave permanent scars, which, of course, give rise to cicatricial areas of alopecia on the scalp.

Morbid Anatomy. Lupus pernio and the sarcoid nodules consist of lobular masses of epithelioid cells, lymphocytes, and occasional giant-cells, separated by strands of connective tissue. As has been said, nodules, having the same histological structure, occur in the lymphatic glands, tonsils, the medulla of the bones of the extremities, and lungs. In the bones they lead to destruction of the osseous tissue, and give rise to characteristic areas of absorption, which appear dark in radiographic plates. These areas are mostly circular and sharply defined, but they may be irregular if the destructive process is extensive. They are seen chiefly in the phalanges, and in the metacarpals and metatarsals near their extremities, but may also occur in the bones of the carpus and tarsus, and even at the ends of the long bones. As the deposits occur primarily in the bone-marrow, this may be extensively affected without there being necessarily any changes in the bony tissue.

Ætiology. In Schaumann's opinion the origin of his benign lymphogranuloma, of which lupus pernio and nodular sarcoid are the cutaneous manifestations, is an infection with the *filterable* form of the tubercle bacillus, probably of the bovine type. He inoculated into guinea-pigs the sputa of three patients, and only after passage through several animals was he able to produce the classical form of experimental tuberculosis and cultivate the bacillus, which in two of the cases was of the bovine type, in the other of atypical form. He also claims in favour of a tuberculous causation the fact that in true benign lymphogranuloma the Von Pirquet reaction is invariably negative, the patients being, in fact, less sensitive to tuberculin than normal persons, and he believes it impossible for the tuberculides, which are associated with a high degree of cutaneous allergy and strongly positive tuberculin reactions, to coexist with benign lymphogranuloma.

In some of Schaumann's cases pulmonary tuberculosis developed, and this involvement of the lungs caused the cutaneous sarcoid lesions to disappear, and the Von Pirquet to become positive. It should be remarked, however, that tuberculides and even lupus vulgaris also usually disappear if actively progressive phthisis ensue, and, with the extension of the lung disease, the Von Pirquet reaction diminishes, and finally becomes negative.

Treatment. The writer has obtained satisfactory results in some cases with injections of gold compounds, as indicated for the treatment of lupus erythematosus. Gray has found intramuscular injections of sodium morrhuate of great value, and in one case under the writer's care—the most extensive and characteristic example of benign lymphogranuloma that he has seen—they were given, in combination with iodine and cod-liver oil internally and artificial sunlight baths, and the ultimate result was very striking.

Darier advises *intradermal* injections of tuberculin with novarsenobillon intravenously. Schaumann has failed to obtain results either with the latter or with arsenic by mouth. Hudelo, Montfaur and Leforestier have recorded success in a case of lupus pernio with injections of large doses of cacodylate of soda. Recently Lomholt has reported disappearance or improvement of the lesions with injections of antileprol.

SOFT SORE

(*Soft Chancre, Chancroid*)

A soft sore or chancre is a round or oval ulcer, which develops very rapidly after a short incubation period, and is auto-inoculable. At the site of invasion by the specific infecting organism (Bacillus of Ducrey-Unna) a small inflammatory

papule appears within twelve to twenty-four hours, which soon becomes converted into a pustule on a bright red base. On rupture of the pustule, the characteristic ulcer is formed—*i.e.*, within four or five days from the date of inoculation. *The base* of this ulcer consists of greyish granulations, covered with a yellow, creamy, purulent film; *the edges* are sharply cut or undermined, and careful examination will show slight crenation—a valuable diagnostic sign; *the base* is œdematous, but not indurated like that of a chancre; *the periphery* of the lesion is bright red. The ulcer exudes a purulent secretion, from which inoculation of adjacent areas of skin takes place. It is, therefore, rare to see a single lesion, multiple ulcers, arising either from simultaneous inoculation at more than one point, or from auto-inoculation from an original single sore, being the rule. By the confluence of several lesions, the size of which varies from a pea to a finger-nail, a considerable area of ulceration may result.

The neighbouring *lymphatic glands*, on one, or more rarely, both sides, are, as a rule, enlarged and painful within a few days from the appearance of the sore or sores, and there is a tendency for one gland in particular to be involved, which is very apt to soften and break through the skin, producing the soft or chancroidal bubo.

The situation of soft sores varies, but the vast majority are seen on the genitals and adjacent parts. In men the prepuce, the corona and cervix, and the frenum, which may be perforated, are most commonly affected; in women, the vestibule, the fourchette, the labia minora, the glans clitoridis, and the anus. By auto-inoculation, neighbouring regions, such as the pubis, internatal cleft, and inner surfaces of the thighs, may be involved. Extra-genital soft sores are excessively rare, and usually, though not invariably, arise by auto-inoculation from genital lesions.

Complications. Reference has already been made to suppurating bubo; in addition lymphangitis, abscess of the dorsal lymphatics of the penis (bubonulus), phimosis, paraphimosis, phagedena, and gangrene may result. Phagedena arises both from the actual sores, and also from a suppurating bubo.

Ætiology. The cause of soft sore is a strepto-bacillus described by Ducrey and Unna. It is a short Gram-negative bacillus, easily stained by methylene-blue. It is with difficulty grown artificially, but has been cultured on peptonised human skin and certain other special media. The organism may be successfully inoculated on monkeys. Infection usually takes place directly by sexual intercourse, but may rarely be indirect.

Diagnosis. The chief characteristics of soft sore are the short incubation period, the tendency to rapid ulceration, the auto-inoculability and the resulting multiplicity of the lesions, the early involvement of the lymphatic glands and their liability to suppuration, the lack of induration of the base, the crenated edge of the ulcer, and the painful course of the affection. It must be distinguished from a syphilitic chancre, herpes progenitalis, the lesions of scabies, mucous patches, tertiary gummatous ulceration, and epithelioma.

The following differences between hard and soft chancres should be noted (Pusey):—

Hard Chancres	*Soft Chancres*
Incubation period two to five weeks.	Incubation period two or three days; becomes an ulcer in four or five days.
An erosion or superficial ulcer, with sloping edges and scant secretion.	An angry-looking ulcer with a bright-red halo, undermined edges, crenated border, and profuse purulent secretion.
Indurated cartilaginous base.	Slight inflammatory induration.
Is almost painless.	Often very painful.

Hard Chancres	*Soft Chancres*
Is not auto-inoculable.	Is auto-inoculable, and therefore multiple lesions of different ages and sizes are common.
If multiple, due to multiple primary inoculations, the lesions being of the same age.	
Adenitis is bilateral.	Adenitis usually unilateral.
Adenitis indolent and painless; the enlarged glands are multiple and discrete.	Adenitis acute, painful and inflammatory, and likely to result in suppurating bubo.

It must be remembered, however, that a simultaneous inoculation with Ducrey's bacillus and the *Treponema pallidum* may occur, and for this reason every soft sore should be considered as potentially a hard chancre. Frequent and persistent examinations for the spironema of serum taken from *the edges* of the ulcer, after a preliminary cleansing of the surface, should be made.

Treatment. The patient should, if possible, be kept at rest, since exercise favours suppurative adenitis. The ulcer should be cleaned several times daily with hot solutions of perchloride of mercury (1 in 2,000), potassium permanganate (1 in 1,000), or carbolic acid (1 or 2 per cent.), and iodoform or aristol powder then applied freely. Another method is to destroy the ulcer by swabbing it thoroughly with pure carbolic acid, applied with a swab of cotton-wool; an acute inflammatory reaction occurs, and a slough is formed and shed, leaving a healthy wound.

RHINOSCLEROMA

This is a dense infiltration of the septum and alæ of the nose, rendering it as hard as ivory, thick, and rigid. The surface is smooth or irregular, the colour normal or brownish red; the mucous membrane is affected as well, and the orifices may be blocked by its swelling. By extension the upper and lower lips, the gums, epiglottis, larynx, trachea, jaws, and soft palate, which may be perforated, may become involved. The changes are a dense infiltration of the corium and papillæ with plasma cells, the presence of large translucent degenerated cells (Mikulicz cells), and bacilli, the bacilli of Frisch, which have a close resemblance to the pneumonia bacilli of Friedländer, and are found chiefly in the Mikulicz cells, but also in the plasma cells and tissue. Removal by the knife or destruction by caustics may be required, but X-rays should be tried first.

The majority of cases have occurred in southern Russia, Egypt, Italy, and "on both shores of the Danube" (Castex). Several have been reported in America, only one of which was indigenous.

Erysipeloid. This eruption was first described by Morrant Baker as "erythema serpens," and later by Rosenbach, who gave to it the name under which it is now known. It is usually seen on the hands, but may occur on the face and elsewhere. Recent researches have shown that it is due to accidental infection of the skin with the bacillus of swine-erysipelas, which is saprophytic on animal matter. The eruption begins as an erythema surrounding the point of inoculation, usually a cut or scratch. It spreads peripherally, while clearing in the centre. The colour is bluish-red, and the border is raised and well-defined. By the development of new areas irregular circinate figures may result. Subjective symptoms are slight, as a rule, but itching and some pain may occur. The infection runs a definite course of some two to four weeks.

Apart, however, from this mild form of the disease, another more serious (**25**) is occasionally seen. The eruption may spread widely and involve at different times almost the entire skin. Lymphangitis and arthritis with general malaise and fever accompany it, and, although spontaneous recovery usually follows in some weeks, the course may be chronic. An acute, septicæmic variety, with

arthritis and endocarditis, has occurred in veterinary surgeons accidentally inoculated when immunising swine against the infection.

Ætiology. The disease occurs principally in those who handle meat, fish, crustacea, hides, and bones. Gilchrist recorded 323 cases in which a bite or injury from crabs was responsible, the incubation period being two days. It is rare in England, but in America is an occupational disease of importance, particularly in those engaged in the fish industry.

Treatment. The affected area should be painted with iodine or ichthyol. In severe cases injections of an immune serum have proved of value.

Diseases Due to Fungi (Mycoses)

The dermatomycoses are described elsewhere, *i.e.* Actinomycosis on p. 99, Blastomycosis on p. 102, and in the section dealing with Diseases of the Tropics, p. 1028.

EPIDERMATOMYCOSES

FAVUS

In this disease, rare in England, the fungus attacks the epidermis and the hair follicles; it may at first form patches like those of ordinary ringworm, but soon there appears a small, bright yellow, circular disc, with a depressed centre and a gradually thinning margin. This, the "favus cup," is caused by the fungus elements separating the layers of the epidermis and lifting them up, except at the central point, where the hair follicle joins the skin. This characteristic lesion may occur on the scalp, or on any other part of the body, the forearm for instance, determined by contagion; and it is conveyed not only from man to man, but to man from domestic animals—rabbits, dogs, cats, and others. When numerous cups have formed, they become aggregated together, and produce a thick continuous yellow crust, with an irregular honeycombed surface, giving off an offensive odour resembling that of mice. The hair sacs are destroyed, the hairs fall out, and baldness results; moreover, the favus masses often become a nidus for pediculi, and eczema and impetigo complicate the original lesion. If the masses are examined under the microscope, after soaking in liquor potassæ, the mycelium and spores (conidia) of the *Achorion schönleinii* are seen. The conidia are larger and more varied than those of the ringworm fungi, and the mycelium is shorter and more jointed.

The *nails* may be also invaded by the fungus of favus. They present an appearance similar to that in ringworm and sometimes a distinct cup forms under the nail. The nail may be examined in the same way as in ringworm.

Two other species of achorion have been seen in man in rare cases: *Achorion Quinckeanum*, the fungus of mouse favus, and *Achorion gypseum*.

Treatment. The crusts must be softened by oil or poultices and removed; parasiticides and epilation are needed, and for most cases the Röntgen rays should be used as for ringworm. The nails, if affected, may be treated in the same way as when they are diseased by the microsporon or trichophyton. The disease is very obstinate, and after apparent cure often breaks out again. It is well to care for the general health by good food and tonic medicines.

RINGWORM (*See Plate 59*)

Tinea or ringworm is the term used for an infection of the skin, hair, and nails with various species of fungi. All of them have segmented mycelia and form "spores," the size of which has been utilised rather unscientifically as a basis for classification. For clinical purposes, however, we recognise: *Microsporons* or small-spored ringworms, which include the *M. audouini*, responsible in the great majority of cases for ringworm of the scalp in this country and for

some of tinea circinata, and other species which infect animals and indirectly human beings, *e.g. M. felineum, equinum, canis vel lanosum : Trichophytons* or large-spored ringworms. These are divided into *endothrix* varieties, in which the fungus is found only inside the fully infected hairs, and *ecto* or *ecto-endothrix* varieties in which it is seen both inside and outside the hair. The former apparently affect only man and birds ; the latter occur in many animals (horses, dogs, cats, cattle, deer, and birds), but may be communicated to man. *Epidermophytons*, which do not invade the hair, but grow only in the horny layer of the skin and in the nails. The best known of these is the *E. inguinale*, which is peculiar to man, and is the cause of tinea cruris or " dhobi itch " and of the common intertriginous ringworm of the hands and feet.

These fungi can be cultured on artificial media, and it is their cultural characteristics that enable us to classify them scientifically.

Clinically ringworm is classified to some extent according to the site affected. Thus we speak of *Tinea tonsurans* (ringworm of the scalp), *T. circinata* (ringworm of the glabrous skin), *T. sycosis* (ringworm of the beard), *T. unguium* (ringworm of the nails), and *T. cruris* (ringworm of the crutch, also termed " eczema marginatum," " dhobi itch," and " Burmese ringworm ").

Tinea tonsurans (*Ringworm of the head*). This disease is the great scourge of schools and allied institutions among the poorer classes. It is frequent in children, rare in infancy, and not easily caught by adults. It spreads by contact, and by the use of hats, caps, brushes, combs, and towels used in common.

It generally first appears as a round patch on which the growth of hair seems thinner than elsewhere. On close examination the skin is seen to be pink, perhaps a little swollen, and covered with minute branny scales. Besides the thinly scattered long and healthy hairs are seen a number of broken stumps of hair, opaque, black or dark brown in colour, twisted and bent. By rubbing a patch with chloroform the stumps are rendered whitish and more easily visible. If an attempt be made to extract one of these broken hairs with a pair of forceps, it will almost certainly break off short ; if then moistened with a drop of liquor potassæ and placed under the microscope, the condition is explained. The substance is quite opaque, the natural structure of the hair is unrecognisable, and the hair seems to be converted into a mass of fungus spores (conidia). This is, however, only a sheath of spores surrounding the hair, which is itself occupied chiefly by mycelium tubes running in a longitudinal direction. These may be more readily observed in hairs which are less completely diseased.

The patch spreads by the implication of hairs at its circumference, and fresh patches form in other parts of the scalp. As these enlarge they become more completely denuded of long hair, though they nearly always present a considerable quantity of the short stumps which have been described ; and these may be surrounded and mixed with scabs, crusts, or sebaceous matter, or with a fine whitish powder, of which probably the fungus elements form a part. The patches spread slowly ; some may heal in the centre as they extend at the edges ; or the patches may coalesce, and nearly the whole scalp may be affected. Sometimes, on the other hand, one or two patches persist, without improvement, but without spreading. The disease may last for years, but eventually dies out, and the hair is perfectly restored. There is rarely much inflammation ; but occasionally the hair follicles inflame, coalesce, and form a red or pink swelling which is soft and boggy to the touch, and discharges pus from a few points ; the hairs are loosened and fall out, and the patch may remain bald when the other parts of the scalp have recovered. The condition is called *kerion*.

Probably the fungus invades the hair close to the scalp, and pushes down towards the bulb. The hair in the follicle is thus weakened or destroyed, and as it is forced outwards by the newly formed epithelial plates, it breaks off. The newly formed epithelium is, in its turn, invaded as soon as it gets into the horny condition. It was shown by Sir Frederick Taylor and Thin that the fungus

only invades the hair itself, and cannot be found in the cells of the root sheath or in the structures of the hair follicle.

Recently the **diagnosis** of scalp ringworm has been rendered much simpler owing to the fact that hairs and scales, infected by ringworm fungus, fluoresce more brilliantly than normal hair or the scales of other diseases, such as pityriasis simplex or psoriasis, when exposed to ultra-violet rays of wavelengths between 3,600 and 3,300 Ångström units. These are obtained by filtering light from a mercury-vapour lamp through Wood's glass. Exposure of an infected scalp to the rays in a dark room will cause the hair and scales on the areas involved to fluoresce with a brilliant green tint. By this method not only can early cases be detected with ease, but it can also be utilised to determine whether a child is cured after treatment, previously a difficult problem.

In this country ringworm of the scalp is due to the *Microsporon audouini* in about 90 per cent. of cases. It occurs almost exclusively in children and dies out spontaneously at puberty; a few cases have, however, been reported in adults. In other countries trichophytic or large-spored ringworm of the scalp is commoner, and this is seen both in children and adults; moreover, microsporons of animal origin, usually the *M. felineum*, may invade the adult scalp, as in the case of an elderly woman, seen by the writer, in whom infection had occurred from a Persian kitten.

The clinical appearances of ringworm of the scalp due to infection with a *Trichophyton endothrix* differ from those of microsporosis. Two types of the disease are met with: (1) The infected hairs, intermingled with normal long hairs, are greyish, and broken off at a distance of 2 to 4 mm. from the scalp, the surface of which is covered with dry or greasy scales, containing twisted stumps of diseased hairs. This variety is due to the *Trichophyton crateriforme*. (2) The affected areas are studded with black points formed by infected hairs which are broken off level with the scalp or twisted on themselves in the mouth of the follicle. This is the " black-dot " ringworm of English writers. It is due to the *Trichophyton acuminatum* or the *Trichophyton violaceum*. The broken hairs, extracted with a needle from their follicles and examined microscopically, will reveal masses of large spores lying in the substance of the hair (endothrix).

Infection of the scalp with the endothrix fungi much more easily escapes recognition than microsporosis, owing to the absence of definite scaly patches of some size, and to the fact that the infected hairs are intermingled with normal ones. Moreover, the stumps do not fluoresce with Wood's Light. Confusion with alopecia areata is also more likely to arise than in microsporosis.

Ectothrix trichophytosis of the scalp may be contracted from animals, and almost invariably results in kerion, which undergoes spontaneous cure.

Tinea circinata, or ringworm of the glabrous skin, is met with (1) in children with *Tinea tonsurans* and those in contact with them, the fungus responsible being usually the *Microsporon audouini* or a *Trichophyton endothrix*: (2) in children without ringworm of the scalp and in adults, who have contracted the disease either directly or indirectly from infected animals. The fungus is then often of the ectothrix variety, but cases are now commonly met with in which the *Microsporon felineum*, contracted as a rule from blue Persian kittens, is responsible, and, as has been said, this may involve the scalp even in adults.

The clinical features of a patch of *Tinea circinata* depend to some extent on the species of fungus, the ectothrix varieties causing more intense inflammation than the others. The latter give rise to erythematous scaly lesions, almost exactly circular in contour with sharply defined edges. The patches spread at the periphery, and tend to heal spontaneously in the central parts, which therefore appear depressed in contrast with the raised margin; in this way the circinate configuration, from which the disease derives its name, arises. Very often vesicles or pustules appear, and are usually situated just inside the spreading edge, but may occur elsewhere; occasionally concentric circles of vesicles are

met with. The ectothrix fungi cause a severe inflammatory reaction, the patches being bright red, œdematous, and covered with vesicles and pustules, which dry up to form sero-purulent crusts.

The evolution of the lesions is rapid, and the size which they attain varies from that of a two-shilling piece to that of the palm of the hand. By confluence of adjacent patches polycyclical figures may result. The diagnosis of *Tinea circinata* should always be confirmed by examining microscopically scrapings from the edge of a patch or the roofs of the vesicles, soaked in liq. potassæ. The mycelium will be seen as branching, wavy lines, which must not be confused with the outlines of the horny cells. At a certain focus they have a greenish tint, and transverse septa, granules and vacuoles may be recognised ; apart from the mycelia, groups of refractile spores are seen.

Tinea marginata (*Tinea cruris*, *Eczema marginatum*, or *Burmese Ringworm*). This form of ringworm, due to the *Epidermophyton inguinale*, of which at least three varieties exist, is very common in tropical countries, where it is known as dhobie (washerman's) itch, owing to the fact that it often results from infection of the underclothing during washing. It occurs chiefly in the groins, but may also involve the axillæ, and may spread from the groins backwards over the perineum and buttocks and upwards over the lower part of the abdomen. It may begin like an acute intertrigo, but more commonly the primary lesions consist of a few circinate patches, which coalesce to form red symmetrical, semicircular areas, with sharply defined and slightly raised edges, on the inner surfaces of the thighs and the contiguous parts of the scrotum. As the disease spreads at the margins, recovery tends to occur in the centre. The lesions are much more extensive, more inflamed, and more obstinate than those of tinea circinata. The disease has become much commoner in England of late since the War, and it often occurs in epidemics in schools, colleges, and other institutions. The usual source of infection is doubtless the water-closet seat.

The epidermophyton fungus is also responsible for a very important condition known as *eczematoid ringworm of the extremities*, in which the infection involves the toes, the soles, the fingers, the palms, and sometimes the nails. On the feet it usually begins as indolent, scaly patches between the toes, spreading outwards on the lower and sometimes the upper surfaces towards the heads of the metatarsals ; the edges consist of the raised horny layer, while the skin within them appears reddened and glazed or actually raw. Frequently eczematous vesicles are formed, so that the condition resembles pompholyx, and sometimes recurrent acute attacks of eczema occur, usually in hot weather, with much inflammation and the formation of numerous vesicles and bullæ. Secondary streptococcal infection may result, and lead to lymphangitis spreading up the leg. Most cases of so-called intertrigo of the toes, and many cases of eczema of the feet, are really examples of eczematoid ringworm, and in a doubtful case the under-surfaces of scales from the margins of the patches and the roofs of vesicles should be examined under the microscope for the fungus. On the hands the disease may resemble an erythemato-squamous eczema of the palms, or it may occur at the roots and sides of the fingers, as on the toes, and may spread upwards to their dorsal surfaces. Acute attacks resembling pompholyx are not infrequent, especially in hot weather. These vesicular lesions may contain the fungus in a state of active growth, or they may represent an eczematoid reaction of the epidermis to the fungus elements or toxin (epidermophytin) absorbed into the circulation from a site of active infection, and reaching distant parts of the skin through the blood stream (eczematoid epidermophytide). Thus recurrent attacks of such vesicular lesions on the fingers and palms are common in association with chronic epidermophytosis of the feet. Moreover, eczematoid patches of the nummular type, usually situated on the ankles and legs, may be due to the same cause. In these cases the epidermis is sensitised to the toxin of the fungus, and, if an intradermal injection of trichophytin or epidermophytin be

made into an unaffected part, *e.g.* the anterior surface of the forearm, an erythemato-urticarial reaction will arise at the site of injection within twenty-four hours, which may be replaced by an eczematoid reaction after an interval of a few days. Focal reactions in the existing eczematoid lesions may also occur. It is to the researches of Whitfield and Sabouraud that we owe the recognition of the parasitic origin of this form of eczema of the hands and feet, and the discovery is of great importance, since many unrecognised cases have been, and still are, treated for years as gouty eczema, or intertrigo, or pompholyx.

Tinea sycosis (*Ringworm of the beard, Hyphogenic sycosis*). The hair follicles of the chin and cheeks are here inflamed by the presence of the fungus; they suppurate, and the hairs become loosened. Induration and swelling of the intermediate skin also occur. It differs from sycosis, described elsewhere, in that it first attacks the hairs, and loosens them early, so that their extraction is painless; it spreads more rapidly and produces deeper infiltration. Microscopical examination shows the fungus, in which the mycelium is more abundant than the spores.

Tinea of the nails. The invasion of the nails by a fungus is called *onychomycosis*, and this may be a ringworm or favus. The nail becomes elongated and curved over the end of the finger, with a thick edge, rough, uneven surface, and dirty yellow colour; it is also brittle and readily splits. If fragments or scrapings are soaked with liq. potassæ, and examined under the microscope, branching mycelium and chains of spores of the fungus are seen.

Treatment. *Tinea tonsurans.* Two methods are commonly used:—

(1) Röntgen Rays. These have to be applied with great care and precision in order to avoid injuring the skin, and at the same time to get the full depilatory effect at one sitting. For this purpose the duration and strength of the application can be regulated by *Sabouraud's pastilles*, which are discs of paper thickly coated with an emulsion of platino-cyanide of barium. If the source of the rays is placed 15 cm. from the scalp, and the pastille exactly midway between them, *i.e.* 7½ cm. from the anti-cathode, the desired amount of influence is reached when the pastille acquires a particular fawn tint identical with a test colour supplied. The application is made to a limited area of the scalp at one time, the rest being protected by sheet lead; but time is saved by treating on the same day five points, situated at least 5 inches from one another. After fifteen to twenty days the hair comes out with the slightest traction; and the patch must be constantly washed with soap and water till it is all removed, the diseased hairs falling last. An antiparasiticide, *e.g.* ung. hydrarg. ammon., should be applied to the whole scalp during the defluvium. The head remains bald for five or six weeks, when finer and coarser hairs begin to grow.

(2) Epilation by Thallium Acetate. It has long been known that thallium acetate, given by mouth in sufficient dosage, causes the hair to fall out, and this action of thallium in tinea tonsurans has had considerable vogue as a substitute for radiotherapy. The dose of the drug recommended is 8 mgm. per kilo body weight, and owing to its toxicity, the most careful precautions must be taken to avoid an overdose. It is given in a small quantity of sweetened water in a single dose. At the end of a week the hair begins to loosen, and by the nineteenth day epilation is usually complete. The infected hairs fall less readily than the non-infected, and it is advisable to aid their removal by applying adhesive strapping and then forcibly pulling it away. It is also necessary to apply some antiparasiticide to the whole scalp in order to prevent reinfection of the new hair. Buschke advises the use of a 10 per cent. sulphur ointment from the first day of treatment until the hair falls, and then this ointment and tincture of iodine are applied on alternate days. The new hair grows more rapidly than after epilation by X-rays, probably owing to the fact that thallium, apart from causing the hair to fall, also stimulates its regrowth. The loss of hair produced by the drug has been shown to be due to failure of the process of transition from the

large polygonal cells to the stratified keratinised cells forming the hair. This method of epilation is suitable for the treatment of scalp ringworm in young children in whom the dosage, relative to body weight, would appear less dangerous than in older children. In the latter toxic symptoms are very likely to arise. Of these the commonest are joint pains, which usually begin early in the second week after administration, loss of appetite, irritability, drowsiness, and dryness of the skin. Albuminuria has also been noted. Unfortunately, errors of dosage have been made in some cases with disastrous results. It may be said that the treatment is practically free from risk in children under six years of age provided that (1) the drug is as pure as possible, (2) the child is accurately weighed naked, and (3) the dosage is most carefully checked.

Kerion. Suppurating ringworm of the scalp should never be treated by X-rays or thallium, as it tends to undergo spontaneous cure. Mild antiseptic compresses should be employed, and intramuscular injections of turpentine (*e.g.* Terpichin) or Aolan may be given to hasten resolution of the patches.

Tinea circinata is easily cured by the use of ung. hydrarg. ammon., oleate of mercury, tincture of iodine, sulphurous acid in solution (1 part to 2 or 3 of water), a weak carbolic acid glycerine, hyposulphite of sodium (1 in 8), or some other not too strong parasiticide.

Tinea marginata. Treatment of epidermophyton infection of the groins is usually not very difficult, but relapse will probably take place unless it be thoroughly carried out, and the underclothing be disinfected. For most cases the following method proves successful: The infected regions are sponged twice daily with a lotion consisting of 2 per cent. of salicylic acid in 75 per cent. spirit; at night-time the following ointment is thoroughly rubbed in: ℞. Acidi benzoici gr. xxv, acidi salicylici gr. xv, paraffini mollis ʒij, ol. cocois nuciferæ ad ʒj (Whitfield); in the morning either the ointment is again applied, or the following dusting powder used after sponging with the lotion: ℞. Acidi salicylici 4 parts, acidi borici 20 parts, talc. to 100 parts. It is preferable that the patient should wear a pair of short cotton pants under his ordinary ones during treatment, and, even after apparent cure, the use of the lotion and powder should be continued for a week or so. In resistant cases chrysarobin ointment may be used, or the pigmentum chrysarobini B.P.C., but great care must be taken not to irritate the scrotum.

Epidermophytosis of the Extremities. This condition is usually most resistant to treatment owing to the thickness of the horny layer on the hands and feet, and the liability of reinfection from the nails. The methods employed must to some extent be varied according to the individual patient, but the following has given the writer good results in uncomplicated epidermophytosis of the feet. For about a fortnight a strong salicylic lotion (℞. Acidi Salicylici ʒi, Spt. vini meth. ind. ad ʒi) is applied thoroughly between the toes and on other affected parts morning and evening, and after each application the Pulv. Acidi Salicylici Co. B.P.C. is sprinkled between the toes and in the socks or stockings. This treatment causes massive exfoliation of the infected horny layer, and, when this appears complete, the following method is substituted. At night time the above benzoic-salicylic ointment is rubbed thoroughly between and under the toes and on other affected areas, a pad of lint being used owing to the risk of infecting the fingers. White cotton socks are worn during the night. In the morning the feet are washed, and as much horny layer as can be easily detached is removed mechanically. They are then painted thoroughly with :—℞. Tinct. Iodi mitis 1·0 : Spt. vini meth. indust. ad 3·0, and the pulv. acidi salicylici comp. B.P.C. is dusted between the toes and into the socks. This treatment is carried out for a month, and the powder alone used for the next three weeks. The full treatment is then resumed for another month, and afterwards the patient is advised to use the powder for the rest of his life as a routine during the daytime. The socks should be washed by themselves and boiled with soda during the treat-

ment, and the shoes periodically swabbed out with pure lysol or cyllin. For the hands, the ointment may be applied under cotton gloves during the night, and the iodine painted on in the morning.

In cases with marked eczematisation it is advisable to begin treatment with small fractional doses of X-rays before instituting one or other of the above methods.

Tinea barbæ (T. sycosis). The treatment is similar to that of kerion of the scalp (*q.v.*).

In *onychomycosis* the nails should be scraped thin, softened with alkaline solutions, and soaked in lotions of sulphurous acid, sodium hyposulphite, or mercury perchloride (2 grains to 1 ounce of water), or they may be frequently painted with carbolic acid. The better and quicker method is to remove the nails under an anæsthetic, and dress the nail bed continuously with iodine until regrowth has occurred.

Trichophytides, Microsporides, Epidermophytides, Favides. Comparable to the tuberculides is a group of eruptions associated with infection of the skin by various species of ringworm fungi; their occurrence depends on sensitisation of the skin as a whole to the antigen contained in the fungi and, as a rule, on entry into the general circulation either of the fungus elements themselves, or of the antigen-containing substance (trichophytin, microsporin, etc.). It is possible that, when the eruption is localised to the neighbourhood of the primary site of infection, contact of the antigen with the sensitised skin may occur, not through the blood-stream, but by external auto-inoculation, or *viâ* the lymphatics. These allergic fungus eruptions are most commonly met with in the suppurating forms of trychophytosis (trichophytides) and in epidermophytosis. Microsporides are rare, except in children with microsporon infection of the scalp, in whom the application of X-rays for epilation may result in a temporary acute inflammatory reaction. Favus is, of course, now very uncommon in this country, but favides, similar to the usual lichenoid trichophytide, have been described as occurring, particularly after X-ray treatment of the scalp.

The vesicular eczematoid epidermophytide has already been described. The following varieties of trichophytides have been recognised: (*a*) *The Papular Lichenoid Trichophytide* (lichen trichophyticus). This is by far the commonest, and is comparable to lichen scrofulosorum. The lesions consist of flat or conical papules, usually follicular, reddish or brownish in colour, and sometimes capped by a scale or tiny pustule. Like lichen scrofulosorum, they tend to be grouped, and appear chiefly on the trunk and limbs, rarely on the face. The follicular lesions may develop horny spines (one variety of lichen spinulosus). A corymbose form of the eruption has been described by Jadassohn and Saeves, similar to a corymbose syphilide. (*b*) *The Vesicular and Pustular Trichophytides.* (*c*) *The Eczematoid Trichophytide.* This is merely a variety of the lichenoid type, in which the lesions are closely set, and form scaly confluent patches, similar to the eczematoid tuberculide (dermatitis scrofulosa). (*d*) *The Scarlatiniform Trichophytide.* A generalised erythematous rash, resembling that of scarlet fever, accompanied by fever, enlargement and even suppuration of the lymphatic glands, may rarely precede the development of a papular or papulopustular trichophytide. (*e*) *The Nodular Trichophytide.* Several cases have been described with severe kerion, in which, in addition to a lichenoid trichophytide, subcutaneous nodules, like those of erythema nodosum, appeared. In Brüusgaard's case the fungus was actually found microscopically in the nodules and cultivated from them (**26**). (*f*) *Erythema multiforme trichophyticum.* This is the rarest of all, but authentic cases have been described.

In most cases of trichophytosis the local infection is not severe, and there is little or no constitutional reaction; careful examination of the trunk and limbs may reveal a lichenoid trichophytide, which has usually escaped the notice of the patient. In some cases, however, both the primary local inflammation and

the general symptoms may be intense. There is suppuration with surrounding œdema of the initial lesion, enlargement of the neighbouring lymphatic glands, which may suppurate and break down, pyrexia, generalised adenitis, a palpable spleen, swelling of the joints, a polymorphonuclear leucocytosis, and an extensive eruption of one or more of the trichophytides.

Pathology. A great deal of experimental work has been done in order to determine the exact pathogenesis of these eruptions. Neisser and Plato, in 1902, prepared an extract from ringworm fungi, which they named trichophytin, and which is analogous to tuberculin. In persons with the deep, suppurative type of ringworm, injection of trichophytin produces general and focal reactions, as does tuberculin in tuberculosis, and with it positive cutaneous and intracutaneous tests are obtained, which indicate a specific general allergic state of the skin ; this state persists for years after the infection is cured. Normal controls and those with the *superficial* forms of ringworm give negative reactions. Apart from a general and focal reaction, injection of trichophytin may provoke an outbreak of a trichophytide eruption. Experimental inoculation of the skin of animals, *e.g.* the guinea-pig or rabbit, with certain ringworm fungi (*Trichophyton gypseum, Achorion quinckeanum*) produces lesions which heal spontaneously, leaving a lasting cutaneous allergy that prevents further successful inoculations, or at any rate, causes the secondary lesions to be short-lived and abortive. The same is true in human beings, for a deep-seated trichophytosis confers immunity in the sense that second attacks are very rare ; this, however, is doubtless due to the allergic state of the skin leading to the rapid destruction of the re-inoculated fungus, rather than to true immunity (cp. Koch's phenomenon in tuberculosis).

It has been shown by Bloch, first, that animal immunity to ringworm can only be produced by inoculating the skin, subcutaneous or intraperitoneal inoculations being ineffective ; secondly, that in a sensitised person the sensitiveness is in the skin cell itself, for by transplanting two pieces of skin, one from a sensitised and one from a non-sensitised person, on to a normal person, the piece from the sensitised person, after the graft had healed, gave a positive cutaneous reaction to trichophytin, whereas the other piece and the subject's own skin gave negative results. That in cases of trichophytosis with trichophytide eruptions the fungus elements pass into the general circulation is certain, for positive blood-cultures have been obtained, and the severer forms of trichophytide, *e.g.* the nodose variety, are probably caused by actual embolism of these in the dermic or subcutaneous vessels, and their rapid lysis by the sensitised skin, with liberation of the antigenic substance. Bloch, however, produced a scarlatiniform erythema, and later a typical lichenoid trichophytide, by injection of trichophytin in a boy who had had a severe ringworm infection but was cured. It is possible, therefore, that the milder trichophytides are due to absorption of the antigenic substance from the primary site of infection, and not to the hæmatogenous spread of the actual fungus elements.

We thus see how closely in their pathogenesis the syphilides, tuberculides, and trichophytides are related. These infections may result in a high degree of allergy, whereby the tissue-cells, particularly of the skin, become sensitised, so that, when the dissemination through the blood-stream of the infective organism, or, in some cases, of its toxin, *e.g.* tuberculin and trichophytin, takes place, a variety of eruptions—or cuti-reactions—occur, representing defensive reactions against superinfection, and resulting in the destruction of the organism or toxin *in situ*. Recently eruptions comparable to the trichophytides, but chiefly of the maculo-squamous or eczematoid type, have been described in connection with Monilia infections (levurides).

TINEA VERSICOLOR

This is a common affection of the skin, produced by contagion, and fostered by warmth and moisture. It is more frequent in men, and especially in those

who wear flannel underclothing. It is not often conveyed directly by contact—for instance, from husband to wife.

The disease begins as a small circular spot, of a yellowish-brown colour, which is slightly raised above the skin, and from which a few whitish scales can easily be detached by scraping with the finger nail or a scalpel. The patches extend, and fresh ones form, so that soon a large part of the chest, where it is commonly seen first, is covered with a brown or brownish-yellow irregular patch, with a convex or scalloped margin; and on the healthy skin adjacent are numerous small isolated patches from $\frac{1}{4}$ to $\frac{1}{2}$ inch in diameter. The disease occurs only on covered parts, and is most abundant on the front and back of the chest and the abdomen. The scrapings examined in liquor potassæ under the microscope show epithelial plates with the specific fungus, *Microsporon furfur*, forming a network of branching mycelial threads, scattered among which are little groups of the relatively large conidia, like bunches of grapes. The affection does not cause much trouble beyond some itching, and is frequently ignored by the patient; but the great extent which the discoloration may sometimes reach has led to its being mistaken for Addison's disease and other pigmentary affections such as vitiligo. The peculiar colour, the convex edge, and the ready desquamation of the surface should be quite distinctive, and the diagnosis is at once confirmed by the microscope.

Treatment. It is quickly cured by rubbing in lotions of sodium hyposulphite (1 in 8) or of sulphurous acid (1 in 4), or a paste containing sulphur, resorcin, and salicylic acid. It may, however, return if the same underclothing is used without thorough washing and disinfection.

Erythrasma. This eruption is most commonly seen in adult or aged men of all social classes; it is rare in women and never occurs in children. It causes no inconvenience, apart from slight itching after sweating, and is often discovered accidentally. Its site of election is the genito-crural fold and the inner surface of the adjacent portion of the thigh; it seldom invades the scrotum or pubis, but may rarely occur in the axillæ. It consists of brownish or yellowish-rose patches, hardly raised above the surface of the skin, slightly scaly, and never vesicular; the margins are sharply-defined but, unlike those of tinea cruris, are not raised. Occasionally outlying oval patches are seen on the abdomen and thighs. The disease is only slightly contagious.

The cause is an infection of the horny layer with the *Microsporon minutissimum*, the mycelium of which is very fine and the spores very small. It may be seen by examining scales in liq. potassæ with a $\frac{1}{12}$-inch oil-immersion lens.

The differential **diagnosis** from tinea cruris is not difficult, since the latter is redder in colour, has raised edges, tends to spread down the thighs and on to the scrotum and pubis, is often vesicular, and has a much more rapid evolution. Intertrigo due to streptococcal or Monilia infection is more inflammatory and usually moist. **Treatment.** Whitfield's benzoic-salicylic acid is effective, but must be used for a considerable time to prevent relapse.

Lepothrix (*Trichomycosis palmellina. T. nodosa*). This condition is met with all over the world, usually in those careless of their personal cleanliness. It affects the hairs of the axillæ and pubis, which become surrounded with yellowish, reddish or black concretions, usually forming irregular nodules along the shafts. These are seen microscopically to consist of masses of micrococci, embedded in a homogeneous viscid substance. According to Castellani, the yellow variety is due to a fungus, *Nocardia tenuis*: the red to the same fungus in symbiosis with a red pigment-producing coccus; and the black to the nocardia with a black pigment-producing coccus. Most cases of so-called chromidrosis are due to lepothrix.

Treatment. The affected parts should be cleaned with benzine, and then swabbed with an alcoholic solution of perchloride of mercury (1/2000), or of formalin (2 per cent.). It may be advisable to shave the hair.

Oïdiomycoses During recent years the importance of yeast-like organisms in the causation of certain dermatoses has become increasingly recognised. The pityrosporon of Malassez, which belongs to this group, has already been described. The exact classification of these organisms is difficult, and will not be discussed. They resemble yeasts in that they are round or oval and multiply by budding, but belong to a lower order and are classed as fungi imperfecti. One family, the *Cryptococcaceæ*, includes the genera cryptococcus, torula, and probably pityrosporon. Another, the *Oösporaceæ*, includes oöspora, oïdia, and monilia. The latter form long and branched mycelia when growing in the skin, the former do not. Apart from the pityrosporon, most of the pathogenic organisms so far investigated belong to the genus *Monilia*, of which the thrush fungus, *M. Albicans* and *M. pinoyi*, are the most important.

The types of eruption caused by Monilia may be classified in the following way (**27**): (1) *Generalised Type.* This is met with chiefly in patients undergoing treatment by the continuous bath, which is employed principally in Vienna. The lesions consist of vesicles, papules, and scaly erythematous patches, and involve particularly the axillæ, knees, and hands: but the eruption may be widespread. (2) *Infantile Type.* This is seen in nursing infants, and is often associated with thrush of the mucous membranes (*q.v.*). The eruption usually appears first around the anus, and spreads over the buttocks, genitals, thighs and abdomen, whence it may extend to the axillæ, neck and face. It is composed of vesicles, pustules, and erythematous plaques with central scaling; the vesicles and pustules rupture, leaving a fringe of horny layer, from which the infection may spread to form erythemato-squamous patches with raised borders. This type may complicate the infantile erythema of Jacquet. (3) *Intertriginous Type.* This is the commonest type of all, and has to be distinguished from intertrigo due to streptococcal or ringworm infection. It is seen in the groins, the internatal cleft, the axillæ, under the breasts in women, and in the hypogastric fold of obese persons. The eruption involves chiefly the areas in which the opposing surfaces of skin are in contact, forming scaly patches or superficial erosions with a collarette of undermined horny layer at their edges, but outlying erythemato-squamous lesions also occur. (4) *Interdigital Type.* Formerly known as "erosio interdigitalis blastomycetica," this type is met with most commonly in those whose hands are constantly wet, *e.g.* washerwomen and bar-tenders. The third interdigital space is most likely to be affected. The eruption begins as groups of vesicles, which rupture leaving a raw surface with a margin of thick sodden epithelium. (5) *Infection of the Nails.* Various forms of onychia or paronychia, due to Monilia, have been described. Subungual abscesses and hyperkeratosis of the nail-plate occur, but more characteristic is a paronychia, in which the nail-fold becomes very swollen over a considerable area. Recurrent acute attacks of inflammation with periods of remission are the rule. The nail-plates become dystrophic.

Apart from these types of monilia infection, the writer has met with chronic cases of eczematoid and intertriginous dermatitis of the hands and feet, resembling eczematoid ringworm, due to this organism. They are often extremely resistant to treatment.

Diagnosis. Microscopical examination and cultures are necessary to establish the diagnosis. In potash preparations the mycelia are seen to be long, thin, non-septate as a rule, and with short lateral buds; with them occur numerous groups of spores. On culture the organism grows in profusion and usually in pure culture, which is not the case if it be merely a saprophytic contamination.

Treatment. Surface infections with monilia may usually be treated successfully by painting with dilute tincture of iodine, or by rubbing in the benzoic-salicylic ointment recommended for epidermophytosis. More effective, perhaps, is a 2 to 3 per cent. solution of gentian violet in 25 per cent. spirit. For the paronychia, pure carbolic acid or undiluted monsol is applied beneath the

raised nail-fold on cotton-wool, twisted around a match-stick sharpened flat, and swept from side to side. With monsol the applications can be made daily, with carbolic acid every four or five days.

Spirochætal Diseases

Syphilis	*Treponema pallidum* (p. 104).
Frambœsia (yaws) . .	*Treponema pertenue* (p. 1030).

VENEREAL WARTS

(*Condyloma vel verruca acuminata*)

Venereal warts are seen in both sexes. In men they occur chiefly in the furrow behind the glans penis, and on the corona and frenum, but may involve the whole prepuce and even the urethral orifice. In women they are seen on the vestibule, the fourchette, and the clitoris, and may spread over the whole vulva to the groins, anus, and perinæum. Rarely they are met with in the axillæ and on the scalp.

They consist of papillomatous vegetations, pink or brownish-red in colour, sessile and lobulated, or filiform and elongated. In women they may form enormous cauliflower-like masses, moist and foul-smelling. Being auto-inoculable, they tend to involve contiguous surfaces.

Ætiology. Favre and Civatte have shown that the causal organism is almost certainly a spirillum, which is found in large numbers, both extra- and intra-cellularly. Lack of personal cleanliness, moisture, heat, and irritating discharges, which macerate the epidermis, favour their development. Gonorrhœa is a frequent though not essential predisposing cause, and pregnancy would seem to be a factor of importance.

Anatomy. The vegetations consist of filiform outgrowths of young connective tissue, containing numerous large blood vessels, and covered by a thickened, actively growing Malpighian layer, the cells of which are in a state of rapid multiplication. The horny layer is thinned.

Treatment. Scrupulous cleanliness, and the use of astringent lotions and a dusting powder, containing salicylic and boric acids, may cause their disappearance. In resistant cases the X-rays should be employed, or the vegetations may be removed with a curette.

Protozoal Diseases

Leishmaniasis (oriental sore)	*Leishmania* (p. 1052).
Amœbiasis. . . .	*Entamœba histolytica* (p. 1056).

Amœbiasis of the skin was first described by Engman and Heithaus in a child suffering from amœbic dysentery, and must be excessively rare.

Metazoal Diseases

Various animal parasites may infest the human skin, and give rise to lesions or eruptions, which are, as a rule, characteristic. Lice, fleas, bugs and mosquitoes are examples of parasitic insects; several varieties of acarus, *e.g.* the *Sarcoptes scabiei hominis*, the cause of human scabies, the *Leptus autumnalis* or "harvest bug," the *Ixodes ricinus* or "wood-louse," the *Pediculoïdes ventricosus*, the cause of "grain-itch," and the varieties of Sarcoptes, parasitic on animals such as the dog, cat, sheep, and pig, may all invade human beings. Lastly, certain worms and larvæ may enter the skin, *e.g.* the guinea-worm, the larva of *anchylostoma duodenale*, and the larva of certain dipterous insects—*larva migrans*.

The pediculi or lice which infest the human race are of three species: *Pediculus capitis*, or head louse; *P. corporis*, *vel vestimentorum*, or body louse; and *P. pubis*, or crab louse.

PEDICULUS CAPITIS

The head louse is about 2 mm. long by 1 broad, and breeds amongst the hairs of the scalp. It is of a greyish-yellow colour, and there are black marks on either side at the junctions of the seven abdominal segments. Its ova are found adherent to the hairs and are called nits. They are about ½ mm. in length, whitish, somewhat conical in shape, with the apex always towards the scalp; and they are fixed to the hair by a cylindrical sheath of chitinous material extending some little distance beyond the apex. The irritation of the pediculus leads to constant scratching and pustular eczema, or contagious impetigo. This eruption is most common and severe in the occipital region, and the suboccipital glands are often enlarged as a consequence, and may suppurate.

The **Diagnosis** is not difficult. If the pediculi are not at once seen, the nits, which are readily distinguished on careful examination from scurf, will show at once that there are or have been pediculi. The position of the crusts at the back of the head is also strongly in favour of pediculi.

Treatment. The parasites are rapidly destroyed by vaseline, which blocks their respiratory tubes, or by benzol. Sabouraud recommends a mixture of 50 drops of xylol and 50 grammes of vaseline. This is smeared thoroughly all over the head, and left on for twelve hours; the hair is then shampooed, and the nits removed by combing with dilute acetic acid. A solution of carbolic acid (1 in 40) is also effective; the hair should be saturated with it and wrapped in a towel for an hour or two before shampooing. The secondary impetigo may require treatment with mercurial ointments, but, as a rule, quickly disappears when the parasites are destroyed.

PEDICULUS VESTIMENTORUM (*See Plate 59, B, p. 878*)

The body louse is larger than the head louse, being nearly 3 mm. in length and from 1 to 1½ mm. in breadth. It is of a light greyish colour, except when gorged with blood, which gives it a dark reddish hue. The abdomen, consisting of eight segments, has no black markings. The parasites infest the underclothing of the host, where they may be found in the seams. The ova are deposited in the clothing, but, as was discovered in the war, may be attached to the body-hair, particularly of the pubic region. The fecundity of the females is enormous, and Nuttall estimated that a single parasite during her lifetime produces 275 to 300 eggs, of which seventy are deposited daily. Body-lice can exist without food for three days, and are resistant to cold, but they are killed by a temperature of 80° C.

The bites of these parasites give rise to urticated papules, which are intensely itchy; lice appear to feed chiefly at night time, when, as in scabies, the irritation is most severe. In those persons who are chronically lousy, some tolerance is established, and, although they continue to scratch, little complaint of itching may be made.

As a result of scratching, *linear* excoriations are produced and correspond to the *lignes de grattage*. These are usually best seen over the shoulders. Secondary pyogenic infection is likely to occur, so that crusted impetiginous lesions, and the deep ecthymatous ulcers which complicated the severe cases of pediculosis met with in the war, may develop.

The deeper excoriations are succeeded by pale linear scars.

The sites of election of these various lesions are the shoulders, posterior axillary folds, the flanks, the sacral region and upper parts of the buttocks, and the anterior and outer surfaces of the thighs. In long-standing cases the skin becomes dry, harsh, scaly, and deeply-pigmented ("Vagabond's disease"). The pigmentation, accompanied by excoriations and their resulting scars, predominates on the sites of election, but may become generalised and so intense as to resemble that of Addison's disease. Moreover, it may be present in the

buccal mucous membrane, and, since severe pediculosis may produce asthenia and cachexia, the diagnosis from this disease may be difficult. The localisation of the pigmentation in the mouth and the asthenia suggest that the venom of the pediculi has a toxic action on the endocrine-sympathetic system, and it is of interest that during the war the writer observed several cases of vitiligo in which this pigmentary disturbance had evidently been provoked by pediculosis (**28**).

The main points in the differential diagnosis between pediculosis corporis and scabies (*q.v.*) are as follows :—

Pediculosis Corporis	*Scabies*
Sites of election. Shoulders and *posterior* axillary folds, sacral region and *upper* parts of the buttocks, flanks, anterior and outer portions of the thighs.	Fingers, anterior surfaces of the wrists, elbows, *anterior* axillary folds, nipples (in women), abdomen, *lower* parts of the buttocks over the ischial tuberosities, legs, ankles, and feet.
Lesions. The *scratch-marks* are *linear* blood-crusts corresponding to the *lignes de grattage.*	The *scratch-marks* are pin-point crusts situated at the apices of erected follicles.
Other lesions are urticated papules from recent bites ; impetiginous and ecthymatous sores ; and superficial linear scars.	Other lesions are burrows ; vesicles and pustules ; elongated and indurated papules in the anterior axillary folds, on the scrotum, and over the ischial tuberosities ; eczematisation, impetiginous crusts and boils.
Pigmentation of the sites of election is intense, and may become generalised.	Pigmentation is slight or absent.

It will be observed that the shoulders and back, which are the parts chiefly affected in pediculosis, are relatively spared in scabies. Apart from such conditions as obtain in an army on active service, pediculosis corporis is met with almost exclusively in old persons of both sexes, even those in comfortable circumstances, and in tramps. It has to be distinguished from true senile pruritus and from that dependent on metabolic disorders, *e.g.* hyperglycæmia and renal or hepatic insufficiency ; nervous diseases, such as tabes dorsalis ; psychological disturbances ; and from the prurigo of lymphadenoma, leukæmia, and pregnancy. It should be remembered that typhus, trench and relapsing fevers are transmitted by lice.

Treatment. Ung. hydrarg. ammoniati or ung. staphysagriæ, smeared over the skin, will kill the pediculi. The clothes, in which the eggs are certainly incubating, should be completely changed ; and they must be baked if they are to be worn again. The necessity of removing or destroying ova attached to the body-hair must be remembered. N.C.I. (naphtholine 96, creosote 2, iodoform 2) and pyrethrum powders have been used to prevent reinfection, but both may cause a severe dermatitis in certain subjects.

PEDICULUS PUBIS

The crab louse is smaller than either of the other species, measuring from 1 to 1½ mm. long, and from 1 to 1½ broad. It has an almost square body, and six long legs, with claws by which it clings firmly to the hairs of the part. It is not only found in the pubic and axillary hair, and in that over the sternum, but is occasionally conveyed to the eyebrows, eyelashes, whiskers, or beard. The eggs are attached to the hairs close to the skin. Itching leads to scratching, and an eczematous rash is the result. In many cases bluish-grey macules (*maculæ cæruleæ, taches bleues, taches ombrées*) about the size of a finger nail are seen in the skin of the lower abdomen and thighs, and on the sides of the thorax, if the axillary and thoracic hair is affected. They are absolutely characteristic of

crab-louse infection, though formerly they were thought to be symptomatic of typhus and even typhoid fever. The pigment in these macules is derived from the salivary glands of the louse.

Treatment. The unguentum hydrargyri B.P. is a favourite remedy among the public, and it is very effectual, but it is apt to cause pustular folliculitis or even acute mercurial dermatitis. A safer method is first to soak the infected parts for an hour with a solution of carbolic acid (1 in 40) applied on lint, and then to rub in an ointment containing yellow oxide of mercury, ammoniated mercury, or balsam of Peru for a few days. Benzol, or a mixture of benzol and xylol, kills the parasites instantly, and one thorough application suffices for cure, but it is advisable to employ a mild mercurial ointment afterwards lest some of the ova may have escaped destruction. The pubic hair need never be shaved. It should be remembered that, although infection usually takes place from sexual intercourse, it may be acquired in other ways, as from dirty closet seats.

SCABIES (*See Plate 59, A, p. 878*)

Scabies, or itch, is a multiform disease of the skin, consisting of papules, vesicles, pustules, and sometimes bullæ, due to the irritation of the itch acarus, *Sarcoptes hominis*.

The female acarus is oval in shape, $\frac{1}{70}$ inch in length, presents in front four little nipple-shaped processes provided with suckers on stalks, and behind four similar processes provided with long bristles. The male is smaller, has four suckers in front, two suckers and two bristles behind. The female after impregnation bores her way under the skin in an oblique direction, so that, as the superficial layers of the epidermis are detached by friction, she still remains at the same depth from the surface. As she proceeds she lays her eggs, one or two daily, it is said, and she may thus burrow through the skin in an irregular line for $\frac{1}{3}$ or $\frac{1}{2}$ inch. Such a burrow (*cuniculus*), or "run," may be recognised on the surface of the skin by the following features: At one end the epidermis is broken or frayed, and the free edges are dirty; at the other end is a minute white pointed elevation, in which the acarus lies; the burrow itself between these points is a sinuous black line. The whole burrow may be snipped off with a pair of scissors curved on the flat, or shaved off with a scalpel; and if it be then moistened with liq. potassæ and examined, there will be seen the female acarus, and behind her, filling the burrow, her eggs in every stage of incubation, with minute black spots of excremental matter among them. As the skin desquamates the most developed ova come to the surface, and are hatched. The male does not burrow, but remains on the surface, where he may be sometimes accidentally caught.

Symptoms. As a result of the invasion of the acarus there is considerable itching, with consequent scratching, pus infection, and dermatitis of variable extent and character. The itching is mild or severe, but not generally so bad as that caused by pediculi, and the scratching rarely leaves scars or causes pigmentation. It is worse at night when the patient is warm in bed. The disease causes erection of the pilo-sebaceous follicles, owing to contraction of the pilomotor muscles, and their summits are excoriated by scratching, so that the scratch-marks consist of pin-point blood-crusts at the apices of the erected follicles, thus differing from the linear scratch-marks of pediculosis corporis. They are usually well seen on the abdomen and limbs. In many cases elongated inflammatory papules of considerable size, in which the acarus may be found to lie at some depth, are present. These are pathognomonic, and occur on the anterior axillar folds, the scrotum, penis, over the ischial tuberosities, and around the elbows. Their recognition is of great importance, since their presence clinches the diagnosis even when burrows cannot be detected. Apart from these there occur in the early stages erythematous and urticarial lesions, and later vesicles, pustules, impetigo, ecthyma, and eczematisation; the last may be of the dysidrosiform type on the extremities, but elsewhere consists of crusted patches

of varying size. A vesicle or pustule may form at the extremity of a burrow where the acarus lies. Purulent bullæ are not uncommon on the palms and soles of young children. In women eczematisation of the nipples and areolæ is frequent, and this is nearly always due either to scabies or lactation. A moderate degree of eosinophilia and occasionally a transitory albuminuria indicate that the acari, like pediculi corporis, produce a toxin which is absorbed.

Sites of Election. These various lesions occur principally in the interdigital spaces of the hands and on the lateral borders of the fingers; the palms; the front of the wrists, particularly on the ulnar side; the elbows; the anterior axillary folds; the nipples in women; the abdomen; the foreskin and glans penis; the buttocks; over the ischial tuberosities; the thighs; the ankles and toes; and the soles of young children. Burrows are most likely to be seen on the fingers, wrists, elbows, penis, and in children on the soles. It will be observed that the face, neck, shoulders and back are spared, but in infants the face and the posterior fold of the neck may be involved from contact with the mother's breasts and wrists respectively.

For contagion with scabies to occur it is essential that an impregnated female acarus should be transmitted from an infected person. This may result directly and almost inevitably from sharing the bed of a scabietic, thus accounting for familial epidemics, and for the frequency of a venereal origin of the disease. Indirect transmission through sheets and clothing often occurs, and commercial travellers, who are compelled to sleep in small hotels, where clean sheets are not always provided, are particularly liable to infection in this way. It is doubtful whether it is possible to contract the disease by ordinary contact with an infected person during the daytime, although nurses who tend scabietics confined to bed may do so.

Diagnosis. The position of the lesions is an important guide to diagnosis. An itching eruption of mixed papules, vesicles, and pustules, occurring mainly about the fingers and wrists, and also in the other situations mentioned, should lead to a careful search. If a burrow can be found, the minute white elevation at the cleaner end should be looked for, and its epidermis carefully scratched through with the point of a needle; the acarus may then be picked out, as it readily adheres to the surface of the needle. If this cannot be done, it is best to snip off the whole burrow, and to examine for ova or fragments of the acarus under the microscope. Finally, where there has been much inflammation, so that burrows cannot be found, the crusts may be removed, boiled in a solution of potash or soda, the fluid allowed to settle in a conical glass, and the sediment examined for fragments of acarus.

Treatment. The successful treatment of scabies depends upon the thoroughness with which it is carried out. It is useless to tell the patient to rub in sulphur ointment "where it itches"; it is essential that all infected members of a household should be treated simultaneously; and the patient should be warned that, if there is still irritation of the skin after the prescribed treatment has been thoroughly performed, it will almost certainly be due to the application employed and not to a persistence of the infection.

The following method is usually successful:—

(1) On the first night, the patient should take a prolonged hot bath lasting about twenty minutes, to which Sulphaqua may be added. In the bath the skin of the whole body from the neck downwards should be thoroughly scrubbed with soap in order to open up all the burrows.

After the bath, the following ointment should be rubbed in thoroughly all over from the neck downwards, not forgetting the fingers and toes:—

℞. Sulph. præcip. . . . . gr. 30
Balsam Peruviani . . . . . gr. 20
Ung. Zinci to the ounce.

and the patient should get into old pyjamas, cotton socks and gloves.

(2) On the next two mornings and two evenings, further inunctions with the ointment should be made.

(3) On the third morning, a second bath should be taken, and the patient should put on entirely clean underlinen. It is important that all used under- and bed-linen should be disinfected.

Instead of the above ointment, Mitigal (Bayer) or " Danish " ointment may be employed. It is claimed that a single application of the latter suffices. After the treatment, the patient should apply a soothing cream or a zinc paste for a while.

Norwegian Scabies. This variety was first described by Danielssen and Boeck among lepers. It is characterised by extensive encrustation sometimes involving the whole skin, including the face and back. The crusts are formed of dried pus and scales, and are riddled with burrows containing countless parasites and ova. The nails are distorted and disintegrated, and harbour the acari. The condition was formerly thought to be due to infection with the acarus of the wolf, but is now known to be human scabies occurring in destitute, neglected persons of low mentality.

Animal Scabies (Sarcoptic mange). The sarcoptes of animals (dog, cat, horse, camel, pig, sheep, goat) may be transmitted to human beings, but they never form burrows. The parts affected are those that have been in contact with the animal. The lesions produced are small papulo-vesicles, often surrounded by urticated wheals, and recall somewhat those of papular urticaria. They are intensely itchy. Severe cases of horse scabies in man have been described, the eruption resembling a generalised pityriasis rubra ; innumerable parasites are found in the scales and crusts. As sarcoptes of animal origin do not burrow or breed in human skin, the disease is easily cured, a single inunction with sulphur ointment sufficing, providing the source of infection is removed or treated.

Grain-itch. This is an eruption consisting of urticarial wheals, with a central vesicle or pustule, which may become of considerable size and simulate the lesions of chicken-pox. Itching is intense, and there may be secondary pyogenic infection with slight pyrexia and malaise. A moderate leucocytosis and eosinophilia have been found. The eruption is caused by the *Pediculoides ventricosus*, which may infest straw and grain. It occurs in those who handle these, *e.g.* dock labourers and sailors, and infection from straw-mattresses has been recorded. The mite does not burrow, and is easily destroyed by sulphur ointment ; the clothing should be baked or fumigated.

Copra-itch. An eruption resembling scabies apart from the absence of burrows, and due to the *Tryglyphus longior*, which is present in copra dust. It is treated with sulphur or beta-naphthal ointments.

The following Diseases are Classified according to their Morphology.

THE ERYTHEMAS

The classification of the eruptions to be considered in this second group is admittedly unsatisfactory. Many of them are merely forms of cutaneous reaction to a variety of toxic or irritant substances, either of exogenous or endogenous origin, for example, certain erythemata, urticaria and eczema, and are manifestations of an allergic state of the skin (cp. the tuberculides and trichophytides). Their morphological differences depend upon the particular elements in the skin that are sensitised rather than on the nature of the antigen. It might be preferable to attempt to classify together these non-specific allergic eruptions ; such a group would include urticaria and angeioneurotic œdema, eczema, and certain prurigos, which are often associated or alternate with other allergic symptoms (see toxic idiopathies, p. 138), and some forms of generalised exfoliative dermatitis. In the present state of knowledge, however, it has been thought pre-

ferable to adhere to the morphological classification adopted in the previous edition.

There is little doubt that Erythema multiforme, E. nodosum and E. scarlatiniforme, particularly in their recurrent forms, may be due to sensitisation having occurred to some strain of a *Streptococcus longus*, and the same is probably true of some cases of Lupus erythematosus; but Erythema multiforme, Erythema nodosum, and Erythema scarlatiniforme may also be caused by sensitisation to a trichophyton, and Erythema nodosum, Lupus erythematosus and, perhaps, Erythema multiforme, may in some instances be tuberculides. Therefore, however unwilling one may be to ascribe eruptions with well-defined clinical characteristics to multiple causes, it must be accepted that these forms of erythema are syndromes, and not specific entities.

ERYTHEMA MULTIFORME (*See Plate 58, B, p. 833*)

Some authors are inclined to include under the heading of Erythema multiforme the ill-defined erythemato-urticarial rashes that may result from sensitisation to food-substances (*e.g.* pork, shell-fish), foreign serums (" serum rash "), various drugs, and many bacterial and protozoal toxins, but the classical form of the eruption known as *Erythema exudativum multiforme* is a clinical entity and should be separated from the above.

Symptoms. The eruption, which is often accompanied by sore throat, fever, pains in the joints and muscles, and gastro-intestinal disturbance, appears suddenly, at first almost invariably on the parts exposed to light, viz., the backs of the hands and wrists, the face and neck, and, in women, on the V-shaped area of the upper chest exposed by the cut of the blouse. It is bilaterally symmetrical, and later may involve the forearms, elbows, knees, ankles and feet; occasionally it is more or less generalised. The *mucous membranes* of the lips, cheeks, tongue, pharynx, and vulva are frequently involved, particularly in the bullous form, and in recurrent cases. Moreover, the mucous membranes may alone be affected by periodical attacks for years without any cutaneous lesions developing, and many cases of so-called recurrent stomatitis are really of this nature.

As the name suggests, there is considerable variety in the lesions produced. The most characteristic, seen typically on the backs of the hands and wrists, are raised, flat, disc-like erythematous papules, bluish-red in the centre, bright red or pink at the periphery; on palpation such a lesion gives to the finger a peculiar sensation as of an india-rubber cap stretched over the mouth of a bottle full of water. The centres of the lesions are often white, owing to the exudation of fluid, which may be sufficient to produce a vesicle or bulla (*E. bullosum*), and in some cases large, pemphigoid bullæ, surrounded by an erythematous halo, occur; sometimes actual hæmorrhage takes place in the centre of a papule (*Purpura urticans*). Moreover, the central parts may clear, leaving rings (*E. annulatum*), which by coalescence produce sinuous or scalloped patches (*E. gyratum*). Rarely a ring of erythema is surrounded by another right outside it, and this is followed by another farther out, while the first ring is beginning to fade. The different colours of the rings in various stages suggest the name *E. iris*. As many as four such rings may be seen at the same time, sometimes arranged concentrally around a central bulla (*Herpes iris*), which may occasionally be surrounded by one or more rings of smaller bullæ or vesicles. On the mucous membranes the lesions consist of flaccid bullæ, which are rapidly replaced by extremely painful erosions upon which a diphtheroid membrane forms; in some cases practically the entire buccal and pharyngeal mucous membranes are involved, and the pain and discomfort are such as to render eating almost impossible.

One of the most striking features of erythema multiforme is its tendency to recurrence; these recurrences occur at varying intervals, sometimes annually—as a rule in the spring—, sometimes every two or three months, and rarely a new

attack may begin before the lesions of a previous one have disappeared. Osler long ago emphasised the close association that exists between erythema multiforme, urticaria, purpura and erythema nodosum, and their connection with visceral disease, such as endo- or myocarditis, nephritis, and gastro-intestinal disturbances. This association is easily explained, because one cause of E. multiforme, E. nodosum, and purpura is an acute or chronic streptococcal infection, and urticaria may be due to sensitisation to the same organism. Apart from true erythema nodosum, there may rarely be seen in association with the usual superficial lesions of E. multiforme circumscribed intradermic or subcutaneous nodules, doubtless caused by emboli of streptococci. Another eruption, which occurs so frequently with erythema multiforme, particularly of the recurrent type, that the association cannot be merely fortuitous, is herpes simplex. Several patients have been observed in which a tendency to recurrent outbreaks of the two eruptions has been present, over a long period, and in two under the writer's care injection of an emulsion of herpes virus apparently produced immunity of considerable duration to both.

Ætiology. As has been said, erythema multiforme, like urticaria and some other forms of erythema, even in its most classical form, cannot be regarded as an absolutely specific reaction. The work of Landouzy would seem to prove that it, as well as erythema nodosum, may be a toxi-tuberculide. As the result (**29**) of inoculating guinea-pigs in series with blood taken from four cases during the attacks, Ramel concludes that the eruption is due to a tuberculous bacillæmia, and he considers that a preceding streptococcal infection, such as tonsillitis, is merely a provoking factor. His findings, however, have not been confirmed in this country (**30**). An erythema multiforme type of trichophytide has also been described, but in the great majority of cases erythema multiforme is probably due to sensitisation having occurred to a strain of *Streptoccocus longus*. Its association with acute rheumatism is too frequent to be a coincidence; it occurs in streptococcal septicæmia, and an attack may usher in a fatal streptococcal infective endocarditis. In a series of patients subject to recurrent attacks one or more foci of chronic streptococcal infection were invariably found, specific agglutinins and precipitins were present in the serum, injections of a vaccine prepared from the infecting strain of streptococcus often provoked focal reactions, *i.e.* the appearance of a few typical lesions on the skin or mucous membranes, and removal of accessible foci of infection, combined with the administration of an autogenous streptococcal vaccine over a long period, brought about a cessation of the attacks (**31**). The usual sources or portals of entry of infection are the tonsils, nasopharynx, teeth, nasal sinuses, and intestines, but possibly others, such as the prostate and cervix uteri, may be responsible. It is possible that in some cases erythema multiforme may be a widespread cutaneous reaction to invasion with the virus of herpes simplex. Exposure to sunlight is undoubtedly a factor in predisposing to an outbreak of the eruption and in determining its localisation.

Treatment. The patient should be put to bed, and the heart watched carefully for signs of endocarditis or myocarditis. Sodium salicylate or salicin, combined with alkalies, may be given, or quinine. Locally cooling lotions, such as lotio plumbi or lotio calaminæ, should be applied during the acute stage. In the bullous form of the eruption, when the mucous membrane of the mouth is involved, the pain and discomfort may be relieved by allowing the patient to suck the trochiscus kramcriæ et cocainæ B.P. and the trochiscus acidi carbolici B.P.

When the attack has subsided, a search should be made for some chronic focus of infection, such as the tonsils or teeth, and, if found, this should be dealt with. In recurrent cases a streptococcal vaccine, prepared from the infecting focus, and preferably injected intradermally, should be administered over a long period. For the anæmia, following the attack, iron should be given until the blood returns to normal.

Erythema Annulare Centrifugum. Numerous observers have described under various terms circinate or figurate erythematous eruptions, but these may be included under the descriptive title erythema annulare centrifugum, proposed by Darier. The lesions arise as raised erythematous papules, firm to the touch but less so than those of granuloma annulare. They rapidly become transformed, by spreading peripherally while clearing in the centre, into rings or semi-circles, which attain a varying size and then fade, leaving slight pigmentation with, perhaps, some desquamation. Sometimes gyrate figures are produced by irregular extension or breaking-up of the original annular lesions. The sites of election are the trunk and proximal segments of the limbs. New elements continue to arise, sometimes after an interval at sites of pre-existing ones, but, as a rule, few are present at any one time, and there is little tendency to bilateral symmetry. The affection may last for months or years, with intervals of freedom.

Ætiology. The eruption, in the writer's opinion, may be regarded as a connecting-link between erythema multiforme and granuloma annulare. A comparison may, perhaps, be made with the syphilides, erythema multiforme corresponding to the widespread secondary lesions, erythema annulare centrifugum to the asymmetrical circinate syphilides of the late secondary stage, and granuloma annulare to the serpiginous tertiary lesions. It is probable that, as with erythema multiforme and granuloma annulare, erythema annulare centrifugum is not a specific entity, but a reaction of the skin to more than one toxin. The writer's own observations suggest that, as a rule, it is a streptococcide.

Diagnosis. It has to be distinguished from granuloma annulare, the elements of which are harder to the touch, less acutely erythematous, of much slower evolution, and more persistent: from annular syphilides, which never extend rapidly and are of longer duration: and from erysipeloid.

Treatment. A history of previous acute illnesses, such as scarlet fever, tonsillitis, and puerperal fever, should be enquired for, and the presence of chronic foci of infection sought for and treated. The writer has found that intradermal injections of a streptococcal vaccine, prepared from various strains, are curative, at least in the majority of cases. The initial dose should be small—one to two million organisms—as severe local reactions often occur at the sites of injection; subsequent dosage depends upon the degree of reaction, and an increase should never be made as long as this is marked.

Granuloma Annulare. The elementary lesion of this rather rare eruption is a firm, pea-sized nodule, which is raised about $\frac{1}{16}$th of an inch or somewhat more above the surface. By excentric extension, or by the appearance of new nodules, annular patches of varying size are produced. Their surface is smooth, their edges sharply defined, and the colour ranges from reddish-white to a dull purple. The central areas of the rings are usually stained a dark lilac colour, and may be studded with minute pale nodules, which remain discrete and may persist after resolution of the raised border. By irregular involution crescentic or festooned patches result. The eruption occurs most frequently on the backs of the hands, wrists, elbows, ankles, knees, buttocks, and neck. As a rule, the number of lesions is small, but in two cases observed by the writer they were numerous, and by wide extension involved large areas. The evolution is slow, and there may be little tendency to spontaneous resolution. Ulceration never occurs, and there is no subsequent scarring.

Ætiology. Although usually seen in children and adolescents, granuloma annulare may occur in middle and even late life. Its relationship to erythema multiforme and erythema annulare centrifugum has already been discussed, and in a patient, subject to recurrent attacks of the former, the writer has observed the gradual development of typical granuloma annulare from a patch of erythema multiforme. Moreover, in patients with lupus erythematosus there may occasionally be seen nodular and annular lesions, indistinguishable

clinically from granuloma annulare, which may coexist with or become transformed into those characteristics of this disease. It is clear that all these eruptions are closely related, and, although some consider that they are diseases *sui generis* and caused by infection with unknown specific organisms, it is probable that they represent a variety of non-specific reactions to different toxins. Granuloma annulare is considered to be, like lupus erythematosus, of tuberculous origin by many and this may be so in some cases, but in others it is more probably a streptococcide. Forman and the writer found in a series of eleven cases that 73 per cent. gave positive intradermal tests to *Streptococcus hæmolyticus*, 50 per cent. to *S. viridans*, and one case only (9 per cent.) reacted to tuberculin, the reaction being strongly positive. Moreover, in two widespread cases, observed by the writer, there was no evidence of tuberculosis. In one the eruption followed a severe streptococcal septicæmia after childbirth, and the other had suffered from chronic streptococcal infection for years. Both responded remarkably to intradermal injections of streptococcal vaccine, the reactions to which were initially severe, and this method of treatment has proved successful in other cases.

Morbid Anatomy. There is a central area of coagulation necrosis in the corium, surrounded by an infiltration of lymphocytes, epitheloid, and connective-tissue cells. Plasma and giant cells may be seen. The epidermis is intact.

Treatment. The local application of salicylic acid plaster may cause the lesions to disappear, and they yield to radiotherapy. The patient should be investigated for the presence of tuberculous or streptococcal infection, and treated accordingly. Darier advises tuberculin intradermally, and, as stated, the writer has found intradermal injections of streptococcal vaccine usually curative. It has been observed that a patch often disappears after excision of a small portion for microscopical examination.

ERYTHEMA NODOSUM

This consists of oval or circular solid flat elevations of the skin, from ½ inch to 1¼ inch in diameter, bright or dusky red in colour, gradually shading off into the surrounding skin, tender to the touch, and perhaps pitting slightly on pressure. These occur most often over the whole length of both tibiæ, and not infrequently over both ulnæ. Though rare in other parts, they may be seen on the calf, on the thighs, over the scapulæ, and over the condyles of the humerus. They come out more or less in crops, last seven or ten days, and gradually subside with bruise-like staining. They may become soft and fluctuate, but never suppurate. They are most common in children and people under twenty years of age, and more frequent in girls than in boys. The appearance of the eruption is often preceded by a sore throat or tonsillitis, and is accompanied by some pyrexia, general malaise, pains in the joints, and sometimes by actual arthritis comparable to that of rhematic fever.

Ætiology. Erythema nodosum may be regarded as the dermo-hypodermic counterpart of erythema multiforme, with which it may occasionally co-exist. There has been much discussion in recent years concerning its causation, and chiefly as regards its relationship to tuberculosis. Some consider that it may be due to infection with a specific micro-organism, for example, that which Rosenow claimed to have isolated from the nodes and blood in six patients with the disease, and Trousseau classed it among the exanthemata. There is general agreement that in some cases it may, like erythema multiforme, be a manifestation of streptococcal or rheumatic infection, and occasionally it is associated with endocarditis and pericarditis. Streptococci have been cultivated from the blood during an attack. Others have stressed its frequency in patients with gonorrhœa, and a syphilitic variety has been described. Certain drugs, *e.g.* iodides, antipyrine, may provoke a similar eruption.

Evidence has now, however, accumulated to suggest that in the majority of

instances it is of tuberculous origin. This view was maintained by Landouzy in 1907, and he later claimed (**32**) to have demonstrated a tubercle bacillus in a vessel of a nodule, and to have tuberculised a guinea-pig with another portion of the same nodule. Strongly positive Mantoux tests are obtained in a high proportion of cases. In a series of eighteen patients Forman and the writer (**33**) found that 54 per cent. gave a strongly positive and 38 per cent. a positive reaction to tuberculin—a total of 92 per cent.; whereas in Erythema multiforme only 19 per cent. gave strongly positive and 23 per cent. positive reactions—a total of 42 per cent.

It would seem that Erythema nodosum is usually associated with a recent tuberculous infection, the primary site of inoculation being often small and immediately subpleural, and the hilar glands being rapidly and more extensively involved (**34**). It is probably from the latter that the invasion of the blood-stream by tubercle bacilli, on which the eruption depends, takes place. Not infrequently a history of recent contact with a person suffering from open tuberculosis is obtained. In other cases it may herald the reactivation of a latent tuberculous focus (*cp.* Erythema induratum), or may precede the adult form of pulmonary tuberculosis. Whitwell has recorded a case in which erythema nodosum followed a primary tuberculous infection of the skin with invasion of the neighbouring lymph-glands, tubercle bacilli being obtained from both sites. Subacute cases which form a transition between E. nodosum and E. induratum have been described.

Lastly, E. nodosum may be a rare form of trichophytide.

Bloch obtained focal reactions with injection of trichophytin, and Bruusgaard claims to have demonstrated spores in the nodules of his case, and to have cultivated the Trichophyton gypseum from the lesions, which was the fungus responsible for the original ringworm infection. To sum up, erythema nodosum is an allergic dermo-hypodermic reaction to emboli of circulating organisms, of which the tubercle bacillus would appear to be most frequently responsible.

Morbid Anatomy. In early lesions there is seen thrombosis of the subcutaneous arterioles and a dense infiltration with polymorphonuclear leucocytes of the surrounding subcutaneous fat. In later lesions, the polymorphonuclear leucocytes disappear and are replaced by lymphocytes. Giant-cells may be present during the process of repair, but are fat-phagocytes, and not indicative of a tuberculous lesion.

Prognosis. This must be guarded in cases in which a tuberculous infection is apparently responsible for the eruption. Several instances have been recorded in which manifestations of active tuberculosis have supervened within six months of an attack of erythema nodosum, and in some death from miliary tuberculosis has occurred. The outlook is graver in children and adolescents, since in them a tuberculous origin is more likely, whereas it would appear that in adults infection of the throat with a hæmolytic streptococcus is often responsible.

Treatment. The patient should remain in bed pending the results of investigations, which should include a clinical and radiographic examination of the chest, tuberculin tests, and, in cases suspected to be of streptococcal origin, an estimation of the anti-streptolysin in the blood. Careful inquiry should be made for previous contact with a person suffering from open tuberculosis. Such contact explains the epidemics of Erythema nodosum that sometimes occur in families and schools. Forman observed a family of eight children, five of whom developed the eruption after being in contact with an older member of the family with active phthisis. If investigation reveals evidence of tuberculosis, the case should be notified, and the usual methods employed to combat this disease should be instituted at once. In any case, the patient should be kept under close observation for several months. If infection with a hæmolytic streptococcus appears to be causal, chronic foci, such as the tonsils, should be dealt with, and, should recurrent attacks occur, intradermal injections of an

autogenous or stock streptococcal vaccine should be given, as advised for recurrent Erythema multiforme. In all cases, a vitamin-rich dietary and calcium salts should be prescribed, and the patient should live out of doors as much as possible.

ERYTHEMA PERNIO

(*Chilblain.*)

Chilblains consist of bluish-red tumefactions of the skin, which occur in certain persons on exposure to cold or during a sudden drop in atmospheric temperature. They are seen most commonly on the fingers and toes and on other parts of the hands and feet, but the ears, tip of the nose, cheeks, and, in young girls with erythrocyanosis, the lower parts of the legs may be affected. They may be circumscribed or diffuse. They give rise to sensations of itching, tingling, or actual pain. As a rule they gradually subside, but sometimes the serous exudation in the corium is sufficient to raise the epidermis so as to form a thick-walled vesicle, which ruptures, leaving an indolent ulceration ("open chilblain"); this may become secondarily infected with pyogenic bacteria. Healing takes place slowly with or without scar-formation. In other cases there is no ulceration, but the overlying horny layer becomes thickened and then splits, causing painful fissures. Severe ulcerated chilblains may sometimes completely incapacitate the patient from manual work or even from walking.

Ætiology. Although usually seen in children and adolescents, chilblains may occur in middle and late life. They naturally form more readily in those with a poor peripheral circulation ("chilblain circulation") and a tendency to "dead fingers," dependent upon spasmodic contraction of the arteries, or to acrocyanosis. But some persons of this type never develop chilblains, and conversely the latter may occur in those without this tendency. Cold, particularly damp cold, is the immediate provoking factor, and a sojourn in a damp place or house may cause the appearance of chilblains in a person previously immune. Malnutrition, anæmia, and arterial hypotension are predisposing factors, and many victims are tubercular subjects.

It is clear that underaction of the accelerator group of endocrine glands—thyroid, pituitary, and ovaries—is probably of ætiological significance; a deficiency of the circulating pituitary hormone, which is the chief regulator of capillary tone and appears to decrease the permeability of the walls of the minute vessels, may well be the most important single factor in the genesis of acrocyanosis and chilblains.

Pathology. Normally, exposure of the skin to cold causes contraction of the small vessels and capillaries with consequent pallor; this is followed by a reaction in the form of an erythema, due to vaso-dilatation, which gradually subsides. If, however, the vasomotor tone is deficient, the vessels and capillaries remain distended, and serum, or even blood, escapes from the tissues, the permeability of the walls being increased. Chilblains may therefore be said to result from static erythema with œdema.

Diagnosis. Chilblains have to be distinguished from papulo-necrotic tuberculides, lupus erythematosus, and, when they occur on the legs of girls with erythrocyanosis, from erythema induratum, with all of which conditions they are likely to co-exist, since these are met with in persons with a chilblain circulation.

Treatment. The state of the patient's general health and the mode of life must be considered. A generous dietary with plenty of milk, eggs, and butter, if well tolerated, should be prescribed, and this should be supplemented in winter with cod-liver oil or one of the proprietary vitamin-concentrates. The administration of small doses of thyroid is of undoubted value; this may be combined with large doses of whole pituitary gland, but it is preferable to give intramuscular

injections of pituitrin. In females with irregular or scanty menstruation active ovarian extracts are indicated. Calcium salts appear almost specific in some cases, but are disappointing in others; calcium lactate in doses of 15 to 30 grains thrice daily, the syr. calcii lactophosphat. B.P., or one of the proprietary preparations should always be tried. Vigorous outdoor exercise and simple gymnastics should be enjoined, and warm gloves and stockings must be worn. A course of local and general applications of ultra-violet light is often of striking benefit. Locally, galvanic baths improve the circulation very effectively, and should be given for ten minutes daily. Very good results are also obtained by immersing the affected parts in a mixture of hydrogen peroxide (15 to 20 vols.) and hot water for a quarter of an hour every night, followed by the application of a stimulating preparation, such as iodex or a methyl-salicylate ointment.

Livedo (*Cutis marmorata*). This is another example of the effect of circulatory stasis in the skin. It is seen chiefly on the extensor surfaces of the legs, thighs, and upper arms, and sometimes on the flanks. It consists of a bluish network, with reticulations of considerable size enclosing areas of normal colour. It is made more apparent by exposure to cold. It appears to depend upon the distribution of the main arteriolar territories, the central pale areas receiving a direct supply from the underlying arterioles, and the reticulations corresponding to sites of anastomosis, where the blood flow is naturally more sluggish. The tone of the vessels in the reticulations is also diminished, and they are relatively irresponsive to adrenalin and histamine. The eruptions of measles and secondary syphilis occur first in these reticulations, and the same is true of those due to copaiba and salvarsan, and sometimes of lichen planus and parapsoriasis.

Erythema Ab Igne (*Ephelis ab igne. Cutis marmorata pigmentosa*).—This condition results from frequent exposure of the skin to heat, and is most commonly seen on the fronts of the legs in those who are constantly sitting in front of a fire, and in stokers and cooks. It may also occur on the abdomen or elsewhere from repeated use of hot-water bottles. The discoloration corresponds to the reticulations of livedo, and varies in tint from light brown to a deep reddish-purple; it is partly caused by dilatation of the superficial vessels in the marginal areas, where, as already noted, the circulation is normally more sluggish and the tone of the vessels diminished, and partly by a heavy deposit of melanin in the basal layer of the overlying epidermis. Microscopically there is seen an inflammatory cell-infiltration of the corium around the blood-vessels. Occasionally, the markings are distinctly raised, due, perhaps, to thickening of the vessel walls (Perry).

Erythrocyanosis Crurum Puellaris. This condition, which of recent years, owing to the advent of short skirts and thin stockings, has become very familiar, is a variety of acrocyanosis met with in girls and young women. It is seen on the lowest third of the leg, chiefly on the postero-external surface. The affected part is swollen, cold to the touch, and bluish-red or dark-lilac in colour. On the surface may be seen a pattern of dilated venules. As a rule the patients are fat and phlegmatic, with large bones, thick ankles, and a chilblain circulation. Very often a history is obtained that they grew rapidly and became abnormally fat and big at puberty, probably owing to over-activity of the anterior part of the pituitary gland at that time. The legs as a whole are large and unshapely from excess of subcutaneous fat, and a characteristic feature is the presence of keratosis pilaris and of a bluish halo around each follicle. The patients may complain of aching in the legs, and in winter painful chilblains of large size may form at the site of maximum circulatory stasis. These may be mistaken for the nodules of erythema induratum, since it is in girls of this type with erythrocyanosis of the legs that this eruption is likely to occur should an active tuberculous focus exist. The nodules, however, are firmer to the touch, deeper and more sharply circumscribed than chilblains.

Ætiology. The condition is seen almost exclusively in young girls and women of the type already described, but may occur occasionally in thin subjects. It would appear certain that an endocrine dyscrasia, which may be inherited, is the primary factor. As with chilblains, a deficiency of the posterior pituitary hormone is, perhaps, of chief importance, but thyroid and ovarian insufficiency may also play a part. Amenorrhœa or irregular and scanty menstruation are often present, but not constantly. Exposure of the legs to cold is, of course, the chief contributory factor.

Treatment. The general indications are those already given for chilblains. Warm woollen stockings and anklets should be worn, and, although vigorous exercise is beneficial, the patient should avoid standing for long periods.

LUPUS ERYTHEMATOSUS (*See Plate 60*)

This disease occurs mostly in adults, especially between the ages of twenty and forty, is very rare in children, and is more common in women than in men. Its early recognition is of great importance, since it affects chiefly the face, and, as the lesions often result in scarring, it may cause permanent disfigurement. Various forms of the eruption are recognised, although they may all coexist in the same patient. In the majority of cases the disease begins as a red, injected, desquamating patch, with a well-defined, irregular, and slightly raised edge. If a piece of scale be removed, there will often be seen little horny plugs projecting from the under-surface; these fit into depressions in the epidermis, which, after removal of the scale, are recognised as small pits on the denuded surface of the patch. Dilated venules are usually visible, and in one variety the formation of telangiectases is very marked. As the disease spreads peripherally, involution often occurs in the centre, so that after a while there is a central, depressed, pale scar surrounded by a raised, red, scaly edge. The scar formation is not preceded by ulceration. These cases are usually, but not always, tuberculous in origin. In another variety, which is commonly due to streptococcal infection, there is no scale formation, but the disease appears as raised, œdematous patches of erythema, closely resembling, and, indeed, often indistinguishable from, those seen in *Erythema multiforme*. In this erythematous type scarring is very slight, and may be entirely absent, the patches of erythema eventually disappearing without leaving any trace. Although the eruption is usually of limited extent, it may occur in an acute generalised form from the onset, or, more commonly, after a few chronic patches have been present for some time. In the acute form the recent patches either resemble those of *Erythema multiforme*, or they may be mistaken for eczema, although actual vesiculation is rarely seen.

Distribution. This is important from the diagnostic standpoint. The commonest sites are the malar eminences, the nose, the ears, the scalp, the backs of the hands and fingers, and the vermilion border of the lips. The distribution tends to be symmetrical, and often patches occur on either cheek and across the nose, so that the outline of a butterfly or bat is simulated—a very characteristic feature. The disease may rarely begin on the scalp or on the fingers before the face is involved. On the scalp atrophy of the hair follicles occurs, and patches of permanent alopecia, usually traversed by telangiectases, result. The ears are affected along the edges, which become eroded, irregular in outline, and shrunken, and the inner surface of the auricle is also involved. The mucous membranes of the mouth, nose and conjunctiva may be attacked, but, except for the lips, they are usually spared.

The subjective symptoms may be slight, but there is often great irritation in the patches, and many patients complain of intense burning, particularly after meals, or on exposure to sun or wind. The disease is not infrequently associated with rheumatoid arthritis of varying severity. In the acute generalised form there is pyrexia, sometimes of the septicæmic type, and there may be albuminuria; these cases may terminate fatally.

Ætiology. As will be evident from the above description, the eruption tends to involve those situations in which circulatory stasis is apt to occur, namely the fingers and toes, the backs of the hands, the ears, and the rosaceous or "butterfly" area of the face, and in people with marked acroasphyxia the hands, feet, and ears may be the chief or only parts affected, whereas in those with a pre-existing rosacea the "butterfly" area is likely to be the site of predilection. Frequently, however, rosacea and a "chilblain-circulation" coexist, in which case all the above sites may be involved in the same patient. Since the eruption is produced by circulating toxins—perhaps, even, by an actual bacteriæmia—and is essentially chronic, it is obvious that the inflammatory reaction, which constitutes the lesions, is most likely to appear where there is vascular stasis; moreover, certain areas of skin evidently become sensitised to the toxins, so that recurrence may take place in the identical situations previously involved, when there is a recrudescence of the toxæmia after temporary disappearance of the eruption. As to the nature of the toxins or micro-organisms causing the disease, there are now two predominant views; one, which obtains most favour on the Continent, is that it is a tuberculide, the other that it is a manifestation of chronic or acute streptococcal infection. Many now incline to the opinion that, like other forms of erythema, it is not a specific entity, but that both tuberculous and streptococcal infection (and possibly others) may be responsible in different cases.

In favour of its tuberculous origin in some cases, its occurrence in those with a strong family history of tuberculosis, its association with manifest tuberculous infection of glands, bones, joints, lungs, etc., and the claims that guinea-pigs have been tuberculised by inoculation of the affected tissue may be mentioned (**35**). On the other hand, no trace whatever of tuberculosis has been found in some fatal cases of the disease. Convincing evidence has been produced that in some cases acute or chronic streptococcal infection is the cause (**36**). The primary sources may be the teeth, nasal sinuses, tonsils, and probably the prostate and female genital organs; in many cases there is a secondary and persistent intestinal infection with a *Streptococcus longus*, which may rarely be recovered from the fæces in almost pure culture. In fatal cases a *Streptococcus longus* has been obtained from the blood during life. Certainly the fatal cases reported have resembled clinically streptococcal septicæmia rather than general tuberculosis. It must be remembered that, as in chronic tuberculosis, cases of chronic streptococcal infection have as a rule both primary and secondary foci, and the removal of obvious and accessible sources of infection does not necessarily suffice to cure, owing to the existence of subsidiary foci in lymphatic glands, the intestines and elsewhere.

Diagnosis. The conditions which are most likely to be mistaken for *Lupus erythematosus* are rosacea, *Erythema multiforme* and *Erythema pernio*, eczema, psoriasis, and *Lupus vulgaris*. The distribution, the persistence, the resistance to local treatment, and the tendency to superficial scarring, are the chief characteristics on which the diagnosis rests. From *Lupus vulgaris* the main points of distinction are that *Lupus erythematosus* very rarely begins in childhood, it is usually bilaterally symmetrical, it never ulcerates, and never destroys cartilage, it frequently involves the scalp, the scarring from it is superficial, it only rarely reacts to injections of tuberculin, and the characteristic apple-jelly nodules are absent.

Morbid Anatomy. In *the dermis* is seen a diffuse, but chiefly perivascular infiltration with lymphocytes and small connective-tissue cells, and occasional plasma cells and polymorphonuclear leucocytes. Giant-cells of the phagocytic type have been observed near disintegrated follicles. There is œdema of the papillæ and dilatation of the lymphatics. Some of the blood vessels are dilated, others obliterated, and small hæmorrhages may be seen. In *the epidermis* the rete malpighii is atrophied, and may be reduced to only a few rows of cells, the stratum granulosum being absent at certain points. The stratum corneum is, on the other hand, thickened, and horny plugs fill the openings of the follicles and

sweat-ducts. The atrophy is due to the disappearance of the connective-tissue and elastic fibres. The hairs fall, and the glands, at first dilated, are ultimately destroyed.

Treatment. The treatment of this chronic and disfiguring disease has been rendered far more satisfactory in recent years, since the introduction of gold compounds, such as Sanocrysin, Krysolgan, Solganal, and similar preparations. In the majority of cases the results are good, but in some they are disappointing. It would seem that those cases in which the eruption appears to be of tuberculous origin respond more readily than those apparently due to streptococcal infection. The dosage of these gold compounds depends upon the preparation employed, and the tolerance of the individual patient. Occasionally toxic symptoms—fever, general malaise, pruritus, and a generalised erythematous or lichenoid rash, with involvement of the buccal mucous membrane—may arise, as in other forms of metallic intoxication; the occurrence of such symptoms probably depends upon a failure of hepatic function, and they are more liable to occur in alcoholics, or others with manifest hepatic insufficiency. The administration of glucose, 2 to 3 ounces *per diem* in divided doses, for two or three days before each injection, appears to have a prophylactic effect, and full doses of calcium gluconate are also recommended. In some cases injections of bismuth preparations appear more effective than those of gold salts, and recently intravenous or intramuscular injections of antileprol have been employed with success.

Internally iodine in increasing doses appears to do more good than any other drug that has yet been tried. It should be given as a 10 per cent. solution in rectified spirit, and should *not* be combined with iodide of potassium. Of this solution 5 drops daily in milk should be taken at first, the dose being increased gradually up to 40 drops in divided doses *per diem* if well tolerated. Very much larger doses have been given without ill effect, but instances of intolerance are met with. Cod-liver oil is often of great benefit, but is apt to upset the digestion. Instead, one of the proprietary vitamin concentrates may be taken, and the patient should be given plenty of milk and other foods rich in calcium. Quinine and salicin appear sometimes to be of value, especially in the more acute cases. When the eruption appears to depend on chronic streptococcal infection, accessible infective foci should be sought for and dealt with, and the subsequent administration of an autogenous streptococcal vaccine over a long period in suitable dosage would appear of definite value. In severe cases prolonged rest in bed, preferably out of doors, should be insisted upon. Judicious heliotherapy or artificial light baths are in some cases of striking benefit, but it is advisable at first to protect the actual eruption from the rays, which may, until tolerance is established, aggravate it and cause it to become acute.

Locally. In the acute and hyperæmic cases cooling lotions such as those of calamine and lead should be applied. In more chronic cases, without much infiltration, continuous compression with non-flexible collodion, to which 2 per cent. of salicylic acid may be added, sometimes results in improvement and even disappearance of the patches. Chronic patches of the fixed type may be treated more energetically. The scales should be removed with soft soap and spirit, or a salicylic acid plaster, and the patches may then be painted with tincture of iodine, while quinine is simultaneously administered internally (Hollander). Or the patches may be rubbed once a week with a glass rod dipped in a mixture of lactic acid 4 parts, carbolic acid 1 part. Repeated applications of solid carbon dioxide snow for fifteen seconds with moderate pressure, though causing a severe reaction, may bring about the disappearance of chronic patches. Ionisation with zinc or copper sulphate, scarification, and even cauterisation, have been used with varying results. The X-rays and the Finsen light are more likely to do harm than good. It should be remembered that local treatment, though of great value, does not prevent recurrences, and for this reason every effort should be made to locate the underlying infection responsible for the disease.

ROSACEA

(*Acne Rosacea—Gutta Rosea*)

In the earliest stage of the disease there is periodical flushing of the face, occurring usually after meals or on exposure to heat and cold. At first the hyperæmia affects the nose and malar regions, but later it extends to the centre of the forehead and the chin. After a while the flushing tends to become permanent, although it varies in intensity at different times, and eventually telangiectases appear; they are particularly numerous in persons with a feeble peripheral circulation. In most cases the flushing is accompanied by seborrhœa, and sometimes by hyperidrosis, and secondary inflammation is very apt to occur around the pilo-sebaceous follicles, resulting in the formation of pustules and papules, which cause great disfigurement. Fresh outbreaks of these inflammatory lesions occur periodically, and in women they are apt to be most numerous just before the menstrual periods; an indigestible meal or indulgence in alcoholic liquor may invariably provoke an outbreak in certain cases. Although the disease is usually most evident on the nose and cheeks, it may affect chiefly the chin, particularly in women; in such patients, crops of indolent, red papules and pustules continually appear in this situation. This variety is said to be associated with ovarian or uterine disorders. In another variety of the disease the skin, instead of being greasy, is dry, and superficial, red, scaly patches, intermingled with small pustules, appear on the hyperæmic areas. In some cases of cirrhosis of the liver intense rosacea, with severe secondary staphylococcal infection, may involve not only the "flush-area," but also the posterior parts of the cheeks and forehead, and even the ears and submaxillary regions. Two examples of this kind have been seen by the writer in young girls with cirrhosis.

In long-standing cases of rosacea the condition known as rhinophyma may arise. It is seen most commonly in men of alcoholic habits, whose employment exposes them to cold winds. The nose becomes covered with large, lobulated or pendulous protuberances, separated by deep furrows; their colour is deep violet, and their surfaces traversed by large dilated veins, and pitted by the dilated follicles of the hypertrophied sebaceous glands.

The dyspeptic symptoms of patients with rosacea sometimes depend on chronic gastritis with hypochlorhydria. There is a feeling of fullness after meals, flatulence, and sometimes heart-burn and a sensation of nausea. The appetite is often poor, and the bowels constipated. On the other hand, subjective symptoms of dyspepsia may be absent.

An important complication of rosacea is the occurrence of ocular lesions, which are met with in about 15 per cent. of cases. Chronic blepharitis, however, which is so common in seborrhœic subjects, is seen with greater frequency. The ocular lesions may be classified as follows:—

(1) Simple dilatation of the conjunctival vessels, the conjunctivæ being included in the rosaceous area of the face; (2) phlyctenular conjunctivitis; (3) corneal ulceration, resulting from the breaking-down of phlyctenules; (4) diffuse keratosis.

The last three are evidently the result of a pyogenic infection, comparable to that which occurs on the skin of the rosaceous area, but there is not necessarily any parallel as regards the intensity of the two, and occasionally the eye-lesions may precede the active manifestations of rosacea. Although successful treatment of the latter usually leads to a cessation of the ocular inflammation, the corneal ulceration may be severe and intractable, and the resulting scars cause permanent impairment of vision.

Anatomy. In the early stages there is merely dilatation of the capillaries in the corium, particularly around the pilo-sebaceous follicles and the sweat-glands, with some small-celled infiltration. The papules are formed by chronic inflam-

mation around the follicles. In rhinophyma there is enormous hypertrophy of the sebaceous glands, with new formation of fibrous tissue.

Ætiology. Rosacea may occur in adolescence, but usually begins in the third or fourth decade, diminishing or disappearing in later years. It is far commoner in women than in men, and the menstrual periods and the menopause undoubtedly aggravate the tendency when it exists. Two types of the disorder may be recognised, according to whether the hyperæmia is active or passive. In the former case the affected area is bright red, and the flushing is intensified by indigestion, hot drinks, exposure to heat, or emotional disturbance; in the latter there is passive congestion, so that the colour is bluish or purple, and exposure to cold is the chief aggravating factor. The passive form is also met with in those with chronic cardiac or pulmonary disease. In both forms, however, circulatory disturbances are common, in that the peripheral vasomotor tone is unstable. The extremities are often cold, or alternately hot and cold, and many patients, particularly women, are subject to "dead fingers," such as are seen in Raynaud's disease. In the passive form a "chilblain circulation" is the rule, and the rosacea may be merely part of this, there being stasis in the superficial vessels of the nose and malar regions on exposure to cold. Ætiologically this is distinct from true rosacea, although the two may co-exist.

Recent observations (**37**) suggest that in the latter the usual immediate cause of the reflex flushing of the rosaceous area is an increase of tension in the stomach wall, which may be due to (*a*) delay in emptying, (*b*) feeble peristalsis, (*c*) hypotonia, which renders the stomach liable to distension, (*d*) over-rapid peristalsis, and (*e*) gastric spasm. Consequently anything which produces gastric distension, such as bulky, insufficiently-masticated meals, white bread, and a large quantity of fluid, or which interferes with normal peristalsis, will provoke the flushing. Contributory factors, of which there are many, *e.g.* menstruation, the menopause, painful disorders of the female pelvic organs, chronic infections, and psychological disturbances, such as the anxiety state, probably owe their effect to their action on the gastric tone. It has been shown (**38**) that prolonged anxiety causes hypotonicity of the stomach and inhibition of peristalsis, and that a similar condition occurs in women during the premenstruum. It is uncertain to what extent a definite gastritis is present. Numerous observations upon the results of fractional test meals in patients with rosacea have been made and it has been established that there is no correlation between the gastric acidity and the rosaceous tendency, since the secretion of hydrochloric acid may be absent, deficient, normal or excessive. Although the administration of hydrochloric acid is often of striking benefit, it may be equally so in cases with hypochlorhydria and with a normal or even excessive secretion of acid. Its action, therefore, probably depends upon its influence on the gastric tone and peristalsis. Alkalies, given before meals, and carminatives doubtless act in the same way. The frequency of rosacea in chronic alcoholics and tea-drinkers may be partly due to gastritis, partly to hypotonia and distension from large quantities of fluid, and partly to aggravation of the flushing by alcohol and hot fluids.

Diagnosis. Rosacea may be distinguished from *Acne vulgaris* by the absence of comedones, and by the fact that it appears later in life. The two conditions, however, frequently coexist. In *Lupus erythematosus* there are usually well-defined patches, with raised borders and adherent scales, and superficial scarring is apt to result. The diagnosis from the rosaceous tuberculide has already been discussed. Confusion with syphilitic eruptions should not arise.

Treatment. The patient must avoid heavy meals, the taking of large quantities of fluid, and eating when tired. White bread should be taboo, for it has been demonstrated in a patient with a jejunal fistula that, whereas when crisp toast was eaten only a small amount of liquid material appeared at the fistula, if white bread was taken large doughy lumps were passed. Other soft starchy foods should also be avoided, such as milk- and suet-puddings, heavy

cakes, and porridge. Alcohol should be taken very sparingly or not at all, and strong tea or coffee and other hot drinks must be forbidden. Oral, tonsillar, or naso-pharyngeal sepsis must be most carefully sought for, and dealt with if present. Examination of the gastric juice by the fractional method is always desirable, and in some cases an X-ray examination of the whole alimentary tract is indicated. In most cases the best results are obtained by giving an alkaline mixture before meals, *e.g.* R. Sod. Bicarb. gr. xx., Tinct. Rhei Co. ℥xl., Tinct. Zingiberis ℥xxx., Aq. chlorof. ad ℥i: and full doses of dilute hydrochloric acid (30 to 40 minims), either during or after the three principal meals of the day. Other drugs that are sometimes of value are bismuth and ichthyol; both should be given on an empty stomach. The possible influence of emotional stress and an uncongenial environment must always be considered, and judicious psychotherapy is sometimes of striking benefit. In women with menstrual irregularities, and during the menopause, active ovarian extracts are indicated. Locally, the main indication is to check seborrhœa and the resulting secondary infection. In mild cases a weak ichthyol cream or paste may be applied at night-time and calamine lotion during the day. In more severe cases a paste containing sulphur, salicylic acid, and resorcin may be applied at night. Lassar's paste, containing 2 per cent. of yellow oxide of mercury, is of value if there is much pustulation. Dilated venules may be destroyed by electrolysis or by repeated light freezing with carbon-dioxide snow. In rhinophyma excellent cosmetic results may be obtained by removal of the hypertrophied tissue with the knife. Small doses of X-rays are sometimes of value.

URTICARIA

The essential lesions of the eruption of "nettlerash" (*Urtica*, a nettle) are wheals (*pomphi*, hives). These are firm, convex elevations of the skin, pink in colour, or with a white centre, where the œdema is most intense, surrounded by a red areola or "flare"; they may be round, oval or linear, and sometimes form gyrate figures. In size they vary from small, sharply-defined papules (*U. papulata*) to large plaques of wide extent. Rarely a vesicle or bulla may form on the surface of the wheal (*U. bullosa*). In giant urticaria (*U. gigans*) the serous exudation is subcutaneous (angeioneurotic œdema), and more or less circumscribed nodules of the size of a hen's egg, or larger, occur, or there may be diffuse swelling of parts such as the eyelids, lips and extremities. Both in ordinary urticaria and the giant form the individual lesions are ephemeral, lasting from a few minutes to some hours. The eruption is accompanied by intense itching, so that the patient cannot forbear from scratching himself, thereby often causing new wheals to arise (*U. factitia*).

A distinction must be drawn between this factitious urticaria and dermographism. The former, as has been said, is produced by scratching or rubbing the skin of a person in an urticarial state. On the other hand, certain people, who are not urticarial, develop similar wheals, even on gentle stroking of their skin. This phenomenon is known as *dermographism*, and it differs from true urticaria in that there is no accompanying itching. The tendency to dermographism, however, is a matter of degree, and a considerable proportion of normal subjects show some whealing as a sequel to firm stroking.

Ætiology. The wheal, however produced, is a complex reaction, named by Lewis (**39**) the "triple response." It comprises (*a*) a primary and local dilatation of the minute vessels of the skin, (*b*) a widespread dilatation of the neighbouring arterioles, resulting in the "flare," and brought about entirely through a local nervous reflex, and (*c*) locally, increased permeability of the vessel walls, with exudation of serous fluid rich in albumin. Occasionally there is round-celled infiltration round the dilated vessels. This complex reaction can be evoked by stimuli of very different kinds, namely mechanical, thermal, electrical,

and chemical, but it is probable that, *whatever the exciting cause*, the wheal is due to the liberation of histamine or a histamine-like substance in the skin. Typical wheals can, of course, be experimentally produced by injecting a solution (*e.g.* 1 in 3,000) of histamine into the skin.

The urticarial or dermographic wheal may be regarded as a purposive local reaction to injury ; by means of the " triple response," upon which its formation depends, there is an increased blood-flow and lymph-supply to the injured area, which " will tend to wash away or dilute injurious substances, and will bring leucocytes more quickly through the vessels of the affected region " (Lewis).

The urticarial wheal is one of the commonest cutaneous reactions towards irritant substances, either when applied locally to the skin or when absorbed from within, and to injury by physical stimuli. Apart from histamine, a large number of chemical substances—acids, alkalies, formaldehyde, the salts of certain metals and alkaloids, iodine, mustard oil, cantharidin, etc. —will produce wheals if injected into the skin. Here, as a rule, the question of sensitisation, to be referred to later, does not arise, and the same is true for nettle-stings, and to some extent for those of stinging-insects. On the other hand, in the case of bites from insects, such as fleas, mosquitoes, gnats and lice, the factors of sensitisation and immunity must be considered. Persons bitten for the first time by rat-fleas show no reaction, but, after repeated bites, marked local reactions occur, the persons having become sensitised (**40**). Immunity may develop in those who are repeatedly bitten by certain insects over a long period. Thus natives, in areas where *Simulium* flies are plentiful, become immune to their bites (**41**), and it is well known that those who are constantly exposed to the bites of fleas, lice and bugs, in time show little or no reaction.

With regard to urticaria of internal origin, it must be remembered that, apart from a purely urticarial eruption, with or without its subcutaneous variety, urticarial wheals may occur in various conditions of toxic origin, such as dermatitis herpetiformis, the different forms of prurigo, and in light sensitisation. In many instances, for example, drug-, food- or serum-rashes, the eruption is polymorphic, there being erythematous patches of varying hue and configuration, mingled with urticarial wheals, and sometimes eczematisation. A mixed urticarial and eczematous eruption very commonly follows the ingestion of certain foods, particularly fish.

Urticaria and angeioneurotic œdema are essentially neuro-vascular reactions, dermic in the former, hypodermic in the latter : the *epidermis* remains intact, except that in the rare bullous urticaria it is raised entire or infiltrated by the intense serous exudation. In eczema, on the other hand, as will be seen, the essential factor is *epidermal* sensitisation, and an eczematous reaction of the skin is an epidermo-dermal one. It is easy to understand how a mixed urticarial and eczematous eruption can be provoked by the same antigen, if both the dermal and epidermal tissues are sensitised to it.

Urticaria of internal origin is presumably always an indication that the person is in a sensitised or allergic state ; in some cases the eruption is provoked suddenly and for the first time after a hot bath or violent exercise, whereby no doubt there occurs a flooding of the cutaneous vessels with the circulating antigen, and in certain chronic cases the attacks only take place when congestion of the skin is produced by a physical stimulus, or under the stress of some emotion. The actual eruption is doubtless due to the liberation of histamine by the contact of circulating antigen with the sensitised dermal tissue, *i.e.* in response to injury. In a person sensitive to a given substance, *e.g.* fish or egg, the injection of a diluted extract of the antigenic substance and of a solution of histamine into the skin give exactly similar reactions simultaneously. Moreover, the histamine renders the area of skin to which it has been applied refractory to the antigenic solution, and the latter renders its area refractory to histamine.

The number of substances capable of causing an urticarial eruption of internal origin is enormous ; they may be classified as follows :

(1) *Food and Drinks.* As common examples may be mentioned fish, crustacea, bivalves, pork and sausage, eggs, mushrooms, nuts, cereals, certain fruits and vegetables, wines and other beverages. The antigens in these substances are not themselves proteins, since they are contained in a protein-free dialysate of the substance in question, as has been shown, for example, with egg (**42**). In some cases sensitiveness to a certain food is so great that merely taking it into the mouth may provoke an attack. In others an outbreak may depend upon incomplete digestion with consequent absorption of the antigen unchanged ; in patients with achlorhydria the administration of hydrochloric acid may prevent an attack even when a food which usually causes urticaria is taken. Some patients are sensitive to one food only, others to several, and in others again, although it is clear that the antigen is absorbed from the alimentary tract, no particular foods can be incriminated.

(2) *Drugs.* Numerous medicinal substances may provoke urticarial or erythemato-urticarial rashes, *e.g.* the balsams, opium, quinine, salicylates, iodides, the barbitone group of hypnotics, arsenic, arsenobenzol, and many others.

(3) *Therapeutic Sera.* Serum sickness, of which urticaria is a prominent symptom, is due to the horse-serum, not to the contained antitoxin, hence the danger of serotherapy in those already horse-sensitive.

(4) *Bacterial Infections.* Chronic urticaria may be dependent upon some focal infection, *e.g.* infected teeth, tonsils, or nasal sinuses, chronic appendicitis, cholecystitis or prostatitis, to *B. coli* infection of the urinary tract, and to the presence of abnormal coliform bacteria in the intestine.

(5) *Animal Parasites.*—Intestinal worms, hydatids, and parasitic protozoa. W. Jadassohn has shown that the actual antigen of the ascaris worm, which provokes violent urticaria, asthma, or eczema in sensitised persons, is not destroyed by heat and is dialysable ; as in the case of food antigens, therefore, it is not a protein.

Both when the antigen is absorbed from the alimentary canal, and in some cases, at any rate, when it is of parenteral origin, the proteopexic and detoxicating functions of the liver probably play a predominant *rôle* in preventing allergic reactions, such as urticaria. The liver, in fact, may be regarded as the first line of defence, and when this fails, the skin, owing to its ability to form antibodies and to fix those circulating in the blood (as evidenced by the Prausnitz-Küstner reaction), may take on a vicarious protective function. Urticaria and other cutaneous manifestations of allergy may be regarded as antigen-antibody reactions designed to destroy the former, thereby protecting other more vital organs. In serum sickness, in certain prurigos, in some cases of acute urticaria and angeioneurotic œdema, and in urticarial and other eruptions secondary to metallic intoxication (arsenobenzol, bismuth, gold, &c.), a positive Van den Bergh reaction of the biphasic type is often found, with excess of urobilin in the urine, deposition of urates, and other indications of hepatic insufficiency. It has been shown that glycogen is essential for the antitoxic and other functions of the liver, and this may partly explain the value of glucose in preventing metallic intoxication, and in the treatment of certain allergic conditions.

During an acute attack of urticaria the various phenomena included under the term " hæmoclasic crisis " occur, and the same biochemical changes in the blood and urine that characterise other manifestations of the allergic state (*see* p. 138). There is retention of fluid, the wheals representing local accumulasions in the dermis.

Apart from the essential factor of sensitisation, there may in certain cases be others predisposing to urticaria, such as calcium deficiency and psychological disturbances. Certainly some cases are benefited by the administration of calcium

salts, and in an urticarial subject an attack may be provoked by an emotional upset (cp. asthma, prurigo).

Treatment. An acute attack of urticaria, occurring for the first time, usually follows the ingestion of some food, such as fish, shell-fish or pork, the antigenic substance not having been destroyed by digestion, and having escaped fixation and destruction by the liver; the possibility of it being due to some drug, *e.g.* a hypnotic, or to the injection of a therapeutic serum must, however, be considered. If the patient is seen shortly after a suspected food has been taken, an emetic may be given, and for the immediate relief of symptoms Liq. adrenalini hydrochlor. 5 to 10 minims, or, better, a compound of adrenalin and pituitrin, should be injected deeply in the subcutaneous tissue, and repeated at intervals if necessary. Intravenous injections of calcium compounds, *e.g.* calcium gluconate or *afenil* (calcium chloride-urea), are also effective and may be given daily for a while. It is advisable that the patient should remain without food for twenty-four hours, except that he may be given glucose dissolved in hot water. Unless there is intolerance of milk, the diet should then be restricted to four tumblers per diem of this fluid, sweetened with glucose, for two or three days. A purge, such as calomel gr. 2–3, followed by a dose of the aperient sulphates in hot water the next morning, should be given at the outset of this treatment.

In cases with chronic urticaria or recurrent attacks an attempt should be made, by closely questioning the patient or, if necessary, by performing cutaneous tests, to incriminate certain foods, and a thorough search should be instituted for sources of focal infection. It may be advisable to investigate the gastric secretion of hydrochloric acid by a fractional test meal, and the fæces for abnormal strains of bacteria, evidence of excessive putrefaction, undigested food, and intestinal parasites. A total and differential leucocyte count may indicate latent sepsis, or, if there be eosinophilia, hydatid disease. A complete examination of the urine, specimens being collected at different times throughout a period of twenty-four hours, may reveal the cycle of changes already described in allergic conditions, and give a clue to rational treatment. Coliuria should be treated with hexamine or other urinary antiseptics.

Diet. The dietetic treatment of chronic urticaria naturally demands the exclusion of foods which appear to provoke the attacks, and very acid fruits, fatty foods, except butter and plain cheeses, recooked meat and fish, crustacea and shell-fish, and concentrated sweetstuffs should be avoided. Some cases appear to benefit from temporary vegetarianism, but in the majority a dietary rich in protein, with restriction of carbohydrate and fat and a plentiful supply of vegetables and of the less acid fruits, is advisable. The fluid intake should be limited to two pints *per diem* exclusive of that obtained from fruit and vegetables, salt should be taken very sparingly, and glucose should be substituted for cane-sugar. The following may be cited as an example of such a dietary, which may be modified according to the tastes and idiosyncrasies of the patient. *Breakfast:* Lean ham (3 oz.) or liver (2 to 3 oz.) or kidney with, if desired, one egg. Large slice of wholemeal toast, or two pieces of Vitaweat. Butter. One apple, pear, or orange. One large cup of weak tea, or one large cup of coffee and milk (equal parts). *Lunch:* Sardines (oil to be discarded) 2 oz., or liver (2 oz.), or fresh fish (3 oz.) or chicken (3 oz.). Plain cheese. Salad (lettuce, tomatoes, beetroot, etc.). Wholemeal toast or Vitaweat as for breakfast, with butter. Apple, pear, or orange, or stewed fruit. One glass of water. *Afternoon:* One glass of milk. Piece of plain cake. Fruit. *Dinner:* Three oz. of lean meat, or fresh fish, or chicken; or 1½ oz. of fish and 1½ oz. of meat or chicken. Vegetables as desired (all greens, carrots, parsnips, turnips, onions, leeks, etc.). Wholemeal toast or Vitaweat as above. Fresh fruit. One glass of water, tonic water, or weak whisky and soda. *Avoid or restrict:* Sugar, jam, marmalade, honey, sweets, pastries, puddings, rich cakes, soups, fats (except butter as allowed), pork, bacon, sausages, strong tea and coffee, beer, wines. *Notes:* Liver should be

taken on at least three days a week if possible. One glass of milk and at least one salad should be taken daily. The menus for lunch and dinner may be transposed if desired. The fluid intake should be restricted to that indicated above, unless thirst is experienced, when more may be taken. Glucose in powder should be substituted as far as possible for ordinary sugar.

Calcium salts, *e.g.* the gluconate, chloride, carbonate, lactate, or the compound calcium-sodium-lactate, should be given. They have a diuretic effect and lessen the tendency to serous exudation. It may be advisable to prescribe them in combination with ergosterol for a while.

Often some method of desensitisation is necessary. Peptone taken orally one hour before each meal is occasionally efficacious, but it is preferable to give it in increasing doses by intravenous or intramuscular injection every three to seven days. Autohæmo- and autosero-therapy are often successful, but the blood should, if possible, be withdrawn just before the outbreaks of urticaria occur. Injections of the substance P. of Oriel have been successful in some cases in which other methods have failed.

Lastly the effect of physical exhaustion and psychical disturbances as predisposing factors in urticaria, as in other allergic conditions, must not be forgotten. A complete rest, followed by a change of surroundings, or judicious psychotherapy may succeed when all other means have failed.

URTICARIA PIGMENTOSA

Under this term are included two types of eruption, which are clinically, and in all probability ætiologically distinct. They are usually referred to as the juvenile and adult types.

Juvenile Type. The eruption consists of round or oval macules and papules, the colour of which varies from light fawn to dark brown. They tend, when numerous, to lie with their long axes in the lines of cleavage. The pathognomonic sign of the disease is that the lesions, when vigorously rubbed or scratched, become reddened, swollen, and form urticarial wheals. The majority of cases are accompanied by itching, and dermographism is frequently seen. The disease usually begins in early infancy, and often disappears or becomes much less evident at puberty; it may, however, persist indefinitely, and its first appearance may be delayed until puberty or even adult life. Most of the lesions are situated on the trunk and buttocks, but the limbs and head may be involved. Histologically there is œdema of the cutis, as in ordinary urticaria, increased pigmentation in the deeper layers of the epidermis, and a dense infiltration of *mast cells*, which is absolutely characteristic of the disease.

Adult Type. The lesions are macules or slightly elevated papules of a characteristic reddish-brown colour, sometimes with a tint of lilac. On the whole they tend to be smaller than those of the juvenile type. They occur most commonly on the anterior surfaces of the forearms and on the trunk, and may be sparsely scattered or present in large numbers over a wide extent. As in the juvenile type, friction causes them to become urticated, but usually to a far less degree. Histologically mast-cells are found in the dermis, but are relatively few in number.

Ætiology. *Juvenile Type.* The condition is commoner in males than in females, and may be familial. Some authors incline to regard it as related to the leukæmias, in view of the fact that, apart from the enlargement of the liver, spleen, or lymphatic glands noted in certain cases, blood-changes have been observed of the lymphocytic or oftener the myelocytic type. This view is, perhaps, in accord with the characteristic mast-cell infiltration of the skin.

Adult Type. This may probably be regarded as a chronic form of urticaria. Its appearance may be preceded by attacks of ordinary urticaria, and has been known to follow food-poisoning. Further research along biochemical lines would probably decide its relationship to the allergic group of eruptions.

Treatment. The lesions in the juvenile type can be made to disappear by freezing with carbon-dioxide snow, but the treatment must be prudently applied in view of the fact that it has in some cases provoked a nitritoid crisis.

PRURITUS AND PRURIGO

The word *pruritus* merely indicates the symptom of *itching*, which may be idiopathic in the sense that it is not the result of any visible change in the skin, or may be one of the subjective manifestations of a definite eruption. Under the term *prurigo* are included a variety of clinical entities, in which pruritus is the cardinal symptom, but certain characteristic lesions also occur in the skin, either primarily or as the result of scratching and rubbing. Thanks to histological researches (**43**), we can now distinguish between these primary and secondary lesions in the different forms of prurigo.

PRURITUS

The sensation of itching is as indefinable as those of taste, smell or touch. It is not known for certain whether the sensory nerves of the skin are concerned in its production, or whether, as seems more likely, it is a manifestation of involvement of certain fibres of the autonomic nervous system. It will be remembered that one of the earliest symptoms of experimental anaphylactic shock in animals, in which there is a profound disturbance of the vegetative nervous system, is violent itching, and the same is true of conditions comparable to anaphylactic shock, such as serum sickness, urticaria, and certain forms of prurigo. The degree of itching varies from a mild and even pleasurable sensation, as that provoked by tickling, to the terrible paroxysms in which the unfortunate victims lose all control, and tear their skin unmercifully in an attempt to obtain relief. Pruritus may be more or less generalised or localised to certain areas, and as a rule it is paroxysmal. In the idiopathic forms, the prurigos, and that accompanying scabies or pediculosis corporis, it is usually nocturnal.

Ætiology. The causes of pruritus are very numerous, but may tentatively be classified after Darier as follows :—

Pruritus of External Origin. Under this heading may be included the itching provoked by mechanical means (tickling, contact with certain materials, such as wool, etc.), and by physical or chemical agents ; by the activity or bites of animal parasites, *e.g.* lice, bugs, acari, oxyuris ; and contact with certain plants, *e.g.* the nettle, or animals. Such itching may be regarded as physiological and purposive, since by scratching the irritant in question may be removed, but, even so, the degree of itching varies greatly according to the individual affected. *Infection* of the skin either by bacteria or the higher fungi may also in certain situations be the cause of a localised pruritus. This is particularly the case at muco-cutaneous junctions, and in the natural folds of the skin. Thus many cases of pruritus ani or vulvæ are due to infection of the parts with pyogenic cocci, particularly a streptococcus, and with ringworm fungi or monilia ; and infection with these organisms is the cause of intertrigo of the folds, which may be accompanied by severe pruritus. *Pruritus in Certain Eruptions.* A large number of eruptions may be accompanied by itching, some constantly, others occasionally. As examples of those in which pruritus is almost invariably present in some degree may be cited : urticaria, eczema, lichen planus, dermatitis herpetiformis, acne necrotica, and the premycosic stage of mycosis fungoides. It is a remarkable fact, however, that in lichen planus the itching may be so severe as to render the patient almost insane, or it may rarely be entirely absent. In psoriasis and the syphilides it is seldom present, but in the former it may occasionally be considerable. It is therefore clear that pruritus is often more dependent on the individual affected than on the eruption with which it is associated. *Toxic Pruritus.* Under this

heading may be considered the pruritus that is provoked by certain drugs, either when given by mouth or by injection, *e.g.* belladonna, morphine, cocaine, caffeine, the barbitone group of hypnotics, and certain arsenical preparations; by foodstuffs, even without urticaria; and by the toxins of animal parasites, such as the intestinal worms and hydatids. As regards drugs and foodstuffs, personal idiosyncrasy, or, more accurately, the question of sensitisation, is of paramount importance. *Autotoxic Pruritus.* The term autotoxic implies that the substance or substances to which the pruritus is due are of endogenous origin, their presence in the blood being dependent on some error of metabolism, the existence of certain organic diseases, or of a source of toxic absorption. It is impossible in the present state of our knowledge to state exactly the nature or composition of the actual substances responsible for the pruritus in cases belonging to this group. The question will be more fully discussed in the section dealing with the prurigos. *Diabetes*, or simple hyperglycæmia, is frequently associated with pruritus, which may disappear when, under suitable treatment, the blood sugar is reduced to normal limits. It is, however, by no means a constant symptom, nor is it certain that the excess of sugar in the blood is the cause of the pruritus. A localised pruritus of the genitalia in both sexes, associated with an infective dermatitis usually caused by a monilia, may be due to the passing of saccharine urine. *Renal disease*, particularly chronic interstitial nephritis and the arteriosclerotic form, is another predisposing cause, and pruritus, with or without a concomitant eruption, may herald an approaching uræmia. *Jaundice* is almost always accompanied by severe itching, due to the presence of bile-salts in the blood, and a high *cholesterinæmia*, which may be associated with xanthoma, is sometimes found in patients with pruritus. It is notorious that *gouty* persons tend to itch, and this symptom may promptly be ameliorated by a suitable dietary and other measures designed to reduce the uric acid content of the blood. *Constipation* is also an apparent factor, and many cases are relieved by intestinal lavage and aperients.

Various researches (**44**) upon the increased irritability of the skin, provoked by a deficiency of calcium, suggest that a disturbance of the normal equilibrium of mineral salts in the blood and skin may sometimes be causative. The *rôle* of certain disorders of the *endocrine glands* is difficult to evaluate, but pruritus is common in Grave's disease, and in women after ovariotomy or at the menopause. *Focal sepsis* is certainly responsible in some cases, and dramatic cessation of either a general or localised pruritus may follow removal or treatment of a chronic source of infection. In lymphadenoma and the leukæmias pruritus may also be a distressing symptom, and may occur with or without actual cutaneous lesions. Lastly must be considered what may be called the *psychological* factor in pruritus, since the degree of itching varies greatly in different cases, and in idiopathic pruritus the patient is usually highly strung and prone to worry unduly. Both in generalised pruritus and in the local form, which in time develops into circumscribed prurigo (*q.v.*), this psychological element is usually apparent. In pruritus localised to the genital organs, particularly in women, it may be the predominant, if not the only causative factor. In many such cases careful inquiry will elicit a story of unrequited love, a broken-off engagement, or unhappy marital relations. Such an explanation must not, however, be assumed until all other possible causes, for example, a local bacterial or mycotic infection, or a reflex source of irritation, have been considered.

The special characteristics and the treatment of certain regional forms of pruritus, *e.g.* pruritus ani, will be considered in the next section.

PRURIGO

The term *prurigo* is used to designate those cases of idiopathic pruritus, either general or local, in which characteristic changes take place in the skin of the affected parts, and also certain clinical entities or syndromes that may be distin-

guished by their primary and secondary lesions, by the distribution of the sites involved, by seasonal, racial, or age incidence, and by their relationship to accompanying symptoms or diseases. These latter comprise prurigo simplex acutus (urticaria papulosa, lichen urticatus, strophulus), the prurigos of Besnier and Hebra, prurigo nodularis, prurigo senilis, prurigo æstivalis and hiemalis, and the prurigos of lymphadenoma and leukæmia. In considering the cutaneous lesions associated with the various forms of prurigo, we have to distinguish between those that result from scratching and rubbing, and those that are primary. Civatte's histological studies indicate that in urticaria papulosa, the prurigo of Hebra, in summer prurigo, and in some cases of lymphadenoma, there are primary papular lesions, arising independently, but subsequently altered by scratching: whereas in the simple prurigo that complicates a general or local pruritus, and in other forms, the visible changes in the skin are due entirely to scratching and rubbing.

Symptoms. The *immediate* effect of scratching by a normal person on healthy skin is to produce a fugitive erythema, which may be accompanied by serous exudation, so that a wheal is formed (dermographism); this reaction is due to the liberation in the skin of a histamine-like substance in response to injury. In eczematous subjects, in whom the epidermis is in a sensitised state, continued scratching of a healthy area of skin may of itself give rise to an eczematous reaction (traumatic eczema). The later effects are of two types. In one the patient's nails tear away pieces of epidermis, producing the familiar "scratch-marks," illustrated by scabies, pediculosis corporis, dermatitis herpetiformis, and the prurigo of Hebra. In the other group there may be no such visible signs of scratching, *e.g.* in lichen planus, pruritus senilis, urticaria and pediculosis pubis.

Civatte has shown that in slight excoriations, produced by scratching, the early changes take place in the *lower* layers of the epidermis and in the papillary body; in deeper excoriations there is a crust formed by a mass of coagulated serum, infiltrated with leucocytes and red corpuscles, which is embedded in the epidermis. Beneath it the horny layer and granular layers—and at its centre the whole epidermis—are absent. From this it is clear that moderate scratching perforates the healthy epidermis *from the depth towards the surface.* Some scratch-marks are punctate and situated at the summits of *the follicles,* which in pruritus are often erected by contraction of their pilomotor muscles; these excoriated follicular papules, which are well seen in scabies, must not be confounded with the true papules of prurigo. In other cases, as, for example, in pediculosis corporis, the scratch-marks are linear, and independent of the follicles.

Apart from excoriations, however, there are two types of lesion that result from long-continued scratching, namely *prurigo papules* and *lichenification* (*lichenization* of Besnier). These two forms of reaction to scratching often coexist in the same patient.

(1) The *prurigo papule* varies in size between that of a millet seed to that of a pea: on the whole it tends to be larger than the elementary papule of lichen planus. Usually hemispherical, it may, like the latter, be plane. Its colour varies, being sometimes almost that of the normal skin, sometimes reddened or bluish-red, or yellowish-brown. Its surface may be smooth and shiny, or scaly: often it is excoriated from scratching and covered with a blood-crust. Histologically these papules are characterised by acanthosis of the epidermis, with hypertrophy of the granular and horny layers, and an infiltration of the dermis with leucocytes and eosinophiles.

(2) *Lichenification.* This change in the texture of the skin, due to repeated scratching over long periods, has been minutely described by Brocq. It may be more or less generalised, or strictly localised to certain regions (circumscribed prurigo, lichen simplex chronicus of Vidal). The skin of the affected part is markedly thickened, and the natural lines are accentuated, thus giving the picture of a mosaic, composed of lozenge-shaped, polygonal, or square areas, the

surfaces of which appear polished and shiny. Sometimes, however, they may be covered with fine scales, or, after the paroxysms of scratching, by blood-crusts. The colour of lichenified skin varies. In quiescent periods the area affected often only differs from that of the surrounding healthy skin in being slightly more pigmented: sometimes it is dark-brown or greyish-brown, sometimes even depigmented, but after a paroxysm it is usually reddened and excoriated. At the edges of a patch of lichenification there is almost always a zone of brownish pigmentation, which merges imperceptibly into the healthy skin beyond; in this zone are often seen small discrete shiny papules, flat and hardly raised above the surface. This state of lichenification may arise *de novo* on normal skin as a result of the scratching and rubbing provoked by a pruritus, or it may complicate a pre-existent dermatosis, such as eczema, seborrhœic dermatitis, intertrigo, or lichen planus, which is then said to be *lichenified*. It is often difficult in a given case to distinguish between a primary prurigo, which has become *eczematised*, and a primary eczema, which has become *lichenified*. To such cases the non-committal term " eczema-prurigo " is often applied.

The different forms of prurigo, as met with in practice, may now be dealt with.

Prurigo Simplex. The term *prurigo simplex* (excluding prurigo simplex acutus or papular urticaria of young children) should strictly be reserved for those cases which do not fall into the special categories to be described later, and in which the earliest symptom is an idiopathic pruritus, *i.e.* one neither dependent on a recognisable external cause, such as invasion by animal parasites, a mycotic or bacterial infection, nor resulting from intoxication by drugs or foods. In describing the localised forms of prurigo simplex, however, it is more convenient to include pruritus ani and vulvæ, which may depend on a purely local cause.

Circumscribed Prurigo (*Lichen simplex chronicus of Vidal, Neurodermatitis*). The characteristic changes in the affected area of skin are those of *lichenification* (*q.v.*). The sites of election are the occipital region of the scalp (this localisation is almost confined to women), the back or sides of the neck, the antecubital fossæ, the elbows and upper portion of the posterior surface of the forearms over the ulna, the outer surfaces of the thighs and legs, the popliteal spaces, the genital organs and groins, the sacral and coccygeal regions, the internatal cleft and perineum.

The early symptom is a simple pruritus, intermittent and at first often slight; gradually the itching becomes more intense, until veritable paroxysms, usually nocturnal, occur, and the patient scratches or rubs the part furiously. This may be done unconsciously during sleep, until the crisis wakes him.

When fully established, a patch of circumscribed prurigo presents three zones: an ill-defined, hardly thickened outer one of pigmentation, with some exaggeration of the natural lines and some discrete shiny plane papules or " facets ": a middle one in which the natural lines are more exaggerated, the intervening portions of skin taking the form of papules, shiny and excoriated: and a central one, in which these changes of lichenification reach their maximum, infiltrated, hyperpigmented or depigmented, and scaly or macerated, according to the region involved. Often one cannot distinctly recognise these zones. On parts such as the eyebrows, the axillæ, the pubis and the extensor surfaces of the arms and legs, the hairs become worn away by the constant rubbing, and stand up stark and straight like the bristles on a brush.

A patch may last for years, the infiltration increasing with time. Sometimes new ones arise, the older ones ceasing to itch and undergoing resolution, leaving an area of pigmentation. Not only is there usually an associated hyperpigmentation of the surrounding skin, but circumscribed prurigo is frequently seen in patients with vitiligo. Although the objective appearances of a patch of circumscribed prurigo are those of lichenification, already described, in pruritus ani and vulvæ they are modified owing to the special structure of the parts.

In pruritus ani the area affected usually corresponds roughly to the corrugator

cutis ani muscle, but extends sometimes actually into the rectum. In men the itching often spreads forward to the median raphe of the scrotum, and in women to the vulva. In some patients, though their pruritus be severe, there may be but little objective change in the perianal skin. As a rule, however, this is thickened, sodden, whitish in colour, and thrown into infiltrated folds, between which are often found superficial fissures. Sometimes the surface is inflamed, eczematised and crusted. In long-standing cases atrophic changes are apt to occur, and the skin becomes pale and dead-looking, like old parchment.

In pruritus vulvæ the pruritus may be strictly localised to the upper portion of one or both labia majora, which becomes lichenified, or, more commonly, the labia majora and minora and the part surrounding the clitoris are all affected. As a result of long-continued scratching, the parts become thickened and hypertrophied ; they may be dry or sodden, or excoriated, eczematised and crusted. Frequently the skin of the mons veneris, groins, and inner surfaces of the thighs presents the typical appearances of lichenification, and the pruritus spreads downwards to the perianal region. As in pruritus ani, atrophy is likely to supervene in chronic cases, particularly in elderly women, and the appearances simulate those of kraurosis vulvæ.

Histologically the changes in the lichenified skin of circumscribed prurigo are far less apparent than would be expected. There is some cell-infiltration in the papillary body, with acanthosis and lengthening of the interpapillary processes in the epidermis.

Diffuse Simple Prurigo. In cases of more or less generalised pruritus there may be surprisingly little change in the skin, even though the pruritus be of long standing. On the other hand, there may be a variety of visible lesions—discrete prurigo papules, extensive areas of lichenification, linear scratch-marks, excoriated follicular papules, and eczematisation. The skin as a whole tends to become harsh, dry, thickened, and pigmented : in some patients the pigmentation is so intense, particularly around the neck and in the flexures, as to recall that of Addison's disease.

As in the circumscribed form, the paroxysms of itching are periodical ; although they may occur during the daytime, usually as a result of emotional stress, undue exertion, a change from a cool to a warm environment, or *vice versâ*, they most commonly begin in the evening when the patient is tired, when he undresses at bedtime, or in the early hours of the morning.

Treatment. Successful treatment both of the local and general forms depends entirely upon investigation of the individual case. External provoking factors, and the diet, mode of life, psychological state, and the metabolism, as revealed by examination of the urine and blood, of the patient must be considered ; and sources of toxæmia, such as focal sepsis and excessive intestinal putrefaction, should be sought for. In the generalised form, and in some cases of circumscribed prurigo, apart from suitable general and local treatment, one of the various methods of desensitisation may be indicated, *e.g.* intravenous or intramuscular injections of peptone, and autohæmo- or autosero-therapy.

Local treatment is chiefly of value in the circumscribed variety, and the application of crude coal-tar, or radiotherapy usually gives the best results. The former, previously washed to remove excess of alkali, may be painted on neat, allowed to dry, and then powdered ; or it may be diluted with acetone-collodion, or prescribed in a paste. Radiotherapy is invaluable, both as an antipruritic, and for causing resolution of chronic infiltrated patches of lichenification, but disastrous results have occurred from too frequent applications. In generalised pruritus, except in those cases in which it is associated with excessive dryness of the skin, as for example from the excessive use of alkaline soaps or other defatting substances, local treatment has a purely palliative effect, but cooling lotions or creams containing phenol, menthol, and tar, may cause a temporary cessation of itching and enable the patient to sleep.

The local treatment of *pruritus ani and p. vulvæ* demands a thorough investigation of the cause; for example, intestinal worms, hæmorrhoids, fissures, dyschezia, and infection of the parts with bacteria or fungi. Glycosuria must always be excluded in cases of pruritus vulvæ. It predisposes to infection of the parts with a monilia, which may produce an acute eczymatous dermatitis. It cannot be too strongly emphasised that radiotherapy should never be employed until the most likely cause has been determined, and then only after other measures have failed. Many causes of pruritus ani are due to an intertrigo of the internatal cleft, caused either by infection with a streptococcus, accompanied by streptococcal fissures, or with the epidermophyton or a monilia, and appropriate treatment by painting with diluted tincture of iodine or a solution of silver nitrate, or by rubbing in a benzoic-salicylic or sulphur-salicylic ointment, will be curative; in women it is commonly secondary to a vaginal discharge, due often to a chronic cervical infection, and in every case an expert pelvic examination should be insisted upon. In some case of *p. ani and p. vulvæ* no local cause can be found, and the possibility of a psychical origin should be considered. Both in cases due to an infective intertrigo, and in others, one of the most valuable local applications is a crude coal-tar paste, which should be applied thoroughly at night time, a simple paste or dusting-powder being substituted during the day.

PRURIGO SIMPLEX ACUTUS

(*Urticaria papulosa. Lichen urticatus. Strophulus.*)

This eruption is met with almost exclusively in young children between the ages of one and eight years, but occasionally it is seen later, or even in adolescence. Ordinary urticaria is very rare in infants. The eruption consists of bright red urticarial lesions in the centre of which is a small indurated papule, which persists after the surrounding erythema and œdema have subsided, so that a number of these small, shotty, brownish papules may be seen mixed with recent urticarial wheals. The rash causes intense irritation, and, as it is apt to be most profuse in the evening, the child often lies awake at night scratching and rubbing himself; during the day-time itching may be absent or slight. As a result of scratching the papules become covered with small blood-crusts, and secondary infection with pyogenic cocci occurs, resulting in the formation of pustules, impetiginous lesions, and sometimes ecthymatous sores. The eruption may then imitate that of scabies very closely. Sometimes exudation may be so great that actual vesicles are formed, or very rarely bullæ, and this vesicular form of papular urticaria is not infrequently mistaken for chicken-pox.

In chronic cases the papules, conical at first, are apt to become flattened, shiny, and angular, and they frequently have a central pit; they may thus resemble the papules of *Lichen planus* very closely. Indeed, cases that have been thought to be examples of *Lichen planus infantum* have later proved to be really *Urticaria papulosa*, although true *Lichen planus* does very occasionally occur in young children. In some children acute attacks of papular urticaria occur occasionally, usually in summer-time, and between the attacks there is absolute freedom from the eruption; in others the disease is chronic, acute exacerbations appearing from time to time. It is usually, however, most severe in hot weather. As a rule it does not continue beyond the age of seven or eight years.

Ætiology. Like ordinary urticaria and the chronic forms of prurigo, papular urticaria is one of the cutaneous manifestations of the allergic state. It is met with in two distinct types of children—the fat, or, perhaps, more strictly the "watery," indolent, often rickety child with a tendency to chronic catarrh of the mucous membranes and offensive stools from excessive putrefaction, and the thin, nervous, emotional child. Not infrequently other allergic symptoms may precede, coincide with, or follow papular urticaria, as described under the prurigo

of Besnier. The actual eruption must usually be due to an antigen, which, reaching the sensitised skin, provokes a characteristic reaction in the dermis, upon which the elementary lesion, the papule, depends. It is probable that in the majority, if not in all cases, the source of the antigen is the alimentary tract, as in Besnier's prurigo. Clinical experience suggests that the antigen is not specific for the disease, but may rarely be so for the individual, for in the majority of cases no evidence of specific food-sensitiveness can be obtained, but occasionally one food, and one only, is found to provoke the attacks—for example, bananas or eggs. A very striking feature of the disease (**45**) is that the eruption disappears promptly when the child is admitted to hospital, cannot be reproduced there, but reappears when he returns home. This, however, is to a certain extent true of other allergic diseases. Threadworms often thrive in the unhealthy catarrhal bowel of urticarial children, and it has been suggested that the worms may produce the antigen. There is a diminution of the serum calcium, and administration of calcium salts has been advocated. Teething has been considered an important ætiological factor, and it is likely that the nervous unrest and sleeplessness that accompany it, by reacting on the digestive system of sensitised children, favour the absorption of antigen and so provoke the attacks: one cannot, however, exclude the possibility of a direct effect by reflex irritation.

Morbid Anatomy. Apart from impetiginous or pustular sores, due to a superadded pyogenic infection resulting from scratching, the lesions of papular utircaria are three in number—the urticarial wheal, the central papule, and more rarely, the vesicle or bulla. Of these, the papule is the most characteristic. It is formed by an œdema of the dermis, accompanied by an infiltration with lymphocytes around a vessel: this infiltration follows the course of the vessel from its origin in the dermis up to the corium and in its ramifications in the papillary body. This vessel forms the axis of the papule, the acuminate form of which is explained by the cellular infiltration, which spreads out at its summit, and is comparable to a nail plunged vertically in the dermis. Apart from the lymphocytes, there is an infiltration of the corium with eosinophile leucocytes, both around the vessels and distant from them.

In some papules these changes in the dermis are found alone, but in the majority the epidermis is involved. The epidermic lesions appear due entirely to scratching, and vary according to the degree of traumatism; there may be merely a slight œdema of the malpighian layers with mononuclear exocytosis, or a definite cleavage of the malpighian body with the formation of an intra-epidermic vesicle, the roof of which is constituted by the intact horny layer and upper malpighian layers, the floor by the lower part of the rete, or finally by a bulla resting directly on the papillary body, which becomes replaced by a serous crust. The large bullous lesions, sometimes met with in papular urticaria, occur chiefly on parts where the horny layer is thick and less likely to be ruptured.

Diagnosis. The disease has to be distinguished from scabies, Hebra's prurigo, varicella, and *Lichen planus*. From scabies the diagnosis may be difficult, but burrows can almost invariably be found in children with scabies, if carefully sought for. Hebra's prurigo chiefly affects the lower extremities, avoids the flexure surfaces, and is usually accompanied by inguinal adenitis. Careful observation should always prevent confusion between bullous *Urticaria papulosa* and chicken-pox: *Lichen planus* is extremely rare in children, and the papules are not preceded by urticarial wheals.

Treatment. Successful treatment depends largely on the investigation of the individual case. The stools should be examined for threadworms, excess of mucus, and undigested foods, and also bacteriologically. In the fat, pasty, catarrhal child, cane-sugar and soft starchy foods, particularly ordinary bread and milk puddings, should be excluded from the dietary: lactose or glucose should be substituted for cane-sugar, and farinaceous foods given in a form that necessitates thorough mastication. In the thin, nervous child, whose stools

usually reveal excessive putrefaction, meat and fish should be excluded or reduced to a minimum, and a dietary prescribed containing plenty of crisp farinaceous food, vegetables, cooked fruits, and lactose or glucose. Careful enquiry must be instituted as to whether any particular foods, such as bananas, acid fruits or eggs, appear to provoke the attacks, and, if necessary, cutaneous food tests should be made.

Internally, small doses of calomel or grey-powder at night time and mist. alba dm. i—oz. ½ should be prescribed for a few days, or an alkaline bitter mixture, containing the compound tincture of rhubarb, given half an hour before the three principal meals. After this preliminary treatment, calcium lactate in the form of syr. calcii lactophosphat. is often of great value. The temporary use of a chloral and bromide mixture at night time is justifiable in severe cases. Peptone in the form of peptonal or peptalmine, given one hour before meals, appears sometimes to be successful. The clothing should be light and porous, and the child be kept out of doors as much as possible. Real or artificial heliotherapy is invaluable in obstinate cases. During the attacks a warm bath, to which 1 or 2 oz. of liq. picis carbonis may be added, should be taken in the evening, and the skin afterwards powdered with warmed starch powder. If septic infection of the skin has resulted from scratching, boric baths and a boric or weak mercurial ointment will control it.

PRURIGO OF HEBRA

(Prurigo ferox vel agria)

This form of prurigo, first clearly described by Hebra, presents such characteristic features that, like the prurigo of Besnier, it must be regarded as a well-defined clinical entity. Unfortunately, although absolutely distinct, these two varieties have been confused. Hebra's prurigo, which is rare, begins, as a rule, in early childhood from the second to the fifth year: whether it sometimes supervenes upon ordinary papular urticaria is doubtful. The elementary lesion is a papule, which differs both in its clinical and histological features from that of papular urticaria. When unaltered by scratching, this papule is small, very hard, and dry; it is felt by the touch more easily than it is seen, for it projects but little, and hardly differs in colour from that of the skin in which it appears embedded. Under the influence of scratching, however, it becomes excoriated, and its character is masked by an overlying blood-stained crust, which, on separating, may leave a small scar.

When fully established, the disease presents a characteristic picture. The affected parts of the skin are chiefly the extensor surfaces of the limbs, the thighs and legs more than the arms, and to a less extent the trunk and face. The joint flexures are spared, in contradistinction to the prurigo of Besnier, as also are the palms and soles. As a result of the long-continued and violent scratching, the skin of the sites involved becomes harsh, thickened, and deeply pigmented. It is covered with excoriations, some linear, some pin-point and follicular; the elementary papules can be distinguished, but are surmounted by crusts, and mingled with them are the whitish scars of former lesions. Secondary eczematisation or impetiginisation are common, and deep ecthymatous sores may complicate the picture. The lanugo hairs become worn by the scratching, and either stand up like short bristles or disappear entirely. On the less-affected parts of the skin there is seen the follicular erection found in other forms of prurigo, and due to the contraction of the pilo-motor muscles. The inguinal and, to a less extent, the axillary glands are enlarged. The characteristic changes in the skin and the distribution make it possible to diagnose the condition with the eyes shut, by passing the hands over the patient. A considerable degree of eosinophilia in the blood is present. The victims of this variety of prurigo are poorly nourished, apprehensive, and ill-cared for; the constant irritation and consequent loss of sleep react upon both their physical development and their mentality.

There is a relatively mild form of the disease (prurigo mitis), in which the elementary papules and the distribution are identical, but the secondary excoriations, lichenification, and pigmentation are less evident, and the glandular enlargement slight.

Ætiology. Hebra's prurigo is more frequent among boys than girls. It would seem that race, since it is commonest in central Europe, and poverty are the predominant predisposing factors. That it is an allergic manifestation, comparable to papular urticaria and Besnier's prurigo, is certain, but it is not known whether the antigen responsible is specific, or whether the disease, like urticaria, is a special form of cutaneous reaction to a variety of antigens. In one case ascarides appeared to be the source. The writer, confirming the observations of other authors, recently admitted a case to hospital, and, although no treatment of any kind was ordered, the prurigo ceased at once, and at the end of a week the skin had undergone a remarkable change for the better. Relapse occurred at once on his return home.

Morbid Anatomy. As in papular urticaria, the essential lesion is a papule, in which the primary changes are dermic, those in the epidermis being secondary to scratching. The initial papule is formed by a dense infiltration of the corium with *polymorphonuclear* leucocytes, which undergo rapid degeneration after leaving the blood-vessel. This mass of degenerate leucocytes forms the centre of a more diffuse infiltration of polymorphonuclear cells, which occupy the whole corium and the papillary body, but these cells do not show degenerative changes. Among them one finds a few lymphocytes around the vessels. There is a little or no œdema, but some proliferation of fibroblasts. The epidermal changes vary in different cases. They may be those of diffuse lichenification, or the necrosis of the malpighian layers, with cavitation, already described in papular urticaria.

Diagnosis. This presents no difficulties, the distribution, the pigmentation, the excoriated harsh skin, and the associated glandular enlargement being characteristic. It will be noted that the antecubital fossæ and popliteal spaces, which are the sites of election in the prurigo of Besnier, are spared.

Treatment. The essential treatment, in the present state of our knowledge, is to remove the child from its home surroundings, and to send it to live an out-of-door life in the country on a generous mixed dietary. Hebra regarded the condition as incurable, and this may be so if the child is compelled to remain at home, but the writer has not seen a case in which the prurigo did not rapidly cease on removal to hospital.

PRURIGO OF BESNIER

This form of prurigo is a well-defined clinical entity, of particular interest to general physicians owing to its frequent association with asthma and other manifestations of the allergic state. A considerable proportion of patients are *ichthyotic*, and in a still higher proportion the condition has been preceded by *infantile eczema* of the allergic type.

The life-history of the patient is frequently as follows :—Soon after birth may be apparent the dryness of the skin, which heralds the ichthyosis that is not as a rule well marked until two or three years of age. In the first few months, but sometimes later, appears infantile eczema, the onset of which may coincide with a change from breast-feeding to a diet of cow's milk, or may almost immediately follow *vaccination*. At about the age of two years the eczema tends to change its characters and distribution. It leaves the face and head, the trunk, and the extensor surfaces of the limbs, and becomes, so to speak, concentrated in the antecubital fossæ and popliteal spaces, on the backs of the wrists and hands, and sometimes around the mouth and in the folds of the neck and groins. Constant rubbing and scratching leads to *lichenification* of the skin in these situations, and the clinical picture of Besnier's prurigo is established. Sooner or later *asthmatic* attacks, often diagnosed erroneously as bronchitis, and other allergic

manifestations supervene (*q.v.*). The symptoms of this hypersensitiveness, or state of allergy, vary according to the particular structure or tissue that is sensitised.

The majority of children with Besnier's prurigo are thin, pale, nervous, restless and introspective, but it may be seen in the fat, indolent child with signs of hypothyroidism. In a characteristic case the skin is ichthyotic, harsh, and of a curious sallow, greyish tint. The pilo-sebaceous follicles of certain areas stand out owing to contraction of the pilo-motor muscles, as in other forms of prurigo. Although the itching may be widespread, it is most intense in the antecubital fossæ and the popliteal spaces, on the backs of the wrists and hands, the dorsal surfaces of the ankles, around the mouth, on the forehead, particularly over the eyebrows, in the folds of the neck, in the groins and on the genitals, and sometimes over the elbows and knees ; in many cases it is confined to the antecubital and popliteal regions. The skin at these sites exhibits the changes already described as *lichenification ;* after a paroxysm of itching, eczematisation with serous oozing, fissuring, and sometimes secondary impetiginisation are seen, but in intervals of comparative calm simple lichenification with pigmentation constitutes the sole objective signs. The pigmentation, however, is not confined to the lichenified areas, but may be generalised, and so intense, for example on the neck, round the eyes, and in the flexures, as to resemble that of Addison's disease, and, like it, may be accompanied by a low blood-pressure and muscular hypotonia.

The vermilion borders of the lips are usually of a greyish-blue or lilac tint, as is seen also in cases of light-sensitiveness. The muscular hypotonia is revealed by the faulty stance adopted when the child stands upright. The front of the chest is flat, and descends in an inclined plane towards the protuberant lax abdomen, the point of maximum projection forwards being just below the umbilicus : the back is arched, the scapulæ winged, and there is lordosis. The child is usually apprehensive, restless, easily exhausted, and extremely sensitive to its surroundings and to the influence of those with whom it comes in contact ; the same is true of the adult cases. The paroxysms of itching or the attacks of asthma, which begin, as a rule, in the evening or at night time, are often provoked by an emotional upset or the anticipation of some displeasing prospect, and may cease automatically in the quiet and well-ordered routine of hospital life, only to return under the disturbing influence of home surroundings.

Ætiology. One of the most striking features of Besnier's prurigo and of the other manifestations of the allergic state, with which it may be associated, is their hereditary transmission and familial incidence. Enquiry will almost always reveal the presence of ichthyosis, hay fever, or asthma in the parents and near relatives, or a history of infantile eczema, cyclical vomiting, urticaria or prurigo in their childhood.

Recent researches have done much to explain the pathogenesis of Besnier's prurigo, and of all the forms of prurigo it is the one of which we possess the most exact knowledge. It is clearly due to sensitisation of the skin to antigens, which, as in many cases of urticaria and probably in Hebra's prurigo, are usually, if not always, derived from the alimentary tract, escaping fixation and destruction in the liver. In urticaria, simple prurigo, and Hebra's prurigo, the reaction, resulting from contact of antigen with the sensitised skin, takes place primarily and essentially in the dermis, whereas in eczema and Besnier's prurigo, it is epidermodermal, *i.e.* both the dermal tissue (probably neuro-vascular) and the rete Malpighii are sensitised.

As regards the nature of the antigens, it is probable, as was pointed out in the section on urticaria, that the actual antigenic substances, although derived from proteins, are themselves non-protein in nature and of relatively simple composition. Persons manifesting the abnormal hypersensitiveness that results in the multiple symptoms of allergy referred to would seem to have a limited power of dealing effectively with foreign proteins, both when taken into the alimentary

tract or when they reach the system parenterally. In the case of food-proteins, it is probable that their delayed or incomplete digestion is an important factor, and diminution or lack of gastric hydrochloric acid has been noted in a considerable percentage of these persons; apart from this, the failure of the liver to fix and destroy proteins and their derivatives, including their antigenic moiety, is clearly the essential factor. When this function of the liver fails, antigens reach the blood-stream and react with the antibodies in sensitised tissues, of which the skin is the most important, and these reactions, represented by the cutaneous manifestations of the allergic state, are really protective in nature, since they result in the fixation and destruction of the circulating antigens. In other words, the skin, and, to a less extent, other tissues take on a vicarious protective function when that of the liver fails.

In infantile eczema, and possibly in Besnier's prurigo, it would seem likely that sometimes, as in certain cases of urticaria, the antigen responsible is specific in that it is derived from one food-substance (*e.g.*, wheat, oat, cow-milk), but in the latter, at any rate, this is certainly exceptional. It is found (**46**) that in patients with Besnier's prurigo, one can evoke the hæmoclasic crisis by the oral administration of various proteins and peptones, or by injection of their own blood. Examination of the blood and urine reveals the same changes that characterise other manifestations of the allergic state (*q.v.*).

Apart from the factor of sensitisation, however, the importance of psychological disturbances can hardly be exaggerated in these patients. The asthma-eczema-prurigo syndrome is particularly likely to occur in the "only child." Rogerson (**47**) has clearly shown how the home environment may affect these children. Out of twelve severe cases, selected at random, five were entirely relieved of their symptoms by psychotherapy of the mother and, to a less extent, of the child itself, and in five others there was marked and progressive improvement.

Morbid Anatomy. The microscopical changes in a patch of Besnier's prurigo naturally vary. In the quiescent stage, they are merely those of lichenification, namely acanthosis and hyperkeratosis: during a period when the itching is severe, the lesions of eczematisation—vesiculation—and of scratching, viz. rupture of the rete beneath an intact horny layer, or serous crusting when this is broken, are observed.

Diagnosis. Once a case of Besnier's prurigo has been seen and its salient features appreciated, there should be no further difficulty in diagnosis. From the prurigo of Hebra it is easily distinguished by the inverse distribution of the chief sites of election—extensor surfaces of the limbs in the former, antecubital and popliteal spaces in the latter. Moreover, the characteristic lesions in Hebra's prurigo are the papules, whereas in that of Besnier they are diffuse plaques of lichenification with eczematisation.

Treatment. Besnier, in his original writings, emphasised the chronicity and resistance to treatment of the form of prurigo that now bears his name.

Observations upon a large number of cases have confirmed the value of the following principles of treatment, based largely on biochemical researches (**48**); (1) The treatment *par excellence* is a completely out-of-door life in a fairly bracing climate with judicious heliotherapy: some cases do well by the sea, others are better among inland hills. The clothing must be light, and, as the physical condition improves, vigorous exercise should be taken. The influence of cool air and sunlight on the whole skin is potent in stimulating the accelerator endocrine glands, chiefly the adrenals and thyroid, and is doubtless an important factor in restoring the metabolism and endocrine-autonomic balance to normal. Under these conditions, even though no dietetic restrictions be enforced, the patient's whole appearance and temperament are transformed. His skin, even though previously ichthyotic, becomes soft and supple, and its horny layer thin and translucent. The prurigo and asthmatic attacks cease. The tone of the muscles

is restored, with consequent improvement of the stance and increased physical vigour, and the patient loses his irritability and apprehensiveness, and becomes calm, bright and happy. This physical and mental transformation is accompanied by a restoration of the metabolic functions to normal, as revealed by biochemical examinations of the blood and urine. Unfortunately, if the patient be compelled to return to a sedentary indoor life in unhealthy or unhappy home surroundings, relapse is liable gradually to occur. Psychological investigation and treatment, both in children and adults, may be of paramount importance.

(2) *Diet.* A lacto-vegetarian diet has been recommended, but the writer has recently observed that a dietary such as that recommended for the treatment of chronic urticaria is usually of great value in these cases. Foods to which the cutaneous tests reveal hypersensitiveness should, of course, be excluded.

(3) In some cases, a preliminary detoxication treatment is advisable. For this purpose small doses of calomel ($\frac{1}{8}$ to $\frac{1}{6}$ gr.) at bedtime, and an alkaline saline containing the aperient sulphates on rising, and an hour before midday and evening meals, should be given for a fortnight, and afterwards the calomel or a blue pill may be taken on one or two nights a week, followed the next morning by the saline.

(4) It is of great importance to stimulate the skin and thereby the adrenal-thyroid-sympathetic system, by outdoor exercise in very light clothing, alternate hot and cold baths or douches, and by real or artificial heliotherapy.

(5) In some cases thyroid gland in suitable doses by mouth is of great value, and in very nervous, worrying patients, who sleep badly, a mixture containing bromide and sal volatile should be given thrice daily for a while.

(6) Local treatment of the pruriginous areas is of secondary importance, but the most effective measures are the X-rays, given in fractional doses at suitable intervals, and the application of crude tar, either in a paste, or as a paint, pure or diluted with 1 to 3 parts of acetone-collodion. In mild cases a clean paste, containing the ether-soluble fraction of crude tar, may be substituted. It cannot, however, be too strongly insisted that local treatment alone is only palliative, and it is better to avoid employing radiotherapy except when only a few lichenified patches are present.

(7) Lastly may be considered the various methods of so-called desensitisation. Autohæmotherapy is sometimes helpful, from 3 to 15 c.c. of blood being withdrawn from a vein and injected just before clotting commences into the gluteal muscles. Intravenous or intramuscular injections of a carefully-prepared solution of peptone, given at intervals of from three to seven days in increasing doses, may be successful. In some cases good results have been obtained by hypodermic injections of a stock or autogenous mixed bacterial vaccine prepared according to Danysz' method from intestinal bacteria, or by the deliberate production of protein-shock by means of intravenous injections of *B. coli* or typhoid-paratyphoid vaccine, or of solutions of various vegetable proteins. The writer, however, has found that weekly injections of an autogenous preparation of the substance P. of Oriel, beginning with very minute doses, *e.g.* 0·1 c.c. of a one-in-one-million dilution, provide the most effective method of desensitisation, and this has been confirmed by others. The dosage, however, must be carefully controlled in order to avoid unpleasant reactions.

PRURIGO NODULARIS (Hyde) (*See Plate 61, D*)

(*Lichen obtusus corneus. Urticaria perstans verrucosa*)

This condition, concerning which some confusion still exists, is characterised by the presence of large discrete papules, scattered irregularly, sometimes in groups, chiefly on the limbs, but also on the trunk and occasionally on the face. These papules are hemispherical, hard to the touch, and may attain the size of a nut. Their surface, usually excoriated and covered with blood-crusts, becomes

warty from hyperkeratosis, and irregular. Each is usually surrounded by a halo of pigmentation, and sometimes by a small area of lichenification. In cases in which the itching is very severe, the papules may become surmounted by bullæ, doubtless caused by vigorous scratching. The lesions may disappear, leaving a depigmented macule, bordered by the zone of hyperchromia. Apart from the papules, the skin is usually normal, but may be excoriated, and areas of circumscribed lichenification may be present independently of the papules. The itching, entirely absent in one recorded case, is usually intense, paroxysmal, and chiefly nocturnal, but periods of relative freedom occur, for example when the patient is on holiday.

Ætiology. Like other forms of prurigo, the condition is doubtless allergic in nature, but the nature and origin of the antigen are unknown. It is commoner in women than in men, and, as with other allergic symptoms, psychical influences, such as worry, grief, or shock, are of importance. The duration may be said to be indefinite, as treatment up to the present is admittedly of little avail.

Diagnosis. This presents little or no difficulty as a rule, but the eruption must be distinguished from *hypertrophic lichen planus*, in which the lesions are usually larger and flatter, and often accompanied by the ordinary papules elsewhere or by involvement of the buccal mucosa, and from the condition which may be labelled *lichen obtusus vulgaris*, and is merely a hypertrophic or giant form of lichenification (circumscribed prurigo). The eruption sometimes termed *lichen obtusus corneus* is identical with prurigo nodularis. There are thus three entirely distinct conditions, which are frequently confused: (1) The hypertrophic form of lichen planus, situated as a rule on the legs below the knee, particularly on varicose legs. (2) Lichen obtusus vulgaris, or the hypertrophic form of circumscribed prurigo, also usually seen on the legs, but occurring as well on the thighs, genitals, buttocks, and in the groins. This condition is commonly localised to one or two areas, and the horny papules are closely set on a plaque of lichenification. (3) Prurigo nodularis or lichen obtusus corneus, in which the papules are discrete, and disseminated irregularly, but more or less bilaterally symmetrically on the limbs.

Morbid Anatomy Civatte has confirmed histologically the distinction between lichen obtusus vulgaris and prurigo nodularis. In the former the microscopical appearances are solely those of lichenification. In the latter these are also seen, but they are superadded to a lesion situated deeply in the dermis, which is the essential part of the papule of prurigo nodularis. This lesion consists of a dense infiltration of various types of cells, histiocytes, polymorphonuclear leucocytes, eosinophiles, plasma cells, and mast-cells. Giant cells may also be found.

Treatment. This is usually very unsatisfactory. The application of X-rays to the lesions may give relief from itching for some time and cause them to disappear, but relapse is the rule. A long holiday may result in an entire cessation of the itching with effacement of the papules. Covering the affected parts with an occlusive dressing, such as Unna's paste, may also cause their disappearance.

SUMMER PRURIGO

Under this term, first employed by Hutchinson in 1879, are included conditions that are certainly distinct from one another both clinically and ætiologically. Tentatively one may classify them as follows: (1) *The Juvenile Group.* This includes (*a*) the severe bullous eruption *Hydroa vaccinoforme*, which is usually associated with hæmatoporphyria congenita, and can hardly be described as prurigo, (*b*) the mild papular type to which Hutchinson first applied the name "summer prurigo," and (*c*) the more severe variety of this, in which vesicles and bullæ, as well as papules, occur, and which clinically appears to be intermediate between the first two. (2) *The Adult Group.* This includes the cases of light-

sensitisation, in which susceptibility to light develops for the first time in adult life. In these patients the reaction of the skin to light is usually eczematous in character, indicating *epidermal* sensitiveness, and lichenification of the affected areas results from constant rubbing and scratching; the reaction may, however, be mixed, urticated papules being mingled with a diffuse eczematous dermatitis. More rarely, a simple urticaria (urticaria solaris)—*i.e.*, a purely dermal reaction—may be the response to exposure to light. All these varieties of eruption have this in common, that they occur only, or are most intense, in summer, and that they are provoked chiefly by exposure of the skin to light; heat in some cases would also seem to be a predisposing factor. The differences in their clinical characteristics depend no doubt partly on the particular sensitising substance responsible, and partly upon the tissue sensitised, whether dermal, epidermal, or both.

***Hydroa Vaccinoforme* (*Bazin*).** This rare, congenital, and sometimes familial eruption usually manifests itself in the first year of life after exposure of the skin to sunlight. It consists of lesions beginning as erythematous papules, papulo-vesicles, or directly as vesicles and bullæ, which may be hæmorrhagic or become pustular. They are umbilicated, and dry up to form brownish crusts, beneath which the centre of the lesion is found to be necrotic. On separation of the crust there is seen an ulcer, which eventually heals, leaving a varioliform scar. The eruption occurs on parts exposed to light, and the scarring may cause considerable destruction of the ears, alæ nasi, and fingers. Fresh outbreaks occur every summer, the eruption subsiding to a great extent in winter; after puberty the attacks may cease.

Ætiology. The great interest of this condition is its association with the very rare inborn error of metabolism, hæmatoporphyria congenita. Examination of the urine and fæces shows the pigments described by Fischer—uro-porphyrin in the urine, sterco- or copro-porphyrin in the fæces. The teeth may be coloured pink, and on transillumination, the bones are seen to be darker than normal from the presence in them of the porphyrin pigment. The blood changes indicate great activity of the bone-marrow, and the spleen and liver may be enlarged. It is the shortest ultra-violet rays, those with a wavelength of between 400 and 300 $\mu\mu$, that provoke the eruption. Presumably in these cases the porphyrins are the agents that sensitise the skin to light, for the injection of porphyrin experimentally into a normal person has been shown to have this effect. In cases of hydroa vaccinoforme without hæmatoporphyrinuria, it appears likely that porphyrins may be present in the stools. A similar eruption may occur in sulphonal poisoning, in which there is also hæmatoporphyrinuria.

Pathological Anatomy. The primary change appears to be an enormous dilatation of the blood vessels in the corium, with serous and cellular exudation, which destroys the rete Malpighii and forms a bulla beneath the horny layer. Necrosis of the corium takes place owing to hæmorrhage from and thrombosis of the vessels.

Treatment. As hæmatoporphyria congenita is an inborn anomaly of metabolism, no treatment, apart from the protection of the skin from light, is of any avail. Quinine possesses the property of shutting off the ultra-violet rays, and may be applied as an ointment (℞. Quininæ (alkaloid) 5·0, Acid. Oleic. 20·0, Acid Stearic. 100·0, Pot. Hydrox. 5·0, Aq. dest. 400·0), to exposed parts. After applying this, a dusting powder, *e.g.*, ℞. Quin. Sulph. 1·0, Talc. 15·0, suitably tinted, may be dusted on. More effective is a lotion containing tannic acid: *e.g.* ℞. Acidi Tannici 10·0, Spt. vini meth. ind. 25·0, Aq. dest. ad 100·0.

***Summer Prurigo* (*Hutchinson type*).** (*Hydroa æstivale of mild type* (*Colcott Fox*). *Dermatitis recurrens æstivalis* (*Radcliffe Crocker*).) These mild cases of "summer eruption" are met with in children and adolescents, and their ætiological relationship to hydroa vaccinoforme on the one hand, and to the adult type of light-sensitisation on the other, requires elucidation. The eruption

consists for the most part of discrete papules, resembling those of papular urticaria, pale and almost the colour of normal skin when not scratched. In mild cases these may be the only lesions, but in others there are papules surmounted by vesicles, or vesicles and even bullæ, as in the case described by Adamson (**49**), may appear *de novo* on exposure to bright light. The degree of itching, and consequently the secondary results of scratching, vary in different cases, and the lesions may or may not be followed by scarring. The eruption is situated chiefly on exposed parts, particularly the face and the extensor surfaces of the arms and hands.

Ætiology. In some of these cases, especially when actual bullæ are formed, it is probable that porphyrins, due to an inborn metabolic error, are the sensitising agents to light. In the urine the prophyrins fluoresce strongly with ultra-violet light, and can by this means be more readily detected than by the spectroscope. In other cases there are no porphyrins, and the sensitising substance is unknown.

Treatment. In the cases in which porphyrins are apparently the sensitising substances no treatment, apart from protection from light, is of avail. In others some method of desensitisation should be tried, such as auto-hæmotherapy, and injections of peptone or of the substance P. of Oriel. The last has proved effective in some cases.

Light-sensitiveness of the Adult Type. This is a well-defined clinical entity, distinct from hydroa vacciniforme and from the milder forms of summer prurigo occurring in children. Females are affected more commonly than males, the converse being the case in hydroa vacciniforme. The history usually obtained is that after exposure to strong sunlight, particularly at the seaside, the patient developed an acute dermatitis of uncovered parts with severe irritation, and that subsequently further exposure even to light of moderate intensity caused a recurrence of the symptoms to a greater or less extent. The cases differ according to the degree of their sensitiveness. In some the irritation and the eruption are only provoked by strong sunlight, in others the susceptibility may be extreme, so that the symptoms persist even in winter.

Symptoms. The clinical features of what may be called the adult type of light-sensitiveness are so characteristic that the condition may be diagnosed at a glance. The patient's complexion, even when no active eruption is present, has a sallow, earthy tint, and the vermilion border of the lips is of a characteristic bluish-grey colour. In a case of moderate or great severity, the skin of the face, neck and other exposed parts is definitely thickened, and the natural lines are accentuated, the changes being doubtless partly due, as in ordinary lichenification, to the incessant rubbing and scratching which the intense irritation provokes. The appearances are, in fact, very similar to those seen in the generalised prurigo of allergic origin. The actual eruption, which appears on uncovered parts, when the patient is exposed to light of a certain intensity, is in the early stage an erythema, with a varying degree of serous exudation, the affected areas of skin being bright red and somewhat œdematous. Eczematisation, which is always an indication of epidermal sensitisation, then supervenes, and in an acute attack, numerous, close-set eczematous papules and vesicles arise on the preceding erythematous base. The eyelids are often swollen, as in an eczematous dermatitis produced by chemical or other irritants. Not infrequently urticated papules are mingled with the eczematous lesions, and in rare cases the response to light is a purely urticarial one, there being no eczematisation.

The acute outbreaks are seen most commonly in early spring, and occasionally, after their subsidence, the patients may suffer little inconvenience throughout the summer, except on exposure to strong sunlight. More commonly, however, a chronic eczematisation of the face, neck and the backs of the hands and wrists succeeds the acute phase of the eruption, and the patient experiences paroxysms of intense irritation, which may seriously interfere with sleep. On the nose, malar regions and chin, serous exudation from the eczematous vesicles constantly takes

place, drying up to form yellowish crusts. The skin becomes harsh and thickened from the chronic inflammation, and gradually lichenification results owing to constant rubbing and scratching. On the neck and backs of the hands discrete lichenified papules, similar to those seen in the juvenile cases, are often present. In the more severe cases irritation, with eczematisation and lichenification, may occur on parts of the body other than those exposed to light, and in a small proportion of patients, who have suffered from Besnier's prurigo from childhood, light-sensitiveness may develop in adult life.

It will be observed that the clinical features of the eruption in these adult cases differ materially from those that characterise the juvenile form of light-sensitisation. In the latter the lesions consist of discrete papules, papulo-vesicles and bullæ, which dry up to form crusts, and frequently leave pitted scars. In the former the cutaneous reaction is more superficial and of an eczematous nature, and even in the most severe cases scarring, apart from secondary pyogenic infection, is never seen. It would seem that the early inflammatory changes in hydroa vacciniforme are primarily dermic, whereas in the adult form the reaction is, as has been said, more superficial, and due to epidermal sensitisation.

Ætiology. The results of investigations (**50**) carried out in these cases may be summarised as follows:—(1) There is no definite evidence that the sensitiveness to light is dependent upon a porphyrin. (2) In a considerable proportion of cases there is either achlorhydria or marked hypochlorhydria (80 per cent. of cases). This tendency is also found in Besnier's prurigo, and may be an important factor. In neither condition, however, is it by any means constant. (3) *The Fæces.* An abnormal intestinal flora has almost invariably been found, with evidence of excessive putrefaction. Of particular importance probably is the presence of non- or late-lactose fermenting coliform organisms of various types. (4) *The Urine.* Very marked excess of indican or urorosein is practically constant. In addition a definite excess of urobilin may be found, and specimens taken at intervals throughout the twenty-four hours may give findings similar to those described in allergic states. (5) *The Blood.* The amino-acid content is usually higher than normal. The Van den Bergh test has given a positive indirect reaction in several cases examined. (6) On X-ray examination of the gastro-intestinal tract after a barium meal, visceroptosis, with delay in the cæcum and some part of the colon, was almost constantly found.

From these data, and from the results of treatment based upon them, it may reasonably be inferred that the substance which sensitises the skin to light is formed in the intestine, escapes fixation and destruction in the liver, and thus reaches the systemic circulation. The nature of the substance is unknown. It may be a product of the action of putrefying bacteria upon incompletely-digested protein, or, as some experiments of Knott would suggest, a soluble toxin elaborated by abnormal coliform organisms of the non-lactose fermenting type.

Treatment. From observations on a large number of cases, the only line of treatment, apart from protection of the areas of skin exposed to light, that until recently has given any permanent relief, has consisted of measures designed to inhibit the growth of putrefactive bacteria in the intestine, and to encourage that of fermentative organisms, such as the *B. Acidophilus.* Cases of slight or moderate severity have been successfully treated as follows: (1) *Diet.* A practically vegetarian dietary has been prescribed, consisting chiefly of all kinds of vegetables and fruits, cooked and raw, crisp cereal foods, butter, plain cheese, eggs in moderation, and a liberal supply of glucose, lactose, or lactodextrin. (2) An initial course of high-colon lavage, followed by non-irritating laxatives when necessary. (3) In cases of hypo- or a-chlorhydria the administration of hydrochloric acid and pepsin, in order to favour rapid and complete digestion of protein. (4) Feeding with *B. Acidophilus* milk or cultures, and lactose. In addition, definite benefit would seem to have resulted from injections of a vaccine of abnormal coliform organisms obtained from the stools, or from the oral admini-

stration on an empty stomach of an antivirus prepared from cultures of such organisms. *Locally.* Considerable protection from light can be obtained by the wearing of reddish veils, and by the application to exposed parts of a cream and powder containing quinine, as advised for hydroa vacciniforme.

PRURIGO HIEMALIS

(*Winter Prurigo*)

This variety of prurigo occurs in autumn and winter, disappearing with the approach of warm weather. The attacks of itching are usually provoked when the skin is exposed by undressing or on rising from bed. The itching is usually most intense on the inner surfaces of the thighs, on the legs below the knees, on the extensor surfaces of the forearms and around the joints. Lichenification and follicular excoriation may result from scratching.

Ætiology. Exposure to cold is the principal provoking factor. Unnatural dryness of the skin, which is intensified by cold weather, is often noted, as in senile pruritus, and the itching then occurs chiefly where the skin is naturally driest, namely on the extensor surfaces of the limbs.

Treatment. In patients with dry skins, the avoidance of alkaline soaps and too frequent hot baths, and the application of an emollient antipruritic ointment night and morning may be successful. Stimulation of the skin by alternate hot and cold douches, and by vigorous outdoor exercise in light clothing, or a course of ultra-violet baths is indicated in resistant cases. Sometimes there are signs of hypothyroidism, and thyroid medication will then improve the texture of the skin and diminish its sensitiveness to cold.

DERMATITIS HERPETIFORMIS

(*Duhring's Disease. Hydroa Herpetiformis*)

Duhring, who introduced this term, gave the following definition of the disorder to which he applied it: "An inflammatory, superficially seated, multiform herpetiform eruption, characterised mainly by erythematous, vesicular, pustular, and bullous lesions, occurring usually in varied combinations, accompanied by burning and itching, pursuing usually a chronic course with a tendency to relapse and recur." The eruption is not a common one, but mild forms of it often remain unrecognised, and it would appear to be on the increase in this country. Duhring rightly emphasised its polymorphic character, and this accounts for the difficulty in diagnosis experienced by those without special knowledge.

The different lesions composing the fully-developed eruption are as follows: (1) Erythematous plaques, usually urticated, circular or irregular and gyrate in outline, and varying greatly in size. (2) Urticarial wheals, or urticated papules resembling those of simple prurigo. (3) Vesicles, or more rarely bullæ, giving rise to the herpetiform appearance. They commonly arise on the erythematous patches, but may form independently of them. Their contents are usually clear at first, but may rapidly become purulent.

To these primary lesions are superadded those produced by scratching, namely erosions, which become covered by blood-stained crusts, and linear scratch-marks, and the skin becomes pigmented. The pigmentation is diffuse on the areas most affected, but occurs also as brown macules, surrounding the marks or superficial scars left by the vesicular or papular lesions. During a period of quiescence it is often possible to establish the diagnosis of dermatitis herpetiformis, even in the absence of active symptoms, owing to the distribution and characteristic grouping of the pigmented patches. The sites of election of the eruption are the shoulders, the upper arms near the axillæ, the lower part of the

back and upper portions of the buttocks, the chest, the forearms and the legs below the knees. The buccal mucous membrane is involved in about half the cases, the lesions resembling those of erythema multiforme. The face, the scalp, and even the palms and soles may all be affected.

The disease is subject to exacerbations and remissions. During an active stage fresh lesions appear in small numbers daily or every few days, or there may be periodical extensive outbreaks, followed usually by intervals of comparative calm. The variety of the eruption seems to depend to some extent on the individual affected. Thus in some patients the herpetiform type of lesion predominates; in others, urticated papules and vesicles; in others again, bullæ of considerable size are the striking feature; and the degree of pigmentation varies considerably. Rarely the bullous lesions, particularly in the flexures, become vegetating, recalling the appearances of pemphigus vegetans. In children the bullous form is the commonest, and doubtless corresponds to the *hydroa puerorum* of Unna, and there is less pigmentation; it may be difficult to distinguish from bullous papular urticaria. The writer has seen the latter followed in adolescence by typical dermatitis herpetiformis.

The subjective symptoms are more complex than mere itching, hence Brocq's term "*dermatites polymorphes douleureuses.*" The patients complain of burning, tingling, or of actual pain, apart from the predominant sensation of itching. Their discomfort increases, as a rule, towards night time, and insomnia is often a serious result. It is considered one of the characteristics of the disease that the state of general health suffers but little, but in severe cases the long-continued irritation and insomnia react considerably upon the patient's mentality, and he becomes nervous, emotional, and even suicidal.

Prognosis. In the majority of cases, although the disease may last for many years, the prognosis is favourable as regards life. In rare instances, however, the eruption may become transformed into a true pemphigus, ultimately of the foliaceous type, with fatal results.

Morbid Anatomy. The erythematous plaques are constituted by vascular dilatation, with œdema chiefly in the papillary layer of the corium. There is perivascular infiltration, consisting largely of eosinophil cells. The larger vesicles and bullæ may be formed by effusion between the entire epidermis and the papillary body, or between the stratum corneum and the rete, or by the confluence of small vesicles in the rete. The serous fluid contains eosinophiles in large numbers, which may later be replaced by polymorphonuclear leucocytes when it becomes purulent. The eosinophilia in the blood varies from 5 to 30 per cent.

Ætiology. It has been suggested (**51**) that dermatitis herpetiformis is due to "sensitisation of groups of cutaneous nerve-endings to some bacterial protein from the bowel," and this view is in all likelihood substantually correct. That the eruption is due to involvement of certain nerve-elements in the skin is suggested by the sensory symptoms, and the herpetiform character of the lesions; that it is allergic in nature is probable in view of the eosinophilia and the fact that the same biochemical changes in the blood and urine that occur in other allergic conditions have been found by Oriel in dermatitis herpetiformis. The beneficial effect of an anti-putrefactive diet, and investigation of the intestinal flora, suggest that in most cases, at any rate, the antigen, to which the nerve-elements in the skin are sensitised, is derived from the bowel. It is probable, however, that the actual antigen is not the same in all cases, the characteristics of the eruption being dependent on the particular nerve-elements sensitised, rather than on the specificity of the antigen. A curious feature of the disease is that the patients manifest an intolerance of iodide of potassium, and, to a less extent, of bromides, both when applied externally and taken orally. A 50 per cent. ointment of potassium iodide in vaseline, applied to healed areas of dermatitis herpetiformis, provokes an acute reaction, but this is not found in true pemphigus. Sodium iodide, however, has not the same effect.

On the Continent the view is held that dermatitis herpetiformis is a variant of chronic pemphigus, and that both are caused by infection with a filterable virus. While admitting that a typical case of dermatitis herpetiformis may become transformed into an equally typical one of pemphigus, and end fatally, the prognosis of the former as regards life is nearly always as benign as that of the latter is grave. Moreover, it is difficult to believe that herpes gestationis, which is indistinguishable clinically from dermatitis herpetiformis, can be due to a specific infective organism, since its occurrence is directly connected with pregnancy, the termination of which is followed by recovery.

Treatment. Severe cases should be kept for a while completely at rest in bed; this alone may suffice temporarily to clear the eruption. As pointed out by Norman Walker (**52**), starvation has the same effect, and he records a severe case in which, after preliminary fasting, a lacto-vegetarian diet has kept the patient practically free from symptoms. The same dietetic rules that are recommended for light-sensitisation (*q.v.*) should be enjoined, and for a while, at least, all forms of meat and fish should be excluded. Glucose, or lacto-dextrin, should be given freely, together with acidophilus milk, in order to diminish intestinal putrefaction. An out-of-door life is advisable when possible, and regular exercise in the fresh air must be insisted upon. *Internally.* *Arsenic*, given in increasing doses, will almost always control the eruption, and may be prescribed as a temporary measure; but it is never curative, often seems to lose its effect after a while, and is dangerous, if persisted with, owing to its toxic action on the liver and its liability to cause epithelioma, several cases of which have been reported in this disease. Quinine in large doses has also been recommended. An initial course of high-colon irrigation is valuable, and the temporary use of small doses of calomel and the aperient sulphates is advisable until a suitable dietary has regulated the bowels. *Locally.* External applications have a purely palliative action, but a sulphur ointment, as advised by Duhring, applied freely for a few days at a time, often gives great relief, *e.g.*, ℞. Sulphur. præcip. gr. xxx. Ung. Zinci ad oz.i. Apart from the above measures, some method of desensitisation is usually necessary. Autohæmo- or autosero-therapy is of undoubted value, as also are injections either of a stock fæcal vaccine, prepared according to the method of Danysz, or of an autogenous vaccine, prepared from the abnormal strains of coliform organisms that are usually found in patients with dermatitis herpetiformis. Recently, however, Barber and Oriel have obtained striking results in several cases by injections of the proteose, obtained by the latter from the urine, in suitable dilutions. This method has in the writer's hands proved itself superior to any other form of desensitisation so far employed. As in pemphigus, injections of germanin have been given with benefit in some cases.

DERMATITIS VENENATA AND TOXIC ERUPTIONS

Many forms of dermatitis can be traced to the direct application of poisonous materials or to their internal administration. Such, for instance, in a mild form is the familiar urticaria of the stinging nettle (*Urtica dioica*), and in a much more severe form the eczematous eruption produced by contact with the leaves of the *Primula obconica*, and with the juice of plants of the order *Anacardiaceæ*, to which *Rhus toxicodendron* and the Indian marking-nut belong. Chrysanthemums, daffodils, lilies-of-the-valley, and many other plants may also cause an acute dermatitis in certain persons. The results of the presence of toxins and allied poisons in the blood are seen in the erythematous eruptions of the exanthems, in the occasional eruptions of pyæmia and septicæmia, in eruptions after vaccination and in the erythematous rashes which sometimes follow the injection of diphtherial and other antitoxins. *Urœmic dermatitis* is a toxic form which is occasionally seen in chronic Bright's disease towards the end of the illness. It often begins as papules or larger elevated patches of red inflamed skin, which

ultimately coalesce, so that the whole body may be covered with red thickened skin. Subsequently desquamation takes place, and some cases have a close resemblance to exfoliative dermatitis. Lastly, we have the poisonous effects of certain drugs when given in undue quality, or unduly retained by inadequate elimination by the kidneys, or in cases of idiosyncrasy.

ERUPTIONS CAUSED BY DRUGS INGESTED

The eruptions produced by drugs are erythematous, urticarial, vesicular, bullous, purpuric, or in some other form; the first four varieties are more common, and especially the first—namely, erythema. The following are the most important:

Antipyrin. A red, papular or morbilliform eruption over the greater part of the body, sometimes with itching and subsequent desquamation. Purpura has also been seen, and sometimes characteristic pigmented erythematous patches.

Arsenic. Urticaria, erysipelatoid rash, or small papules. Herpes zoster and herpes simplex are often provoked by the administration of arsenic either orally or by injection. The long-continued use of arsenic has caused a general pigmentation of the skin, and in psoriasis the healed patches sometimes become very deeply stained. *Keratosis*, or thickening of the horny layer of the epidermis, especially affecting the soles of the feet and palms of the hands, also occurs, and was seen in the accidental poisoning of beer-drinkers by arsenic in 1900.

Borax and Boric Acid. Inflammations of the skin have occasionally followed the internal use of borax, as well as its application to the surface, and to internal cavities. The eruptions are erythematous, and sometimes bullous, or even hæmorrhagic.

Bromides. An acneiform eruption is common as the result of the use of bromides in epilepsy; the pustules are usually discrete, and occur on the face, chest, back, or scalp, and around the hair follicles on the thigh. More extensive lesions occur in exceptional cases in children on the face and limbs; these are large, oval or circular, much-raised patches of deep red colour, covered with a number of pustular points, or the thick scab which follows their rupture. The substance of the patch is soft; it mostly subsides, and the scab is detached, without leaving any scar, but only a rather persistent stain. The lesions often begin some days after the bromide has been stopped, and their appearance is favoured by any disease of the kidneys which hinders elimination of the drug. Arsenic internally is said to promote their cure, and if given with the bromide may prevent their occurrence. Erythematous, papular, and bullous eruptions are also met with (*see* Plate 61, B, p. 922).

Chloral. Erythematous eruptions, diffuse redness or red papules, and occasionally purpura. They occur mostly after long-continued use of the drug.

Copaiba. Erythema, consisting of bright red, roundish or irregular patches, slightly raised above the surface, here and there confluent, somewhat like measles, covering the arms, legs, trunk, and face. Purpura, vesicles, and urticaria are occasionally present. Desquamation may occur after a persistent eruption.

Cubebs seems occasionally to produce a similar rash.

Iodides. The eruptions are erythematous, pustular, vesicular, bullous, nodular, or purpuric. The erythema is papular, and occurs over the trunk, face, and limbs. Pustules are seen like those of the bromide rash, but smaller in size when discrete; and the confluent forms are less common, and tend to be more bullous. Sometimes large bullæ occur, with a very narrow areola around each, and clear serous contents. Like the bromide eruption, it may be delayed for some days after the drug has been stopped, and is more likely to appear if the kidneys are diseased. The addition of arsenic or aromatic spirits of ammonia to an iodide mixture, or taking the dose in half a tumblerful of water, may be tried to prevent its occurrence.

Quinine. Erythematous rashes are most common, either diffuse or papular; an urticarial form is next most frequent; both of these produce severe itching, and erythema may be followed by extensive desquamation. Purpuric, vesicular, and bullous rashes are less often seen.

Other drugs that have more or less frequently caused rashes, mostly of an erythematous or urticarial type, are belladonna, the barbiturates, cannabis indica, potassium chlorate, chloroform (inhalation), cod-liver oil, digitalis, iodoform, mercury, morphia, opium, phenacetin, phosphoric acid, salicylic acid, santonin, strychnia, stramonium, sulphonal, tar, terebene, and turpentine. Erythematous and lichenoid eruptions, and sometimes a severe generalised exfoliative dermatitis, may result from the infection of metallic compounds, such as those of arsenic, mercury, bismuth, and gold.

The **Treatment** should be the withdrawal of the drug and the use of astringent lotions, such as those of subacetate of lead, oxide of zinc, or calamine.

In the eruptions caused by metallic intoxication sodium thiosulphate should be given both by intravenous injection and orally; and calcium gluconate and glucose should also be prescribed.

ERUPTIONS CAUSED BY DRUGS APPLIED EXTERNALLY

Many substances are applied externally in order to cause erythema and vesication for their therapeutic effects, such as cantharides, capsicum, mustard, croton oil, and turpentine. Belladonna, iodine, sulphur, mercury ointments, arnica, chrysarobin, and pyrogallic acid are also likely to cause irritation if too long applied to sensitive skins

An important and frequent cause of dermatitis of the face and neck, and sometimes of other parts of the body, is the use of certain lotions and dyes for the hair. Of these the most important is paraphenylendiamine, which is contained in several proprietary hair dyes and is also used to dye furs. It may produce a most violent dermatitis, which usually begins on the face, ears, and neck, and is apt to cause intense irritation and swelling of the eyelids; in severe cases the eruption may spread on to the chest, back, arms, and even to the lower limbs, and there may be fever, a marked leucocytosis with eosinophilia, and sometimes albuminuria. Numerous other substances, many of which are used in various trades and occupations, will in certain individuals provoke a dermatitis. Of these may be mentioned many aniline dyes, salts of chromic and picric acid, formalin, photographic developers, such as metol, alkalies and acids, and antiseptics, such as corrosive sublimate, biniodide, lysol, and iodoform. Perfumes, such as those of lily-of-the-valley and violets, are frequently responsible in women. In these cases of dermatitis from external irritants (*Dermatitis venenata*) there may be an innate susceptibility of the individual affected, or such susceptibility may be acquired from frequent exposure to the irritant in question. A person, once he has become susceptible, is liable to a recurrence of the dermatitis even after exposure to a minute quantity of the toxic substance, although previously he may have freely exposed himself to it without ill effect.

TRAUMATIC AND SOLAR DERMATITIS

Apart from surgical conditions, *traumatic dermatitis* may be recognised in the marks of scratching, such as are seen in pruritus, jaundice, scabies, and phtheiriasis, to which the reader is referred. These effects are in part due to repeated infections by pus organisms.

Another form of traumatic dermatitis is that intentionally produced in order to *feign* disease, an event most common among young women, who may use nitric acid, mustard, cantharides, iodine, or other irritant. The site of the lesion is generally the breast or a limb, at least a part accessible to the right hand; the

lesion is generally redness with or without vesication or pustulation; but it may be continued until ulceration is produced.

Solar dermatitis (formerly called *eczema solare*) is well known to follow unwonted exposure to the rays of the sun as reflected from the cricket field, the river or sea, and especially from Alpine snowfields. There is intense redness and swelling, with formation of vesicles and bullæ, accompanied by itching and smarting pain, and followed by free desquamation and pigmentation. Of analogous origin is the severe and persistent dermatitis which results from prolonged exposure to the *Röntgen rays*.

ECZEMA

A great deal of confusion still exists as to the precise significance of the word *eczema* (ἐκξέω = I boil over), and there are some who would abolish it altogether, and substitute the term *dermatitis*. If, however, we regard eczema as a form of reaction of the skin, possessing well-defined clinical and histological features, and not as a disease *sui generis*, the difficulty is solved, and the disputes that have occurred among dermatologists from the time of Willan and Bateman as to what is and what is not eczema, now appear trivial, and certainly serve no useful purpose.

Eczema is an inflammatory process involving the epidermis and dermis, and, unlike eruptions such as urticaria or lichen planus, possesses no single characteristic lesion, but consists rather of a number of lesions, which differ in the various stages through which the inflammatory process passes.

Although the evolution of these different stages varies in different cases, it may be traced as follows: The earliest, or *erythematous stage*, is represented by a patch of erythema, the borders of which are usually ill defined, accompanied by a certain amount of œdema of the affected part, and associated with a sense of tension, burning, or itching. Occasionally the inflammatory process progresses no farther, its subsidence being followed by a fine desquamation, after which the skin rapidly regains its normal appearance. Usually, however, a number of small superficial vesicles appear on the erythematous area, and this, the *vesicular stage*, is one of the most characteristic phases of the eczematous process. By confluence of the vesicles actual bullæ may be produced. In situations where the epidermis is naturally thick, as on the palms and soles, the vesicles appear deeply imbedded in the skin, and may dry up without breaking, but as a rule they soon burst, either spontaneously or as the result of scratching, and discharge a clear serous fluid, which is albuminous and stiffens linen, thus giving rise to the *weeping stage*. The fluid, after flowing for a little, dries up into yellowish crusts which adhere to the surface until detached by accident or lifted by discharge underneath (*encrusted stage*). As the inflammation subsides, the eczematous area becomes paler, the discharge ceases, and healing takes place by a regrowth of epidermis. This may occur spontaneously under the crust, which may remain long after recovery is advanced. For some time, however, the formation of the new horny layer is imperfect (*parakeratosis*), so that it remains thin and transparent, and is cast off as large flakes or papery scales (*stage of desquamation*). Eventually under favourable circumstances the skin regains its normal appearance.

As a result of secondary infection of the eczematous surface with pyogenic cocci, the secretion may become purulent, and the crusts formed are then opaque and greenish-yellowish or orange-coloured, as in true impetigo (*impetiginised eczema*).

Lastly, in cases in which the eczematous process becomes chronic, the persistence of the inflammation and constant scratching and rubbing of the parts by the patient lead to thickening of the skin, with hypertrophy of the epidermis

and infiltration of the dermis. This change, known as *lichenification*, has been described under the heading of Prurigo.

Locally, eczema gives rise to itching, smarting, or burning, and in certain positions to pain on movement. The general condition of the patient, even in cases with an extensive eruption, may be but little affected. In acute cases there is often slight fever, and the digestive system may show signs of derangement, such as a coated tongue, foul breath, anorexia, and excessive thirst. In chronic cases the insomnia resulting from the constant itching, which usually reaches its acme of intensity at night-time, may lead to severe mental depression and irritability.

Varieties of Eczema. Although the clinical and histological features of eczematisation are essentially the same whatever the cause, one can, nevertheless, recognise certain varieties of eczema, each of which has special characters of its own. Thus it is often possible to say with certainty, not only from the distribution of the eruption, but also from its appearance, whether an eczema in a given case is of internal or external origin. The acute vesicular eczema produced by irritants, such as turpentine, iodine, formalin, paraphenylendiamine and certain plants, can usually without difficulty be distinguished from that due to an antigen absorbed from within, and it is noteworthy that in the latter the accompanying pruritus is far more severe. Only certain well-defined varieties will be described :—

Nummular Eczema. In the writer's opinion this term should be reserved for a variety characterised by the formation of circular plaques, bilaterally symmetrical, and situated most commonly on the backs of the forearms, wrists, hands, thighs and legs. The elementary lesions are papulo-vesicles of considerable size, which may arise singly ; the plaques result from the confluence of these, but even on the fully-formed plaque the individual vesicles can usually be distinguished.

It would seem likely that in this variety the antigen responsible must always reach the skin through the blood-stream, for it is inconceivable that an external irritant could produce an isolated vesicle, and the striking bilateral symmetry on the extremities suggests a blood-borne toxin (cp. erythema multiforme, psoriasis). The source and nature of the antigen, however, is not always the same. In one group of cases the primary source is in the skin itself ; for example, a chronic infective dermatitis on a varicose leg, or a varicose ulcer, may, usually as a result of some unsuitable local application, give rise to an outbreak of nummular eczema at a distance, *e.g.* on the forearms. Here the antigen—presumably a bacterial toxin or a product of tissue-destruction—is clearly absorbed from the primary focus on the leg, and carried to other parts of the skin through the blood stream. In another group some septic focus other than the skin is the source, *e.g.* the teeth, and in a third group the antigen is apparently either of intestinal origin, or some derivation of protein metabolism ("gouty eczema" of older authors).

Eczema due to Pyogenic Organisms. Unna at one time held the view that eczema was due to infection of the skin with a specific organism—the morococcus—by which term he was probably describing more than one variety of staphylococcus ; but Sabouraud, as a result of careful research, insisted that the primary vesicle of eczema was non-microbic. At the present time it is generally admitted that both staphylococci—particularly the *S. aureus*—and streptococci are capable under certain conditions of producing an eczematous reaction in the skin. (*a*) *Dermatitis Infectiosa Eczematoides.* This staphylococcal condition has already been described. (*b*) *Streptococcal Dermatitis.* This form of eczematous dermatitis is most commonly seen in folds, around orifices, or in the neighbourhood of infected wounds or septic ulcers. A chronic fissure in the skin is often present, *e.g.* behind the ears, between the toes, in the groins, at the angles of the mouth (*la perlèche*), the nose, eyes, or anus, which acts as a chronic focus

of infection. The affected area is reddened, œdematous, and shiny, and at the margin there is often a sharply-defined scaly edge, or there may be some vesiculation. Many cases of so-called varicose eczema or eczema rubrum are really of this nature, although the milder forms of the former are due to the staphylococcus. It should be remembered that chronic or relapsing lymphangitis, leading sometimes to elephantiasis, may accompany streptococcal infection of the skin.

Infantile Eczema. Various types of eruption, loosely labelled "infantile eczema," but of totally different causation, are met with in young children, and from the therapeutic standpoint it is essential to distinguish between them. Thus eczematisation provoked by external irritants, or secondary to pyogenic infection (see above), may occur in infants as well as older children. The intertrigo of Jacquet ("napkin rash"), already described, may be the starting point of an eczematous dermatitis, which may spread widely from the napkin region to other parts. As has been pointed out, such a dermatitis may be due to infection with a monilia, usually the *Oïdium albicans*. Apart from these conditions, however, there are two distinct forms of eczema in infants, which more than others merit the term "infantile eczema." One is really an eczematised seborrhœic dermatitis, the other a true eczema in which the antigen is absorbed from within (allergic type). The former occurs in infants who are likely in later life to develop the various symptoms and infections associated with the seborrhœic state. The latter is usually the earliest manifestation of the tendency to sensitisation, which characterises those who throughout life are liable to the various toxic idiopathies (*q.v.*).

In the seborrhœic type the primary condition is infection of the infant's scalp with the pityrosporon, contracted from the scalp of the mother or nurse. The first symptom is the appearance of discrete scaly patches, situated at first around the hair follicles, and later becoming confluent. These cause irritation, so that the child rubs the scalp, and secondary infection with a staphylococcus takes place. The eruption spreads downwards behind and over the ears to the neck, on to the forehead and central parts of the face, and to the back and chest, as in adults; it may also involve the joint flexures. At first it consists of reddened scaly patches, comparable to the seborrhœic dermatitis of later life, but sensitisation of the skin is apt to occur, so that definite eczematisation complicates the primary eruption. It should be noted that, whereas all infants must be exposed to infection with the pityrosporon, it is only in a certain proportion—the future seborrhœics—that this organism becomes established at an early age, and causes active symptoms. Excess of carbohydrates and fat in the dietary is a predisposing factor, as in older children and adults with seborrhœic infections.

The other type of infantile eczema is an eczema *de novo*, *i.e.* is not secondary to any pre-existing infection of the skin, and is due to sensitisation of the epidermis to an antigen or antigens absorbed from the alimentary canal. A considerable proportion of these infants are ichthyotics, and a family history of ichthyosis, eczema, Besnier's prurigo, asthma, or hay-fever is common. Vaccination would often appear to be a factor in bringing about sensitisation of the skin. Although this form of infantile eczema may be met with in breast-fed infants, it is commoner in those fed on cow-milk, and its onset may date from weaning. The distribution differs from that of the seborrhœic form. It often begins symmetrically on the cheeks, and on the forehead, the central part of the face being spared. On the limbs it tends to involve the extensor rather than the flexor surfaces. The scalp and trunk may be affected, but usually later than the face and limbs. The skin of the eczematous areas appears and feels thickened and œdematous; at times there is vesiculation and oozing, but often this is slight, occurring only after a bout of rubbing and scratching. The most striking feature is the intensity of the itching, which, as in the prurigos, is paroxysmal and commonly nocturnal. During the daytime the infant may be calm and happy, but towards evening the eczematous parts become reddened and œdematous, and he begins to rub himself

in a frenzy of irritation, until towards morning the paroxysm subsides, and he falls asleep. There is thus the same periodicity that characterises other allergic conditions, such as urticaria, the prurigos, and asthma, and this corresponds to the same cycle of changes in the urine throughout the twenty-four hours that have been described in chronic allergic states (*q.v.*). Retention of chlorides, with wide and rapidly occurring fluctuations of the water-content of the tissues, has been found in eczematous, as compared with non-eczematous, infants, and the periodical exacerbations of the eczema and pruritus correspond to the times at which there is retention of fluid with its accumulation in the skin.

Ætiology. The essential factor in the causation of an eczematous reaction in the skin is sensitisation of the Malpighian cells, and, since these cells may become sensitised to a great variety of irritants, which may reach the skin either by direct external contact, or through the blood-stream by absorption from within, it is clearly impossible to detail all the possible causes of eczema. Even when it is provoked by an external irritant, however, there is obviously some factor or factors which predispose to the occurrence of sensitisation. Certain persons are more liable to develop eczema both from external and internal provoking causes than others, and this liability may apparently be inborn (idiosyncrasy) and often inherited or acquired; in the former case the person is often subject to other manifestations of sensitisation (toxic idiopathies). Bloch tested the healthy skin of 1,130 people with substances that commonly provoke an eczematous reaction, and found that 35 per cent. of those liable to eczema reacted, compared with 5 per cent. of non-eczematous persons. This increased susceptibility of the skin in certain subjects is probably connected, like the other toxic idiopathies, with the autonomic nervous system and the mineral salts, which regulate its sympathetic and parasympathetic portions. There is no evidence that the latter is connected with the skin, the functional integrity of which is probably entirely under sympathetic control. Klauder and Brown (**44**), from their investigations of the mineral content of the skin of rabbits, have produced evidence that a high calcium-content and low potassium-content are associated with diminished susceptibility to irritants, and the converse with a heightened irritability. Calcium appears to diminish the irritability both of muscle and nerve-tissue to contact with physical and chemical agents; and it decreases the permeability of the cell-membrane, whereas potassium and sodium increase it, making the cell more receptive for water. The essential lesion in eczema is an œdema of the rete and, as has been noted, during the paroxysms of infantile eczema there is water-retention followed by diuresis. It is quite likely, therefore, that a disturbance of the normal equilibrium between the mineral salts, such as those of calcium and potassium in the skin, with its consequent effect on the sympathetic nerve fibres, may be a factor predisposing to the eczematous reaction. The influence, however, of predisposition or idiosyncrasy is only relative, for whereas only a small proportion of persons who handle *Primula obconica* become sensitised to it, it is possible to sensitise every subject tested by using a concentrated extract of the plant (**42**). Moreover, all those who constantly handle salts of nickel eventually develop nickel-dermatitis. It is clear, therefore, that the tendency to become sensitised is partly dependent on the irritant in question, or on its concentration.

A tentative ætiological classification of eczema may be attempted as follows:—

Eczema due to External Factors. Physical. In certain persons mechanical irritation of the skin by friction, pressure, rubbing and scratching results in local eczematisation; and likewise exposure to great heat, *e.g.* stokers' or blacksmiths' eczema, to extreme cold, particularly cold winds, and to the actinic rays (eczema solare). The œdema of the skin that results from varicose veins ("varicose eczema"), or from renal disease and cardiac failure, predisposes to *local* eczematisation.

Chemical. A very large number of chemical substances are capable of pro-

voking an acute or chronic eczematous dermatitis when brought into contact with the skin, and many of them are employed in various trades and professions. Thus the constant use of highly alkaline soaps and washing soda is a very frequent cause ("washerwomen's eczema"); exposure to salt and brine may produce "butchers' eczema," to metol "photographers' eczema," to antiseptics (particularly formalin, perchloride and biniodide of mercury, lysol) "surgeons' eczema." Grocers and sweet manufacturers are liable to eczema from handling sugar. Aniline dyes, picric and chromic acids, hair dyes (particularly those containing paraphenylendiamine), hair lotions, mouth washes and tooth pastes, turpentine, sulphur, etc., are also common causes.

It has been shown that with chemical irritants, *e.g.* iodine, formaldehyde, quinine, eczema may be produced in sensitised persons both when they are applied directly to the skin, or are given by mouth or by injection.

In "bakers' eczema" the skin of the parts exposed to the flour may be sensitive to some or all of the proteins contained in wheat, or it may be caused by some chemical used in baking. An important point to remember is that in many instances the skin of certain parts may become susceptible to an irritant, whereas other parts remain immune. Eczema due to these external irritants, as well as that produced by certain plants, has already been referred to under the heading of Toxic Dermatitis. Although in these cases the provoking cause of the dermatitis is an external one, other factors must often be taken into account. There is no doubt that the general constitutional condition in some way influences the liability to occupational eczema, and the development of susceptibility to a given irritant may correspond to the onset of ill-health; dyspepsia, associated with oral sepsis and constipation, would seem in particular to be a predisposing cause, and it is probable that incomplete digestion and assimilation, and inefficient excretion of toxic waste products, render the skin more susceptible to external irritation. In some cases, at any rate, when the general health is improved, immunity to the irritant causing the dermatitis is completely or partially recovered.

The seborrhœic state, which will be referred to later, is another important predisposing factor to the development of eczematisation, and its prevalence among our soldiers in France accounted, partly at any rate, for the severity of the secondary dermatitis that so frequently accompanied scabies. Moreover, seborrhœic persons were found to be more susceptible to mustard-gas dermatitis, and they are very liable to eczema after even a moderate use of sulphur ointment for the treatment of scabies.

Lastly, in ichthyosis, and in persons with very dry skins, there is naturally an abnormal tendency to eczema both from exposure to cold wind, and from the use of alkaline soaps, soda, and other chemicals which are fat-solvents.

Eczema of Internal Origin. That eczema may be caused by certain chemical substances, given by injection or taken by mouth, has already been noted, but, apart from this, antigens derived from food-substances, septic foci, and probably from the action of proteolytic bacteria on undigested protein may be responsible. An injection of a foreign serum sometimes excites not only the usual urticarial serum-rash, but also an acute eczema, owing to the epidermal cells having become sensitised to the antigenic substance in the serum. In the same way certain foodstuffs invariably provoke an attack of eczema in some persons, and the same individual may develop urticaria from one food and eczema from another. In children eczema from food-substances is not uncommon, *e.g.* from cow-milk, cereals, such as oats and wheat, cabbage, beans, pork, and beef, and one or more of the other toxic idiopathies are likely to develop as the child grows older.

Apart from food sensitisation, certain cases of eczema, mostly in adults, appear to depend on *focal infection*, and it is probable that in some instances, at any rate, the eczema is a manifestation of bacterial sensitisation. Oral

sepsis particularly is an exciting cause, and numerous cases have now been recorded in which eczema of long standing has disappeared rapidly after removal of infected teeth. The association of *gout* and eczema has probably been much exaggerated, and, although the two conditions may certainly co-exist, it is rare to see a case of true tophaceous gout in a dermatological clinic. Concerning the connection between eczema and *renal disease* little is definitely known apart from that complicating renal œdema, but in uræmia a generalised eczematous and exfoliative dermatitis may arise ; in such cases the amount of urea in the blood is always very high and the eruption is of grave significance, death usually occurring within a few days of its appearance. *Glycosuria* may cause a localised eczema around the vulva, or prepuce, due to irritation by the saccharine urine and the growth of infective organisms, such as moniliæ, but, apart from this, eczema is not uncommon in diabetics. *Retention of fluid*, with its accumulation in the skin, is an important factor not only in infantile eczema, but also in eczemas of internal origin met with in later life. It is predisposed to by an excessive consumption of carbohydrates and fats, particularly if large quantities of fluid are also taken. Several observers have emphasised *nervous shock or strain* as a provocative cause of eczema, and in some persons an acute outbreak may follow a severe shock or period of worry, but the association is probably an indirect one. *Intestinal toxæmia*, associated with excessive putrefaction and indicanuria, is apparently responsible for one variety of eczema, the eruption affecting chiefly the parts of the skin exposed to light, namely, the face, ears, neck, and the backs of the hands ; it is probable that in these cases some toxin is absorbed from the intestines which sensitises the skin to sunlight (*vide* light-sensitisation).

The term *seborrhœic eczema* is often used as synonymous with seborrhœic dermatitis ; the latter is simply a parasitic infection due to the pityrosporon, the *Staphylococcus albus* also growing actively in the lesions, but a true eczematous dermatitis may complicate the primary eruption, due no doubt to the epidermis having become sensitised to the infecting organisms (cp. *dermatitis infectiosa eczematoides*). This eczematised seborrhœic dermatitis represents, as has been said, one variety of infantile eczema, but is also not uncommon in adults. During the war it was a very frequent cause of disability among our soldiers in France, and was often wrongly diagnosed as impetigo.

Morbid Anatomy. The histological changes met with in the skin in eczema vary according to the stage of the disease. In acute eczema there is great dilatation of the capillaries in the papillæ, with œdema and some leucocytic infiltration. The transitional epithelium becomes œdematous, the prickle cells are separated and disintegrated by the serous exudation (*spongiosis*), and thus vesicles are formed. As a result of these changes in the epidermis the process of keratinisation is interfered with. In the more chronic stages there is marked thickening of the interpapillary processes (*acanthosis*), and more and more infiltration of the corium, with connective tissue proliferation ; owing to the imperfect keratinisation (*parakeratosis*), scales consisting of clumps of nucleated cells are formed, and periodically shed. In old patches the thickening of the skin may be very great.

Treatment. Since the possible causes of eczematous inflammation of the skin are so numerous, it follows that successful treatment must depend, as a rule, on accurate diagnosis. Thus many patients have been treated for years for "gouty eczema" of the hands and feet when they were really suffering from eczematoid ringworm, and in recent years recurrent attacks of acute eczema, due to the use of certain proprietary hair dyes, have become increasingly common, and have often been regarded as of constitutional origin. It cannot be too strongly insisted upon that in every case of eczema the possibility of an external irritant being responsible should first be considered. The distribution of the eruption and the history of its onset will usually help one in determining this

point, but, although the cause may obviously be an external one, its discovery may be a matter of great difficulty.

Whatever the cause, the local treatment depends on the stage of the inflammatory process. Thus in acute cases with intense hyperæmia, vesiculation, or weeping, astringent lotions repeatedly applied should be used; when the eczematous surface is drying up, a protective paste or cream should be substituted for the lotion, and in the chronic scaly stage ointments may be employed. The following are suitable lotions in the acute stage: (1) Liq. plumbi subacetat., 1 dr.; Spirit. vini rect., 1 oz.; Aq. dest., ad 8 oz., to which may be added aluminium acetate in a strength of from 1 to 3 per cent.; this should be applied on a single layer of lint, which must be kept continually moist. (2) ℞ Calaminæ præpt., Zinc oxide, āā, 2 dr.; Glycerini, 1½ dr.; Spirit, vini rect., 1½ oz.; Aq. calcis., ad 8 oz. (3) Lotio nigra and Aq. calcis, equal parts. (4) Ichthyol, 3 per cent. in water. In some cases a calamine liniment is preferable to a lotion, *e.g.* ℞ Phenolis liq. ℥ xv.; Zinci oxidi, Pulv. amyli, Calaminæ præpt., āā 1 oz. Ol. olivæ, Aq. calcis, āā 4 oz.

As a paste the well-known formula of Lassar is invaluable: ℞ Zinci oxidi, Pulv. amyli, aā, 2 dr.; Acidi salicylici, 10 gr.; Paraffini mollis alb., ad 1 oz., this may be modified by omitting the salicylic acid, which sometimes proves irritating, and by adding a little lanoline. This paste, or a zinc cream, *e.g.* ℞ Zinci oxidi. ½ oz.; Ol. olivæ vel amygdalæ dulc., ½ oz.; Adip. lanæ. anhyd., 1 dr.; Aq. calcis, 3 dr., may be used alone, or as a base for the incorporation of ichthyol, wood or coal tar, sulphur, resorcin and ammoniated mercury, etc. In subacute or chronic cases, in which these stimulating substances are indicated, the tolerance of the skin towards them must be tested gradually by prescribing them at first in small quantities.

In very chronic patches, in which lichenification has occurred, crude coal tar, pyrogallol, eugallol (the monoacetate of pyrogallol), and even chrysarobin may be employed. Crude coal tar may be painted on neat, or incorporated either with the pigmentum caseini B.P.C. or a zinc paste (*e.g.* crude coal tar, 2 parts; zinc oxide, 2 parts; corn starch, 16 parts; petrolatum, 16 parts); it should never be employed when secondary pyogenic infection has occurred. If used neat, the eczematous surface having been first cleansed with soap and water, the tar is applied as a uniform coating and allowed to dry. The applications may be repeated daily for several days if well tolerated. The above crude coal tar paste is usually by far the most effective local application in the allergic form of infantile eczema. Eugallol is a dark liquid containing 33·3 per cent. of acetone, and should be applied once every few days. Chrysarobin is best employed in an ointment, and its effects must be carefully watched.

The X-rays afford one of the most valuable methods of treating these chronic infiltrated patches. Either a full pastille dose may be given and repeated, if necessary, in a month's time, or fractional doses of a third of a pastille at intervals of ten days. In suitable cases rapid relief from itching is obtained by the use of the rays, and resolution of the thickened patches takes place in a few weeks.

The question of washing must always be considered in the management of a case of eczema, whatever be the cause. Soap should never be used in the acute or subacute stages, but in chronic cases a superfatted soap, with or without the addition of tar or ichthyol, is sometimes of value. Water should be avoided altogether in acute cases, but in subacute and chronic eczema sponging or bathing with a 1 per cent. salt solution seldom does harm, and is often beneficial, for, as Whitfield suggests, the irritant effect of plain water probably depends on the fact that it is hypotonic.

General Treatment. The successful treatment of eczema of internal origin depends upon the thorough investigation of the individual case, and the main principles only can be indicated.

Diet. In widespread or acute cases an initial fast for forty-eight hours is advisable, and the food intake should then be restricted to four tumblers of milk per diem, with some fruit, for three days. An anti-retentional dietary, as recommended for urticaria, should then be instituted, and the total fluid intake should not exceed two and a half pints per diem. Alcohol, strong tea and coffee, and very acid fruits should be avoided entirely. In the allergic form of *infantile eczema* cow's milk must not, as a rule, be given. If the child is being breast-fed, it should be ensured that the mother's dietary contains an adequate quantity of calcium and vitamins, and it is advisable to prescribe for her additional calcium and some preparation containing vitamin-concentrates. If breast-feeding is impossible, some proprietary food, such as Almata, made without cow's milk, should be tried, and additional calcium given in the form of Syr. Calcii Lactophosph. B.P. ℥ 30, t.d.s., with a vitamin-concentrate and orange-juice. The change to a solid dietary should be made as soon as possible, and it may be advisable to perform cutaneous tests with certain foods before planning it. Allergic infants are often hypersensitive not only to cow's milk, but also to some cereals and egg. As Czerny insisted, these children, owing to their tendency to water-retention, thrive best on a diet rich in protein with restriction of carbohydrates, fat and fluids. The following, modified according to individual idiosyncrasies, may be recommended :—

Allowed : Freshly cooked lean meat and fish, chicken, liver, kidneys, sweetbread, and brains ; egg-yolk, cottage or other plain cheese ; all kinds of cooked vegetables, mixed salads, cooked and raw fruit (except very acid ones such as grape-fruit, lemons, pineapple, and currants) ; crisp wholemeal toast, Vitaweat, or Ryvita, butter. One tumbler of milk should be given daily, unless the patient is milk-sensitive. Glucose should be substituted for cane-sugar. Salt should be taken very sparingly. The fluid intake should be restricted to three small tumblers of water a day in addition to the milk and fruit. The diet should be supplemented by a small quantity of a mixed vitamin-concentrate and some preparation of calcium, as advised above.

To be avoided : Porridge, cane-sugar, jam, marmalade, sweets, pastries, puddings, cakes, soups, fats (except butter and cheese), egg-white, pork, bacon, sausage, acid fruits.

Internal Medication. Examination of the urine, specimens being taken at different times of the day, often affords valuable indications for internal treatment. If there is hyperacidity, with or without uratic deposit, alkaline diuretics, combined with the aperient sulphates, should be administered in sufficient quantities to render the early morning urine neutral, the dosage being thereafter reduced. If, however, there is hypoacidity with phosphaturia, acids are indicated, and may be given with a little strychnine. Calcium salts are often of great value, and should be given in combination for a while with full doses of vitamin D. In severe or acute cases they may be injected, as advised for urticaria. Even in eczema of external origin, calcium and vitamin D appear to lessen the hypersensitiveness of the skin. If itching is severe and when there is insomnia, sedatives are essential, *e.g.* calcium bromide gr. 5–10, or luminal gr. ¼, thrice daily, and, if necessary, a hypnotic at bedtime. In such cases intravenous injections of calcium or strontium bromide in a solution of glucose (*e.g.* Ekzebrol) may be of value.

In old people in whom the skin is abnormally dry and the general nutrition poor, and in ichthyotic persons, remarkable improvement is often derived from the administration of cod-liver oil and thyroid gland. The former may be combined with malt or iron, and the latter should be given at first in small doses, which should be increased according to tolerance. The importance of treating oral sepsis can hardly be exaggerated, for cases of eczema, which have resisted all other measures, sometimes yield rapidly after the removal of teeth with root abscesses, or the treatment of pyorrhœa alveolaris. Lastly, in patients with

physical or nervous exhaustion a complete rest, followed by change of surroundings, should be ordered whenever possible.

Desensitisation. Even in eczema of external origin, one or other of the various methods of desensitisation may be of value. In fact, in cases of occupational dermatitis autohæmo- or autosero-therapy may enable the patient to resume his work without further trouble. As has been said, eczema due to food-sensitisation has been successfully treated by injecting subcutaneously an emulsion of the food in question in gradually increasing doses, but, as a rule, in eczema of internal origin, the exact nature of the antigen is unknown, and some method of non-specific desensitisation must be attempted. There is, however, evidence to show that the *serum* of sensitised subjects contains a substance specific for the individual or for another sensitised to the same antigen, so that autoserotherapy should, perhaps, be regarded as a method of specific desensitisation. Autohæmotherapy, on the other hand, which is not so certain in its effect, is probably comparable to injections of non-specific protein. Apart from these two methods, peptone, given either by intradermal, subcutaneous, intravenous, or intramuscular injections, is often valuable, as also are the proprietary products "Aolan" and "Cibalbumin." In eczema the former is best given intradermally in doses of 1 to 3 minims at intervals of three to seven days.

ERYTHEMATO-SQUAMOUS ERUPTIONS

PITYRIASIS ROSEA (*See Plates 62 and 63, B, p. 942*)

Pityriasis rosea (Gibert) is chiefly of importance in that it is so frequently wrongly diagnosed, and yet the eruption is, as a rule, so distinctive that its recognition should rarely be difficult. In probably the majority of cases one or more patches of considerable size precede the generalised outbreak of the eruption by several days, but their appearance may pass unnoticed. These "herald patches," or *plaques primitives*, are larger than the subsequent lesions, and are usually seen on the neck, trunk or proximal parts of the limbs. They are more or less circular, scaly, and have a well-defined border; they are often mistaken for patches of ringworm, or of seborrhœic dermatitis. The generalised eruption appears with comparative suddenness, like that of an eruptive fever, first on the upper thorax, and then successively on the neck, the upper arms, the abdomen and neck, and on the thighs. A few patches may be seen on the forearms, the face, and lower parts of the legs, and occasionally almost the entire skin, even the scalp, may be profusely covered. The lesions begin as small, pink papules, which enlarge by peripheral extension to form the characteristic circular or oval patches. A typical patch consists of an outer, raised pink border, and a central, fawn-coloured portion, which presents a wrinkled appearance; between the two is a fine collarette of scales, the free edges of which lie towards the centre. As each patch enlarges the centre may fade almost completely, so that the appearance of rings is assumed, the rosy tint of the ring contrasting with the slightly yellowish tint of the enclosed area. A very characteristic feature of the fully developed eruption is the way in which the oval patches tend to run obliquely round the chest and flanks, their long axes lying roughly parallel to the direction of the ribs. The outbreak of the disease may be accompanied by slight malaise, with sore throat and mild fever, but usually constitutional disturbance is not present. Itching may be entirely absent, slight, or so severe that the patient cannot sleep. The lymphatic glands may be enlarged, particularly the posterior cervical group.

Ætiology. It is probable that the disease is due to infection with a filterable virus, which is inoculated at one or more points on the skin, and, multiplying there, produces the "herald patches." Then, after an incubation-period of about five to fourteen days, it presumably reaches the blood-stream and causes the generalised eruption. There is convincing evidence that the hypothetical

virus may be conveyed by new underlinen, and this may account for the increased incidence of the eruption in spring and autumn. Cases have been recorded in which a person has become affected after wearing a garment borrowed from another suffering from the disease.

Second attacks are very rare, but occasionally undoubted instances are met with.

Diagnosis. So characteristic is a typical lesion, with its pink border, its collarette of scales, and wrinkled yellowish centre, and so constant the distribution and arrangement of the patches, that the disease can usually be diagnosed at a glance by one familiar with it, and yet errors are often made. It may be confounded in its early stage with tinea circinata or with seborrhœic dermatitis (pityriasis circinata); in its developed stage with a secondary syphilide, or even psoriasis. Tinea circinata yields a fungus on microscopical examination of the scales. Seborrhœic dermatitis consists of greasy, figurate patches, with follicular papules, and occurs chiefly on the mid-line of the chest and back, and often on the scalp and face. Pityriasis rosea should never be mistaken for a roseolar syphilide, since the latter is never scaly, and from the papular syphilide it can be easily distinguished, since the papules of syphilis are darker in colour, are markedly infiltrated, are situate on the distal portions of the limbs as well as on the face and scalp, and are accompanied by other signs of syphilitic infection, such as sore throat, mucous patches, and marked generalised adenitis; moreover, a primary sore can usually be discovered. In psoriasis the scales are larger and present the well-known silvery appearance when gently scratched, and the eruption is commonly present on the elbows, knees and scalp.

Treatment. The eruption disappears spontaneously in from three to eight weeks. If irritated, however, by unsuitable applications, such as sulphur or mercury, the duration is lengthened. The patient should take a daily bath, to which two or three tablespoonfuls of Condy's fluid may well be added, after which the skin should be dusted over with the pulv. acidi salicylici comp. B.P.C., or a weak salicylic ointment may be used. Whitfield recommends the application of the following lotion twice daily: ℞ Pulv. calamin præp., ℥iij; Pulv. zinci oxidi, ℥ij; Sp. vini rect., ℥j; Liq. picis carb., ℥jss; Aq. rosæ, ad ℥viij. It is doubtful whether internal treatment has any influence on the course of the disease.

PSORIASIS (*See Plate 63, A, p. 942*)

This disease consists in the formation of raised red patches, covered with thick silvery-white adherent scales. In a great number of instances the lesions appear first on the knee over the patella, ligamentum patellæ and tubercle of the tibia, and on the elbow over the olecranon. It begins with papules, which enlarge into large flat plaques; quite early the papule is seen to be covered with an opaque scale, and with its enlargement in size the scale becomes thicker, especially in the centre, and silvery white in appearance. The scale is rather firmly adherent, and co-extensive with the red plaque, so that the red colour can often only be seen at the edge. If the scale is removed, it leaves a shining, moist-looking, but actually dry, bright red surface, in which examination with a lens will show a number of deeper red points, the hyperæmic papillæ. The patches are at first round or oval, and enlarge to ½ inch, 1 inch, or more in diameter; fresh patches come out near the first or in other parts of the body. If a patch becomes very large, it may heal in the centre, and thus form a ring; coalescence with other rings will produce serpiginous or gyrate figures. The patches may spread sufficiently to cover large areas of the body continuously, so that the original shape of the spot cannot be detected. The old names given to indicate these different stages have little more than a descriptive value, such as *P. punctata, P. guttata, P. nummularis, P. circinata, P. gyrata, P. diffusa, P. universalis.*

Next to the knees and elbows, the adjacent extensor surfaces of the leg and forearm are most commonly affected, and then the thighs, back, loins, chest, and abdomen; and in all regions a very striking symmetry is observed. The scalp and face are usually attacked when the eruption is at all widespread, but the palms and soles are often spared. The nails are not infrequently involved: they become variously altered, opaque, thickened, pitted, furrowed transversely, or immensely thickened and discoloured (Plate 61, F, p. 922).

The amount of scale varies in different instances or in the same case at different times. In *P. rupioides* the scales are heaped into small conical masses, each on its circular base.

The eruption is usually dry, but may become moist in the flexures, or as the result of irritant applications, and in seborrhœic persons the patches tend to be greasy. Itching is variable, but is not, as a rule, severe. Although it is often stated that psoriasis occurs in persons in perfect health, this is seldom or never true.

The disease breaks out spontaneously, often in early childhood, and, even if not treated, subsides after three or four months, to recur again after a quite uncertain interval. Sometimes the recurrence is twice a year ("spring and fall," as it is often expressed), or a period of years may intervene. In other cases a slight amount of eruption persists, and extensions take place from time to time. During recovery pigment stains mark the situation of the patches, especially after the use of arsenic.

Varieties. *Flexural Type.* Although psoriasis tends to involve principally the extensor surfaces of the limbs, the scalp, and umbilical and sacral regions, it is sometimes curiously localised to the flexures and natural folds of the skin, *e.g.* the internatal cleft, where it may be the cause of "pruritus ani," the groins, the submammary and hypogastric folds, and the retro-auricular spaces. This flexural localisation is usually seen in late middle-age, particularly in obese persons.

Arthropathic Psoriasis. A severe and often very intractable form of the disease is that in which it is associated with multiple arthritis. Clinically, although the general features of the arthritis are those of the usual type of arthritis deformans, involvement of the terminal interphalangeal joints both of the hands and feet is especially common, and a painful inflammatory form of psoriasis of the nails usually accompanies the joint-changes. Intermittent hydrarthrosis of the larger joints is also more frequent than in non-psoriatic arthritis (**53**).

Complications. (*a*) *General exfoliative dermatitis* or psoriasis universalis. There is a generalised erythrodermia, *a capite ad calcem.* Except at certain points, *e.g.* elbows and knees, the characteristic silvery scaliness ceases. The skin remains dry. The hair may fall to a varying extent, and the nails become striated and deformed. There may be an accompanying arthritis. The histological features remain those of ordinary psoriasis, thus differentiating this form of exfoliative dermatitis from others. Some chronic psoriatics are subject to recurrent attacks of this complication. The general condition usually remains good, there being no serious constitutional disturbances. Sometimes the injudicious use of irritating applications, such as chrysarobin or cignolin, may be responsible for the development of this generalisation.

(*b*) A very rare complication of psoriasis is an exfoliative dermatitis, in which serous oozing and visible *pustule-formation* are present. It occurs in combination with a streptococcal septicæmia. This moist and pustular eruption may during the course of the infection become transformed into a dry generalised exfoliative dermatitis of the usual type.

Ætiology. As Civatte has insisted, a comparison of the histological features of psoriasis and of the psoriasiform type of seborrhœic dermatitis, which may clinically resemble each other very closely, suggests that the lesions of the

former are inflammatory reactions produced in the skin by a blood-borne toxin or micro-organism, while those of the latter are due, as, indeed, is known, to an external microbic infection. An inherited and familial tendency to the disease is undoubted (**54**), but observers disagree as to its frequency. Few pedigrees have been published, but at a conservative estimate it would seem that it is present in from 30 to 40 per cent. of cases. Instances are not uncommon in which one or other parent of a psoriatic develops the eruption for the first time in late life. Males are more often affected than females. In Europe and North America the ratio is about 3 : 2. Although beginning most commonly at puberty or in adolescence, psoriasis may be seen in infants, and its onset may be delayed until middle or late life. In women it often appears for the first time at the climacteric, when it tends to affect chiefly the natural folds of the skin.

The actual cause of the disease is unknown. It may, as has recently been suggested, be due to infection with a specific virus, the activity of which, like that of the virus of herpes simplex, is dependent upon factors which vary in different cases. On the other hand, it may be a non-specific cutaneous reaction, like eczema, the tendency to which is inborn and often inherited. In the present state of our knowledge we can merely summarise the known clinical facts, particularly as regards the various provoking factors and the association of the disease with other morbid conditions. In a considerable proportion of cases there is an obvious connection between psoriasis and infection of the throat. Particularly is this so when the eruption appears first in childhood, and it may develop acutely like an exanthem after an attack of follicular tonsillitis or scarlet fever. With subsequent attacks of tonsillitis, further exacerbations occur. It would thus appear that acute streptococcal infection may be the initial provoking factor, or may cause a widespread outbreak when the eruption is already present, whereas other infections, *e.g.* pneumonia and typhoid, usually bring about its temporary disappearance. In adults there is sometimes an apparent relationship between focal streptococcal infection in the teeth, nasal sinuses, or elsewhere, and psoriasis. On the other hand, in many cases of the disease investigation may reveal no evidence of it. In psoriasis arthropathica focal streptococcal infection may certainly be the predominant factor in the causation both of the arthritis and the psoriasis, as in a case observed by the writer in which numerous dead teeth were the source. This, however, does not appear to be so in all cases. Apart from arthritis, other rheumatic manifestations, such as fibrositis and neuritis, are often present in psoriasis, so that lumbago and sciatica are common symptoms. The eruption known as keratodermia blenorrhagica, which is seen rarely as a complication of gonorrhœal arthritis, resembles psoriasis very closely both clinically and histologically, and it has been suggested that it is a variety of psoriasis, in which the gonococcal infection is the provoking cause (**55**). Lastly, the metabolic factor in psoriasis must be considered. In some cases there is found a high urinary acidity with a tendency to heavy uratic deposit, and a marked increase of uric acid in the blood. The patients, many of whom take alcohol to excess, usually complain of considerable itching. Careful dieting, abstention from alcohol, and the administration of alkaline salines bring about striking improvement, or even the complete disappearance of the eruption. Recently it has been suggested (**56**) that psoriasis, like xanthomatosis, is due to faulty metabolism of fat. By employing Bürger's tolerance test, it is claimed that an increase of about 40 per cent. in the total serum fat is found in psoriatics, and that a reduction of fat in the diet to a minimum is curative. The writer has employed this method of treatment in several cases, with good results in some, and complete failure in others. To sum up, the tendency to develop psoriasis is inherited and familial in a considerable proportion of cases. Whatever the actual cause of the disease—if, indeed, it is of specific causation and not merely a non-specific reaction of the skin, comparable to eczema and urticaria—there is no doubt that it is in some cases unfavourably

influenced by acute or chronic streptococcal infection, particularly tonsillitis, and that arthritis or other rheumatic symptoms are commonly associated with the eruption.

Morbid Anatomy. The most striking histological feature is *parakeratosis*, characterised by the disappearance of the stratum granulosum and incomplete keratinisation, so that the horny cells retain their nuclei, and accumulate in visible scales, which are drier than normal. This parakeratosis is not, of course, peculiar to psoriasis, but is more marked than in any other eruption. The rete Malpighii is hypertrophied between the papillæ (acanthosis), which are elongated; above the papillæ, however, it is thinned, only a few layers of cells separating them from the parakeratotic stratum corneum. The papillæ and papillary body are slightly œdematous, and their vessels are dilated and surrounded by small numbers of cells, chiefly mononuclear leucocytes. It would appear, from Civatte's researches, that the primary lesion in psoriasis is a small intra-epidermal collection of polymorphonuclear leucocytes ("micro-abscess" of Munro-Sabouraud). These come from the papillary vessels, traverse the rete Malpighii, and collect in its upper layers. The formation of these "abscesses" disturbs the normal process of keratinisation, and they and the Malpighian cells, among which they lie, are cast off as masses of parakeratotic cells, which form the scales.

Diagnosis. In most cases it cannot be mistaken. Patches of dry *eczema* may resemble it, but the edges are not so sharp, and the scales are not so thick and silvery. Moreover, if the surface be gently scraped, droplets of serum will be seen oozing from the rete Malpighii. In psoriasis of the scalp the scales are often yellow, and look like crusts of impetigo; but psoriasis spreads beyond the scalp on to the forehead or neck, and there is usually psoriasis of some other parts of the body, which will be distinctive. *Lichen planus* and *pityriasis rubra* must be distinguished by the descriptions given. Patches of *tinea circinata* may look like psoriasis, but their small number, want of symmetry, small scales, and the results of microscopic examination will show their nature. *Lupus erythematosus* is recognised by its position on the face, the greater thickening of the skin, the sebaceous plugs and the scars, and *scaly syphilides* by the small size of the lesion, the slight scaliness, the browner colour, and the concomitant symptoms.

Treatment. From what has been said concerning the ætiology of the disease it is clear that an attempt should be made to determine the probable provoking factors in the individual case. If there is a history of recurrent tonsillitis or of scarlet fever, and the tonsils appear to be infected, their enucleation is advisable, and should be followed by the administration of an autogenous streptococcal vaccine. This procedure is sometimes curative. Other possible foci of infection should be looked for, and dealt with, if present, and an investigation of the intestinal flora for pathogenic organisms is always desirable. In plethoric persons in whom the eruption is apt to be extensive and irritable, and the urine hyperacid and concentrated, with uratic deposit, a restricted dietary, complete abstention from alcoholic drinks, and regular exercise, together with the administration of alkaline salines (*e.g.* ℞. Mag. Sulph., gr. 15; Sodii Sulphat., gr. 15; Sodii Bicarb., gr. 25; Pot. Cit., gr. 30; Aq. Menth. Pip., ad. oz. 1; t.d.s., a.c., ex aqua), will usually produce rapid improvement. It may be said that in alcoholics psoriasis is incurable, unless abstention can be enforced. Whitfield has found that, if marked indicanuria is present, the internal administration of creosote may be curative. With regard to diet, no definite rules can be given. In obese persons carbohydrates and fats should be restricted. Some benefit from an almost vegetarian *régime*, and the low fat dietary, advocated by Grütz, is sometimes effective. In severe cases complete rest in bed is advisable, particularly if the patient is suffering from nervous exhaustion.

For acute outbreaks salicin or sodium salicylate are worth a trial, and in chronic cases arsenic—3 to 6 minims of Liq. arsenicalis well diluted thrice daily after meals—may justify its reputation. Thyroid gland, once regarded as almost a

specific, is only of value when symptoms of hypothyroidism are present. Injections of sulphur compounds were at one time popular, and certainly a course of treatment at Uriage, where the natural sulphur water is injected intravenously, and at Harrogate, often gives remarkable results. Injections of Enesol (salicylarsenate of mercury), which is so valuable in lichen planus, have been advocated by Sabouraud, and metallic compounds, such as Psothanol, Sulpharsenol, and Mercolloid, have proved of benefit in some cases. More effective would seem to be gold-compounds, *e.g.* Solganal B. oleosum, with which the writer has recently had some striking results. The method of treatment introduced by Danysz, which consists of injecting bacterial emulsions (killed at 70° C.) prepared from fæcal organisms, in increasing doses at short intervals (three to five days), may prove successful, but often fails. Sutton advises injections of a stock *B. coli* vaccine, combined with vigorous local treatment, and in the writer's hands this has proved to be a more reliable method than any other except the use of gold-compounds.

Local Treatment. Although chrysarobin is by far the most active topical application, it is very irritating and must be used with caution. The same may be said of cignolin, which is in vogue as a substitute at the present time. Oil of cade, Stockholm tar and coal-tar are less rapidly effective. A recent method consists of applying a crude coal-tar paste (Pasta Picis Carbonis B.P.C.) at night time, and irradiating the patches the following day with ultra-violet light. A clean application for general use in ambulant cases, in combination with the other methods of treatment already indicated, is ℞. Liq. Picis Carbonis B. P., dm. 2 ; Hydrarg. Ammon., gr. 5–10 ; Pasta Zinci Co. B.P.C., to oz. 1. For the scalp : ℞. Liq. Picis Carbonis, dm. 2 ; Hydrarg. Ammon., gr. 15 ; Acidi Salicylici, gr. 15 ; Lanolini, dm. 2 ; Vaselin. Alb., ad oz. 1 ; this should be well rubbed in at night time, and the scalp shampooed in the morning. For resistant patches fractional doses of X-rays are temporarily of value, but the patient should be warned of the danger of too frequent applications, for many examples of radiodermatitis are seen in chronic psoriatics. In the majority of cases sun-bathing is beneficial and may banish the eruption completely for several months.

Pustular Psoriasis of the Extremities. It has already been remarked that in rare instances psoriasis may become visibly pustular, for example, in association with streptococcal septicæmia. Recently it has been established (**57**) that a chronic pustular eruption of the palms and soles, which had previously been labelled " acrodermatitis continua of mild type " (**58**), is really, in many instances at any rate, a localised form of pustular psoriasis. The eruption tends to involve the palms and soles symmetrically, the sites of election being the thenar eminences and the central parts of the soles, but it may occur unilaterally or asymmetrically, and single patches are met with. It is characterised by reddened scaly patches, in which intra-epidermal pustules are constantly being formed : these dry up to form brownish scabs, which are gradually exfoliated. In a patch of some standing the clinical appearances, apart from the pustules, are frankly psoriasiform. Sometimes vesicles with almost clear contents are seen, and outlying pustules may occur singly in a normal area of skin. On incising the horny layer overlying a pustule and evacuating the pus, an intra-epidermal cavity is exposed. Cultivation of the pus almost invariably reveals that it is completely sterile, it being exceptional even for colonies of a *Staphylococcus albus* to appear. This eruption may occur alone without lesions of ordinary psoriasis elsewhere, or it may be associated with such lesions, some of which may also develop occasional pustules. Sometimes in a long-standing case of psoriasis, the characteristic pustular form will suddenly appear on the extremities (Plate 64, A).

Ætiology. Observations by the writer and others have shown that in the causation of this condition a streptococcal focal infection, particularly of the tonsils, is of primary importance, and several cases have been reported in which complete removal of the tonsils, or other infective foci, has been followed by rapid

cure or striking amelioration of the eruption, which is notoriously resistant to other forms of treatment. Although occurring usually in adults, it may be seen in children; it is equally common in the two sexes. It is possible that a similar pustular eruption of the extremities, due to focal sepsis, may be independent of psoriasis (**59**). When the identity with psoriasis is certain, it would seem that it is the presence of a streptococcal focus of infection that determines the pustular character of the disease.

Morbid Anatomy. The histo-pathological changes are similar to those of ordinary psoriasis. The chief differences are (1) the far denser leucocytic infiltration of the dermis, which, as in ordinary psoriasis, consists chiefly of mononuclears, at the sites of pustule-formation, (2) the greater disintegration of the rete Malpighii owing to the more extensive exocytosis, there being literally abscess-formation, (3) the denser infiltration of the exfoliated parakeratotic mass with leucocytes, as one would expect. It is this that forms the brownish scabs, resulting from the drying-up of the abscess.

It would appear, in fact, that the visible pustules of pustular psoriasis are merely a greatly exaggerated form of the micro-abscesses of Munro-Sabouraud.

Treatment. In the writer's experience successful treatment depends upon the finding of some source of chronic streptococcal infection. In cases in which no definitely localised focus can be discovered, the throat and stools should be examined bacteriologically for pathogenic streptococci, and, if these are found, an autogenous vaccine should be given. Locally an ointment or paste containing either oil of cade or coal-tar should be prescribed. The eruption is usually resistant to the X-rays.

THE ERYTHRODERMIAS

By the term *erythrodermia* is understood a more or less *generalised* inflammation of the skin, characterised by *redness*, *scaliness* and a tendency to *persistence*. The term is an artificial one, for under it are grouped a number of conditions which, although presenting the above clinical characteristics, are ætiologically quite distinct. It should be observed that (1) the *redness* is essentially of inflammatory origin, and is usually accompanied either by thickening, or by thinning and retraction of the skin; (2) the *scaliness* is an important feature, and the scales may be small and powdery, or so large that literally sheets of them are exfoliated daily; (3) the eruption tends to involve large areas, and often affects the whole integument; the nails and hair may be shed; (4) the majority of erythrodermias are *chronic*, and the severe forms persist till death.

The classification adopted by Darier is the most convenient; thus we have: (1) *Primary erythrodermias*, which develop on healthy skin; (2) *Erythrodermic dermatoses*, in which, owing to the generalisation of one of the erythemato-squamous eruptions described above, erythrodermia results; (3) *Secondary erythrodermias*, in which erythrodermia is a complication, often fatal, of some preceding eruption; (4) *Congenital erythrodermia*, occurring in the newly-born.

The primary erythrodermias alone require description here, and are classified as follows:

A. *Acute Primary Erythrodermia.* This form includes one clinical entity, namely, *erythema scarlatiniforme recurrens*, and is also a rare form of toxic eruption caused in sensitised persons by the absorption of certain drugs, particularly mercury, quinine, chloral, belladonna, opium and picric acid.

B. *Subacute Primary Erythrodermia.* This is merely a more chronic and serious form of the preceding. It is seen particularly in alcoholics and those with chronic renal disease, may be accompanied by progressive wasting, diarrhœa and fever, and is fatal in a considerable proportion of cases. Salvarsan dermatitis may be included under this heading.

C. *Chronic Primary Erythrodermia.* (1) *Pityriasis rubra;* (2) *Premycosic erythrodermia;* (3) *Leukæmic erythrodermia.*

PITYRIASIS RUBRA

It is clear from what has been said that the clinical syndrome of generalised exfoliative dermatitis may result from various causes, and at one time the term *pityriasis rubra* was employed indiscriminately in all cases of chronic generalised erythrodermia. It is best, however, to confine it to a group of cases in which the erythrodermia is *primary, i.e.* does not supervene on any previous disease of the skin, and *persistent,* and which often end fatally. The cause is entirely unknown, and *post-mortem* examinations have failed to throw any light on the ætiology. Such cases were described by Hebra; and Jadassohn, who collected eighteen, pointed out that a considerable proportion die of tuberculosis. Typical tubercles with giant-cells and tubercle-bacilli were found in sections of the skin of one case. It is probable, however, that the tuberculous infection, if it be present, is co-existent with, and not a cause of, the erythrodermia.

Symptoms. The eruption begins as erythematous areas, with slight scaliness but without infiltration, as a rule, in the joint flexures. It extends and in time involves the skin of the entire body. The scales are small on the face, but larger on the trunk and limbs, detached at the margins, and frequently and abundantly shed, so that the bed is filled with dry, papery flakes, amounting to a pint or two in twenty-four hours. There is no exudation of serum, and the skin feels dry and hot, but in some cases there occur periodically profuse sweats, which leave the patient temporarily exhausted. For a long time the subjective symptoms are usually slight; the patients complain of feeling cold, and shivering fits are common, but the appetite is good, at times excessive, and nutrition is well maintained. Itching may be slight or even absent, but is sometimes intense and paroxysmal, causing insomnia. The temperature is apt to be subnormal, but pyrexial attacks are common towards the end. In time definite infiltration of the skin occurs, so that free movement is difficult, the hair of the scalp becomes thinned, the lanugo hair disappears, and the nails are affected. After the eruption has persisted for several months, secondary sclerosis and atrophy of the skin occur. The epidermis is thinned, and the whole skin feels hard and inelastic, fitting tightly over bony surfaces and joints. Its colour tends to become darker and more livid, and increased pigmentation, particularly in the natural folds, is noticeable. In rare cases the skin takes on a characteristic bluish-brown hue, which is seen in no other condition. Gradually the patient's strength begins to fail, he wastes, his sweats increase, his mental state becomes affected, so that he is childish and is a prey to delusions, albuminuria and diarrhœa may be present, and the secondary infective complications—cellulitis, deep abscesses, bronchitis, hypostatic pneumonia, etc.—provoke a pyrexial response of varying degree. Hæmorrhages into the skin and mucous membranes are often seen terminally, and their occurrence in the suprarenal capsules may be the apparent cause of death.

Pathology. It is remarkable what little evidence there is of organic disease *post-mortem* in many cases of this obscure condition. Jadassohn's experience that death usually occurs from tuberculosis has been mentioned, but no signs of active tuberculosis have been found in some characteristic cases. On section the skin in the early stages shows the appearances of a superficial inflammation with parakeratosis. In later stages there is atrophic change, the papillæ and interpapillary processes may be obliterated, the pilo-sebaceous follicles and sweat glands have disappeared, and there is cicatricial contraction of the newly-formed connective tissue, with deposit of pigment in the corium.

PREMYCOSIC ERYTHRODERMIA (*See Plate 61, C, p. 940*)

The various prodromal eruptions that may precede the appearance of the characteristic tumours of mycosis fungoides are mentioned in the descrip-

tion of that disease. One of these is an erythrodermia, beginning as intensely itching red patches, and becoming generalised. The skin is of a vivid red colour ("*homme rouge*"), more livid in the flexures and lower limbs; there is much less desquamation, and the scales are smaller than in pityriasis rubra, and here and there may be small islets of healthy skin, which appear depressed below the surface of the surrounding inflamed and infiltrated integument. The nails are not usually affected, except that they are worn and shiny from constant scratching. The itching is intense, much more so, as a rule, than in pityriasis rubra. The subcutaneous lymphatic glands are enlarged and easily palpable. Eventually, often after many years, the nodular tumours of mycosis fungoides arise, but in some cases the erythrodermia may spontaneously disappear and later recur, or death may result from cachexia or an intercurrent infection before the appearance of tumours.

The histological appearances of premycosic erythrodermia are characteristic. There is a dense infiltration, composed of lymphoid cells, lying in the papillary zone and sharply limited below; the papillæ are broadened and elongated; the interpapillary processes are thinned and often bifid; the horny layer is thickened and in places parakeratotic; and here and there lying in the Malpighian layer are seen little nests of lymphocytes, which are pathognomonic of mycosis fungoides.

LEUKÆMIC ERYTHRODERMIA

Leukæmia, like Hodgkin's disease, may be accompanied by various cutaneous manifestations (**60**). In acute leukæmia, which is usually of the myeloid rather than the lymphoid type, the lesions may be divided into (1) leukæmic tumours; (2) dermatoses of various kinds. Of the latter purpura is by far the commonest, but erythematous rashes, papules, vesicles, hæmorrhagic bullæ, and erythrodermia may occur. In chronic myeloid leukæmia tumours in the skin are very rare; cutaneous and subcutaneous hæmorrhages are seen, usually towards the end, and pruritus has been described. In chronic lymphoid leukæmia tumours are not uncommon, and may be present before the occurrence of leucocytosis, although a differential count usually shows a relative lymphocytosis. Apart from tumours, there are other cutaneous manifestations—the *leucemides* of Audry and Germès; they are polymorphic, and usually accompanied by pruritus. They take the form of *urticaria*, which may be of the papular or vesicular type, *erythemata*, simple or bullous, imitating erythema multiforme or even dermatitis herpetiformis, and *prurigo*, recalling that seen in Hodgkin's disease. It is probable that these various types of eruption, and the erythrodermia to be described, are due to toxins liberated from disintegrated lymphocytes.

Leukæmic erythrodermia is not very rare, and different forms of it have been distinguished. Thus some are relatively acute and febrile, corresponding to the group of subacute primary erythrodermias; others are essentially chronic, and simulate pityriasis rubra; others again are partial, and resemble psoriasis. The commonest variety clinically resembles premycosic erythrodermia very closely, but the itching is usually less intense. Sequeira and Panton have described a series of cases under the term *lymphoblastic erythrodermia*, characterised by a moderate leucocytosis, 8,000 to 30,000 per cubic millimetre, with an increase of the small lymphocytes up to about 75 per cent. There seems, however, no reason to separate these cases from leukæmic erythrodermia. In the differential diagnosis between premycosic and leukæmic erythrodermia the following points should be noted: (1) The blood picture; (2) the histology, that of premycosic erythrodermia being characteristic; (3) The X-rays have little or no effect on leukæmic erythrodermia, but their action on mycosis fungoides is striking, though temporary.

PITYRIASIS RUBRA PILARIS (*See Plate 61, E, p. 940*)

This rare disease should, perhaps, be considered with psoriasis, which it closely resembles. The primary lesion is an acuminate, red follicular papule, with a

broken hair in its centre, and surrounded by a horny collar, which dips into the follicle. These papules are seen best on the hairy parts of the limbs, especially on the extensor surface of the forearm and on the dorsal parts of the fingers. Apart from the primary follicular lesions, red, scaly patches, resembling psoriasis, appear on various parts of the body, and they may extend until a generalised erythrodermia results. The palms, soles, and face are particularly affected. The evolution of the disease varies. The onset is usually sudden, and the eruption spreads rapidly until the whole skin is involved. The erythrodermia may remain generalised for several months, and then disappear slowly or rapidly until the skin returns completely to normal; or the greater part of the eruption may clear, but certain areas, usually the palms, soles and face, remain affected sometimes for years. Two or more attacks may occur in the same patient. The general health is but little affected, but there may be slight fever at the onset, and during the erythrodermic stage of the disease. The inflammation and thickening of the skin give rise to a sensation of heat and burning, and there is great discomfort from cracks on the palms and soles, and from the ectropion, which may result from involvement of the face.

Morbid Anatomy. There is hyperkeratosis of the infundibular parts of the follicles, which thus become plugged with cones enclosing the broken or atrophied hairs. In contrast with psoriasis, the stratum granulosum persists and may be hypertrophied. The rete Malpighii may be thinned or slightly thickened. The vessels of the papillæ are congested, and surrounded by cellular infiltration.

Ætiology. An inherited tendency has been observed in several instances. The writer has seen four examples of the disease occurring in mother and child, and several members of a family in more than one generation may be affected (**54**). This, however, is, of course, also true of psoriasis. The actual cause is unknown. The suggestion that it is of tuberculous origin has little to support it; it is more likely that it is due to an unknown infective organism.

Diagnosis. The follicular lesions must be distinguished from such conditions as lichen spinulosus and the follicular variety of lichen planus. In their absence the resemblance of the red scaly patches to psoriasis is close, particularly as they often occur on the elbows and knees. The early involvement of the palms and soles, however, is a striking feature of pityriasis rubra pilaris. The generalised form of the disease, in which the follicular lesions may be absent, imitates other erythrodermias.

Treatment.—The local treatment is like that of psoriasis, except that chrysarobin should not be employed. Oil of cade is, perhaps, the most effective application. Internally, the administration of arsenic in increasing doses, and of thyroid seem to be of benefit, but the disease often seems to run a definite course without apparently being influenced by any form of treatment. Injections of gold compounds have been of apparent value in some cases.

PAPULAR ERUPTIONS

The term lichen has been long in use to signify any sort of papular eruption, but is now generally restricted to two diseases: one falls in the present group, *lichen ruber planus*, or *lichen planus;* the other is a tuberculide, *lichen scrofulosorum*.

LICHEN PLANUS (*See Plate 63, A, p. 942 and 64, B, p. 945*)

The elementary lesion of *lichen planus* is a papule, of which there are four varieties:—

(1) *The polygonal papule* is formed in a space between the natural lines of the skin, which constitute its boundaries and determine its shape (*cf.* lichenification).

(2) *The obtuse papule* is larger, shiny, and translucent in appearance; in its

centre is a minute depression, sometimes with a horny plug, corresponding to the mouth of the sweat-gland, around which it is formed.

(3) *The plane papule*, not so common as the above varieties, is hardly raised above the surrounding skin.

(4) *The follicular acuminate papule*, the least common of all, is characterised by a horny spine, formed by follicular hyperkeratosis. These follicular lesions, when they occur, usually coexist with other papules, but may be found alone, and probably many cases labelled lichen spinulosus are really follicular lichen planus.

In the majority of cases the fully-developed eruption is constituted by the first three varieties of papule, which by confluence form plaques and figures of varied design. The elementary papules are usually pink in colour, dry and firm to the touch, and their surface has a characteristic sheen or burnish. The fully formed papule and the confluent patches tend to develop a lilac hue, which is almost pathognomonic. Still more so are the opalescent white lines or points, known as Wickham's striæ, which tend to form a network on the surface of the adult papules, both when single or coalescent. They are due to the irregular distribution of keratohyalin in the granular layer of the epidermis, and can be rendered more obvious by sponging the surface of the papules with aniline oil or water, in order to increase the transparency of the horny layer. The confluent patches become covered with fine adherent scales; occasionally the hyperkeratosis may be so marked that at first sight the eruption resembles psoriasis.

In cases of some standing there is usually hyperpigmentation, the papules and plaques becoming darkened, and sometimes surrounded by a brownish halo; and the coexistence of lichen planus and vitiligo is not rare. After resolution of the lesions, their former sites are marked by pigmentation, which is most intense on the lower limbs, and is undoubtedly increased by arsenical medication.

The sites of election in lichen planus are the anterior surfaces of the wrists and forearms, the inner surfaces of the thighs just above the knees, and the legs, but the eruption is often generalised and sometimes more profuse on the trunk than on the limbs. On the palms and soles, owing to the thickness of the horny layer, the appearances are deceptive. The papules are hyperkeratotic, and at first sight resemble vesicles: shedding of their horny covering results in a pitted condition comparable to that seen in the punctate keratodermia of Mantoux, in Darier's Disease, and in arsenical keratosis. Sometimes, however, there are red, scaly patches, or even a diffuse keratodermia. Lichen planus, though rare on the face, is not so uncommon on the scalp as is usually thought; it is often mistaken for circumscribed prurigo, or for lichenified seborrhœic dermatitis. It forms dry plateaux with well-defined steep edges, and a careful examination will reveal the lilac tint and the white striæ. Sometimes, however, the patches are atrophic, and the hair is destroyed. This variety is usually associated with a follicular eruption on the body.

The subjective symptoms vary according to the individual affected. The itching may be intense and continuous, driving the patient to distraction; more commonly it is moderate in degree and paroxysmal, particularly, as in the prurigos, at night time; sometimes it is slight or entirely absent. Occasionally patients complain rather of soreness than of itching. Even when the pruritus is severe there may be little or no evidence of scratching, but in some cases lichenification is superimposed upon, and may mask the primary eruption.

Lichen planus not infrequently involves the mucous membranes, particularly that of the mouth, upon which it occurs in about half the cases. It is important to remember that the mucous membranes may be alone involved, or may be affected before the appearance of cutaneous lesions; and in the mouth the eruption often persists long after it has cleared from the skin. On the *oral mucous membrane* the sites of election are the internal surfaces of the cheeks, opposite the junction of the upper and lower teeth. The lesions consist of milky

white spots, often forming a network or rings ; the white colour is characteristically tinged with blue, and is more opalescent than that of leucoplakia. There may be superficial erosion, so that deep-red patches, which often cause discomfort, are seen, surrounded by a bluish-white network. On the *tongue* patches of varying size or a similar network occur, and the same bluish-white colour is seen. The lesions may involve the dorsum or the sides. More rarely the eruption is extensive, affecting not only the cheeks and tongue, but also the palate, the lips, both on their vermilion borders and inner surfaces, the gums, and even the tonsils. On *the vulva* the patches are also milky white, but on the glans penis the papules resemble more often those on the skin, and commonly form annular figures. The *anus* and *rectum* may also be affected.

The histological changes of lichen planus of the mucous membranes are exactly comparable to those of the cutaneous lesions. The *diagnosis* is of importance, as buccal lichen planus is often mistaken for leucoplakia, tertiary glossitis, or for mucous patches. The colour of leucoplakia is different, lacking the bluish tint of oral lichen, and being *mat* rather than opalescent ; moreover, the surface of the patches appears finely striated. Lupus erythematosus affecting the buccal mucous membrane is not uncommon (about 30 per cent. of cases) ; it occurs on the free border and inner surface of the lips, usually the lower, and on the cheeks, where it may be confused with lichen planus. The white patches, however have a bright red base with purplish stippling, and there is usually partial atrophy. The tongue and palate may be affected.

Varieties. Lichen planus is usually one of the simplest eruptions to diagnose owing to the clear-cut picture provided by the elementary papules, the white striæ, and the characteristic lesions in the mouth. On the other hand, there are anomalous forms of the disease, which may deceive even the expert for a while. Among the most important varieties may be cited :—

(1) The *annular* form (lichen annulatus). The papules tend to group themselves in rings, 6 to 8 mm. in diameter, with a pigmented centre. More rarely a ring may be formed by the peripheral extension, with central involution, of a sinlge papule. This annular variety is common, and the rings are seen chiefly on the wrists and forearms, the flanks, and on the glans penis.

(2) The *gyrate* form (*lichen marginatus seu serpiginosus*), in which the papules extend centrifugally to produce figures comparable to those of erythema annulare centrifugum.

(3) *Lichen striatus* is the name given to the characteristic rows of papules that develop along scratch marks.

(4) *Lichen linearis.* The lesions form long, narrow bands, which may appear to follow the trajectory of a nerve, *e.g.* the small sciatic, internal cutaneous, and ulnar, or may be quite straight, and apparently independent of any nerve distribution. Comparable to these cases are those in which lichen planus develops in a zoniform manner, with a distribution exactly corresponding to that of a herpes zoster.

(5) *Lichen acuminatus.* This is the follicular form of lichen planus already referred to. When the acuminate follicular lesions coexist with plane papules, the variety *lichen planopilaris* is produced. Recent observations indicate that many cases of so-called lichen spinulosus are really the follicular form of lichen planus. Moreover, the association of " lichen spinulosus " with bald, atrophic areas on the scalp has been noted in several instances, and the question arises whether these latter are not atrophic lichen planus, and whether the condition labelled *pseudo-pelade* is not also in some instances atrophic lichen planus confined to the scalp.

(6) *Lichen corneus hypertrophicus, seu lichen verrucosus.* In this variety raised warty plaques are formed, as a rule on the legs, particularly when varicose. They may be discrete, but are usually grouped or even confluent. They are reddish to purplish-brown in colour, and their surface is studded with horny

follicular plugs, or pitted when these have fallen. This hypertrophic form of lichen planus must not be confused with the so-called *lichen obtusus corneus*, which is really prurigo nodularis (*q.v.*).

(7) *Lichen planus atrophicus seu sclerosus* is very rare. The characteristic lesion is an ivory white papule, firm to the touch, and usually neither raised nor depressed. On the surface may be found black, horny plugs, situated in the orifices of the pilosebaceous follicles or sweat-ducts, or the pits that mark their former sites. Histologically there is found a band of sclerosis between the epidermis and the infiltration in the dermis. This atrophic lichen planus is doubtless one form of so-called "white-spot disease," of which the other is guttate morphœa.

(8) *Lichen planus bullosus.* This is excessively rare. The bullæ are formed between the epidermis and the papillary layer. In some cases it appears to be due to arsenical medication.

(9) Lastly may be mentioned a variety in which an acute eruption of erythematous more or less oval patches develops chiefly on the trunk, resembling very closely in its early stages *pityriasis rosea.* It is only when the eruption has been present for some days that the characteristic lichen papules appear in the patches.

Ætiology. The cause of lichen planus is unknown. It is almost certain that, as in herpes zoster, the actual lesions are infective in origin, and caused by involvement of certain nerve-fibres. Like herpes zoster, an outbreak of lichen planus may be provoked by injections of the organic arsenical compounds, and by bismuth and gold preparations. In a case of vitiligo observed by the writer, an eruption of lichen planus, *with an exact zosteriform distribution*, appeared during a course of injections of novarsenobillon, and disappeared spontaneously in about three weeks. Moreover, in some cases of so-called linear lichen planus the eruption appears to follow closely the course of a cutaneous nerve, *e.g.* the internal cutaneous and ulnar, the small sciatic, or the inferior gluteal and popliteal nerves; in others the distribution is comparable to that of a segmental nævus. The undoubted therapeutic action of X-rays applied over the spinal column, particularly over the cervico-dorsal and lumbo-sacral regions, is significant, and it is of interest that in some cases this method of treatment may provoke an acute generalised outbreak of the eruption. The favourable effect sometimes observed of lumbar puncture, with the withdrawal of several c.c. of cerebro-spinal fluid, can hardly be explained otherwise than by some obscure action on the nervous system.

The influence of shock, worry, and grief is in some cases apparent, but the eruption may occur in healthy, happy persons, and in young children.

Morbid Anatomy. The inflammatory process in *L. planus* begins round a sweat duct in the upper part of the corium; there is a dense growth of connective tissue cells, which are, according to some, of granulomatous type. This is followed by increase of the cells of the stratum mucosum, and thickening of the horny layer. There is irregular thickening of the eleidine, which causes the appearance of white striæ, above mentioned.

Treatment. In severe, generalised cases, and in patients suffering from nervous exhaustion, complete rest in bed for a few weeks should be enjoined. The oral administration of arsenic in increasing doses has deservedly fallen into disfavour. Mercury in the form of the liq. hydrarg. perchlor. appears more efficacious, and is usually well borne. Much more certain in their effect are injections of the organic arsenical preparations—novarsenobillon, acetylarsan, soamin, etc.—or of arsenical and mercurial compounds, such as Enesol (salicylarsenate of mercury). Novarsenobillon may be given intravenously in doses of 0·3 to 0·6 gm. at intervals of from one to three weeks, but it occasionally provokes widespread extension of the eruption with considerable malaise. Enesol is injected intramuscularly in doses of 2 to 5 c.c. at intervals of three to seven days.

The toxic effect of these metallic compounds is apparently lessened by the oral administration of glucose, 2 to 3 ounces per diem in divided doses.

On the Continent irradiation of the spinal column is now much in vogue, either by deep, filtered rays, applied obliquely to act on the nerve-roots (Hufschmidt and Pautrier), or by non-filtered rays in doses of 5H to the cervico-dorsal and lumbo-sacral regions with the idea of affecting the sympathetic (Gouin). Both methods may, like injections of arsenobenzol, cause a temporary acute outbreak of the eruption, and, although strikingly successful in some cases, may fail entirely.

Lumbar puncture, with the withdrawal of 6 to 8 c.c. of cerebro-spinal fluid as Thibierge and Ravaut have pointed out, is of value in generalised cases with intense itching. It usually has an almost immediate effect on the pruritus, and in some cases appears to hasten the disappearance of the eruption. To obtain the desired result, two or more punctures at intervals of a few days may be necessary.

Local Treatment. In patients with an acute widespread eruption soothing antipruritic applications should be employed. A daily tar bath may be taken, and a calamine lotion, containing liq. picis carbonis and phenol, subsequently applied freely. In less acute cases a cream, ointment, or paste containing tar, phenol, and ammoniated mercury are of value. Unna's well-known ointment consists of mercuric chloride 2 to 20 grains, phenol 5 to 20 grains, zinc ointment 1 ounce, the quantity of perchloride and phenol being raised according to the extent and thickening of the patches. For chronic patches a strong tar paint or collodion, or a plaster containing perchloride, phenol, and salicylic acid, relieve the itching and may hasten resolution. Obstinate chronic plaques of hypertrophic lichen planus are best treated by a full pastille dose of X-rays, by the filiform douche, or by repeated freezing with carbon-dioxide snow.

On the buccal mucous membrane the eruption is much more resistant to treatment than on the skin, but it may yield to injections of the organic arsenical compounds, particularly of acetylarsan according to Audry. Radiotherapy applied to the nape of the neck and local treatment with radium have been recommended in resistant cases.

LICHEN NITIDUS

This eruption was first recognised as a clinical entity in 1901. Numerous cases have subsequently been described, and the writer (**61**) in a review of the literature has confirmed the view that lichen nitidus is but an atypical variety of lichen planus, with special histological features, and the ætiology is the same.

Symptoms. The elementary lesion of lichen nitidus is a minute papule formed by a more or less sharply defined granuloma, which lies, as a rule, just below the epidermis. These papules are not usually larger than the head of a pin, flat, conical or globular in shape, and slightly raised above the surface. Their colour varies in different cases, and is commonly reddish or reddish-yellow. A very characteristic feature is that they often have the glistening appearance implied by the epithet " nitidus," and appear as minute reddish spots shining through a transparent overlying epidermis. Sometimes they look almost like small vesicles, recalling the sago-grain appearance of cheiropompholyx. On pressing with a glass slide, they remain as opalescent points of a darker colour than the surrounding skin, rendered anæmic by the pressure. Sometimes there is a minute depression in the centre of the papule, but this is by no means a constant feature. At the apex of some papules it is possible by scratching to produce a tiny bright scale. There is, as a rule, no connection between these elementary lesions and the pilo-sebaceous follicles.

As has been said, in many cases the eruption consists merely of these papules, which remain discrete and are unaccompanied by any changes in the surrounding skin. In such cases they usually have a strictly limited distribution, occurring chiefly on the penis in men, the lower abdomen, groins, and inner surfaces of the

thighs, and on the flexor surfaces of the wrists and forearms and backs of the elbows.

In other cases, however, the eruption becomes widespread and loses its primary papular appearance in certain regions. In such a case one can probably always find, by careful examination of the whole body, certain areas where the elementary papules are discrete and typical of the simple form of the disease. In generalised cases they are present on the lower abdomen, groins and thighs, but elsewhere the eruption consists of diffuse pityriasiform or psoriasiform sheets, which are, when once recognised, very characteristic in appearance. Their colour varies in different patients and in different situations, being either reddish-yellow, brownish, or reddish-violet. In the flexures the reddish tint predominates, while on the extensor surfaces of the limbs the patches are often yellowish-brown, or hardly darker than the surrounding skin.

The distribution of these diffuse sheets of the eruption may be widespread, but they are particularly likely to involve the joint flexures, such as the antecubital and popliteal spaces. The anterior surfaces of the wrists and lower part of the forearms, the extensor surfaces of the knees and elbows, the folds of the neck, the submammary region in women, the groins and thighs, the palms and soles and dorsal surfaces of the hands and feet may all be affected. On the knees and elbows the patches are triangular in shape, the apex of the triangle pointing downwards. Here they look not unlike patches of lichenification, but the accentuation of the natural furrows of the skin is absent or but little marked. They differ from psoriasis in that their colour is brownish-yellow, on scratching they become only slightly scaly, and the scales have not the characteristic silvery appearance of psoriasis. In the joint flexures they may also resemble somewhat areas of lichenification, but their colour is usually of a lighter red or reddish-yellow, there is no accentuation of the natural lines of the skin, and there is less thickening.

At the periphery of the diffuse patches one can sometimes see outlying discrete elementary papules, and they may also often be discerned, even in the central parts, by putting the skin on the stretch and thus rendering it anæmic.

Pathological Anatomy. The microscopical features of lichen nitidus are characteristic. A single papule consists of a sharply circumscribed granulomatous infiltration, lying as a rule immediately below the epidermis, which is thinned above it and sometimes actually invaded by it, and consisting of epithelioid cells, small round cells of the mononuclear type, with occasional giant cells, embedded in a stroma of œdematous connective tissue. There may be a definite gap between the epithelium and the area of infiltration, but, as a rule, they merge into one another, and one finds degenerated epithelial cells lying actually in the infiltrate. The epidermis tends to send down acanthotic prolongations on either side of the infiltrate, which may be even completely surrounded by them, a feature that is considered pathognomonic. The vessels going to the little granulomatous nodule have thickened walls, the lumen in some cases being completely obliterated, and around them is a well-defined cellular infiltration. The connective and elastic tissue may be completely destroyed in the centre of the nodules, which usually bear no relationship to the follicles or sweat-ducts. A section taken from a confluent patch will show several such nodules of different sizes and in various stages of evolution.

Treatment. Since recognising the probable identity of lichen nitidus and lichen planus, the writer has treated two extensive cases with intravenous injections of novarsenobillon with satisfactory results. Probably the alternative methods of treatment suggested for lichen planus would be equally efficacious.

PARAPSORIASIS

Under this term, first proposed by Brocq in 1902, has been included a group of eruptions characterised by erythemato-squamous patches of varying size and

distribution, which are very resistant to treatment and the causation of which is unknown. In 1890 Unna, Santi, and Pollitzer described them as *parakeratosis variegata*, and aptly compared them to "a mixture of psoriasis, lichen planus, eczema, and pityriasis rosea." In 1901 Fox and Macleod included under the term "Resistant maculo-papular scaly erythrodermias" the *erythrodermie pityriasique en plaques desséminées* of Brocq; the dermatitis psoriasiformis nodularis of Jadassohn; the pityriasis lichenoides chronica of Juliusberg; the lichenoid psoriasiform exanthem of Neisser; and parakeratosis variegata. Brocq divided his parapsoriasis into *P. en gouttes*, *P. lichénoïde*, and *P. en plaques*, but although this division is convenient, it is very doubtful whether the three types are ætiologically connected, and confusion still exists even as regards their clinical classification.

Parapsoriasis guttata. (*P. en gouttes. Pityriasis lichenoides chronica.*) The eruption involves chiefly the trunk and upper segments of the limbs. It consists of small superficial papules, circular or oval, and varying in colour from pink to reddish-brown or fawn. They are covered by a characteristic mica-like scale, which may give to the lesions a false impression of superficial atrophy. At first sight the eruption might be mistaken for *Pityriasis rosea*, a guttate psoriasis, or a papulo-squamous syphilide in course of resolution, but the adherent scales are pathognomonic. Despite the term pityriasis lichenoides chronica, it has recently been recognised that the disease may have an acute onset and develop rapidly, like *Pityriasis rosea*; as in the latter, a "herald-patch" has been observed in some cases. Moreover, it is now known that *pityriasis lichenoides et varioliformis acuta* (Habermann. Mucha.), which was comparatively common in this country a few years ago, is merely a variety. In this, apart from the lesions already described, vesicles, which tend to become hæmorrhagic or pustular, arise, undergo necrosis, and leave varioliform scars. It may be confused with chicken-pox, particularly as the onset is abrupt and there may be some constitutional disturbance with adenopathy. The acute form of the disease, with or without varicelliform lesions, tends to run a definite course, but its duration, unlike that of *Pityriasis rosea*, is indefinite, varying from some weeks to several months, and recurrences have been reported. In the varicelliform variety the necrotic vesicular lesions may cease to form after a while, whereas the others may persist for a long time.

Ætiology. The disease is seen as a rule in adolescents and young adults, but may occur in children. The acute variety must be due, like *Pityriasis rosea*, to an unknown infective organism, probably a filterable virus, and this is doubtless also true of the chronic form, since there are no valid reasons for separating the two. It is logical, in fact, to regard the condition as a specific disease of infective origin, and as being entirely distinct from the other types of parapsoriasis.

Treatment. There is some evidence that injections of gold compounds are of therapeutic value.

Parakeratosis variegata. (*Parapsoriasis lichénoïde. Lichen variegatus of Crocker.*) This rare eruption is usually distributed widely over the trunk and limbs, and has a retiform arrangement, recalling that seen in livedo and erythema *ab igne*, and due, as in these, to passive dilatation of the capillaries farthest away from the arterial cones. The elementary lesions are papules, varying in colour from reddish-yellow to lilac, some of which may be flat-topped and shiny, resembling those of *Lichen planus*, whereas others are covered by scales, similar to those of *Parapsoriasis guttata*. These papules, which are closely set and tend to become confluent, are most evident on the reticulations formed by capillary stasis. The scaliness in certain areas may be diffuse. The skin of the palms may be hyperkeratotic, but the nails are not affected. Subjective symptoms are slight or absent, but some itching may be present, particularly when the patient is exposed to heat. The eruption usually develops slowly, and is essentially

chronic, but its onset is sometimes sudden and it may become widespread in the course of a few weeks.

Ætiology. Like *Parapsoriasis en plaques* this variety usually occurs in middle age, and is commoner in males. The causation is unknown.

Morbid Anatomy. There is dilatation of the capillaries, with surrounding lymphocytic infiltration, and œdema of the connective tissue. There is also some epidermal œdema without vesiculation, and the horny layer in places is parakeratotic.

Treatment. No form of treatment appears to have any curative influence on the eruption.

Parapsoriasis en plaques. (*Xanthoerythrodermia perstans of Crocker.*) Like the preceding variety this eruption is essentially chronic and unresponsive to treatment. It involves the trunk and limbs, and consists of well-defined patches which vary both in size and contour. Some are roughly circular and of the size of a sixpence to that of half a crown ; others are irregular in outline, considerably larger, and may have finger-like projections or enclose islets of normal skin, thus simulating premycosic erythrodermia. Sometimes diffuse patches occur in the joint flexures. The colour ranges from pale fawn to reddish-brown, and that of a given patch may vary from time to time according to the degree of vascular congestion. The surface reveals slight exaggeration of the natural lines, thus forming a fine mosaic. It is covered by small and adherent scales, which may not be apparent unless it is gently scraped. There is hardly any infiltration, so that the patches are scarcely if at all elevated. Subjective symptoms may be absent, but some patients complain of considerable itching.

Ætiology. The condition is commoner in men than women. Although usually seen in middle age, it may begin in childhood. The cause is unknown. It is possible that it is a rare non-specific reaction of the skin to various toxins, of which, as Civatte has suggested, chiefly on histological grounds, that of tuberculosis may be one. Whitfield has described under the term "Dermatitis colonica" a similar eruption occurring in persons in whom cultures of the stools reveal an enormous preponderance of streptococci. Cure has followed the internal administration of creosote, dimol, or kerol.

Diagnosis. Confusion is most likely to arise with the circinate or flexural forms of seborrhœic dermatitis, and with the pre-mycotic stage of mycosis fungoides. In the former the lesions are more elevated, and the scales are rather larger and more easily detached ; moreover they respond readily to local treatment. In the latter the patches are more infiltrated, and itching is more intense.

Treatment. Exposure to real or artificial sunlight may cause temporary disappearance of the eruption. Apart from this, it is resistant even to strong applications. Injections of a stock *B. coli* vaccine were apparently of striking benefit in one of the writer's cases.

VESICULAR ERUPTIONS

CHEIROPOMPHOLYX

(*Pompholyx, Dysidrosis*)

Definition. A bilaterally symmetrical vesicular or bullous affection of the hands and feet, frequently accompanied by hyperidrosis.

Symptoms. The word *cheiropompholyx* (from χείρ, a hand, and πομφόλυξ, a bubble) should be reserved for an eruption which appears spontaneously and often periodically in certain persons. A dermatitis bearing very close, if not identical, clinical appearances to those of pompholyx, may be produced by various irritant applications and by a ringworm fungus (epidermophyton), but this must be differentiated from the disease to be described.

An attack of pompholyx usually begins with a sensation of itching, burning, or tingling in the hands, and within a few hours the eruption appears as small translucent vesicles situated usually on the sides of the fingers, in the interdigital clefts, and in the palms. These vesicles are deep-seated, unaccompanied by any signs of inflammation, and have been compared to boiled sago grains. In mild cases they may remain discrete, but frequently they coalesce, forming large bullæ projecting beyond the skin. The fluid in the vesicles is clear, alkaline, and contains albumin. The lesions may dry up spontaneously, the overlying skin being shed in dry flakes; in this way the skin of the whole palm may peel off, leaving a pink new skin underneath, which gradually assumes the normal appearance. On the fingers, however, the larger vesicles and bullæ are apt to be ruptured, exposing a raw, moist, tender surface beneath. Secondary infection of the lesions is liable to occur, particularly in uncleanly persons, or in those whose resistance is low; the vesicles then become purulent, and a spreading lymphangitis of the arms with adenitis and fever may result. A peculiarly offensive odour, resembling that of atrophic rhinitis, occurs in these infected cases; this probably results from the digestion of keratin by staphylococci which, growing in the alkaline fluid of the vesicles, liberate proteolytic enzymes.

The eruption may be confined to the hands, but not uncommonly the toes and the soles of the feet are affected, and here secondary infection is the rule. In some cases the disease is accompanied by eczema of other parts of the body.

The duration of an attack varies from a few days to several weeks, but recurrences are common, particularly in spring and summer. Patients subject to the disease are usually in a poor state of health, and are frequently neurotic; the symptoms associated with chronic intestinal toxæmia of the putrefactive type are often evident, namely, pigmentation of the skin, clammy sweat, foul breath, anorexia, and headaches. There is sometimes hypochlorhydria, and the urine contains a considerable quantity of indican in the majority of cases.

Anatomy. The histology resembles that of eczema in that the vesicles are formed in the prickle-cell layer. In the corium the papillary vessels are dilated, and there is some inflammatory cell infiltration around them. According to recent researches the vesicles are formed around, and result from the bursting of the sweat-ducts in the epidermis.

Ætiology. The disease is commonest in early adult life, and is seen, perhaps, more often in women than in men. It is certainly a manifestation of toxæmia, and the frequency with which indicanuria and other symptoms of excessive intestinal putrefaction are present in patients subject to the disease suggests that the toxin may be some decomposition product of protein. Those with sedentary occupations may lose their tendency to the attacks in adopting an out-of-door life with vigorous exercise. In other cases, however, focal infection appears to be causal, since removal of infected teeth or tonsils, or thorough treatment of a chronic sinusitis, has led to cessation of the attacks. The disease occurs most frequently in hot weather, and some persons are liable to one or more attacks every summer.

Diagnosis. True pompholyx must be distinguished from eczematous dermatitis produced by external irritants, and from eczematoid ringworm of the extremities. Differentiation from these two conditions may be difficult, particularly from the latter. It is essential in doubtful cases that scales and the roofs of the vesicles should be examined microscopically, with their under-surface upward, in liquor potassæ, and interdigital epidermophytosis of the feet must be excluded.

Treatment. If, as is usually the case, there is evidence of excessive intestinal putrefaction, the diet should be revised. Patients liable to severe recurrent attacks may well become vegetarians temporarily, and in any case fruit and green vegetables should be taken rather than the heavier meats and sweets. Regular aperients are advisable for a while, such as liquid paraffin, sodium

sulphate, and occasionally calomel in small doses. If hypochlorhydria is present, dilute hydrochloric acid should be given in 30 to 40 minim doses, well diluted, after meals, as this will materially aid the digestion of protein. A thorough search for chronic foci of infection must be instituted, since their successful treatment may prove curative. Locally in the early stages sponging with a 2 per cent. solution of salicylic acid in spirit stops the irritation at once, and then either the pulv. acidi salicylici comp. B.P.C. or pasta zinci comp. B.P.C. may be applied. In cases in which the skin has become raw a lotion containing boric acid, calamine, and glycerine, should be used, and those in which secondary infection has taken place should be treated with weak antiseptic lotions locally, rest in bed, and tonics.

BULLOUS ERUPTIONS

PEMPHIGUS

The term pemphigus (πεμφιξ, a blister) has in the past been somewhat loosely applied to a number of bullous eruptions which ætiologically have nothing in common. Thus *P. neonatorum* and *P. contagiosus tropicus* are due to superficial pyogenic infection of the skin; *P. syphiliticus* is a bullous syphilide most commonly seen on the palms and soles of infants with congenital syphilis; and *P. leprosus* is a bullous form of leprosy.

At the present time the word pemphigus is confined to the following conditions: (1) *P. acutus malignus.* This is a rare acute infective disease, usually fatal, which occurs in those who handle dead meat, and is probably due to infection with a diplococcus. It should no longer be included in the pemphigus group. (2) *P. vulgaris.* (3) *P. vegetans.* (4) *P. foliaceus.* These are probably merely varieties of the same disease—*true pemphigus.*

Pemphigus Acutus Malignus. This disease, which is excessively rare, has been chiefly observed among butchers and farm-hands, and in most cases its onset has been preceded by local wounds on the hands or arms, through which presumably the infecting organism obtained entry. As in true pemphigus, the lesions are large bullæ, arising usually directly from the skin without any preceding erythema; they contain at first clear or slightly blood-stained serum, but later this becomes puriform from secondary infection. New bullæ arise on all parts of the body, and the mucous membranes are usually involved; the skin later becomes excoriated and covered with crusts and fœtid discharge. There is high fever, albuminuria, vomiting, and diarrhœa, and in from two to three weeks the patient usually passes into coma and dies. A few cases have, however, recovered.

The diplococcus, isolated from the bullæ by Demme, Bulloch, and others, is probably the causal organism.

Treatment. The skin should be dressed with mild antiseptic applications, and, if possible, boric acid baths should be given. Quinine is the only drug that seems to have any beneficial effect, and should be given in increasing doses.

PEMPHIGUS VULGARIS

Symptoms. The disease usually runs a somewhat chronic course. The eruption may be preceded in some people by chilliness, nausea, or pyrexia; then the bullæ appear at one or other part of the body, small at first, gradually increasing in size, tense, hemispherical, with clear yellow or slightly turbid contents. The fluid is an albuminous serum, and the turbidity is due to the presence of leucocytes. Around the bleb the skin is at first quite normal, but a narrow pink areola is acquired later, and increases in proportion to the opacity of the fluid. After a few days the fluid is absorbed, or the bleb ruptures, and shrinks down on to its base. From this it is subsequently shed; it leaves a

mark which is injected and afterwards slightly stained, but rarely or never scarred. Sometimes the bleb contains pus or blood, and after its rupture the base may be covered with yellow lymph, or may slough.

The number of bullæ in any case is very variable. There may be but few in one part, or isolated bullæ in different parts of the body; or the whole surface may be thickly covered by blebs, which come out in successive crops, lasting only a few days each, but keeping up the disease for weeks and months. Nearly every part of the body may be affected, but the hairy scalp least of all. The disease may involve the mucous membrane of the mouth, nose, pharynx, larynx, and vulva, producing raw tender areas, sometimes covered by a diphtheroid membrane; the conjunctiva, too, may be attacked, resulting in contraction ("essential shrinking"), which may lead to obliteration of the conjunctival sac and ultimate blindness.

The amount of constitutional disturbance varies according to the extent of the eruption. When this is limited the general health is usually maintained, but in generalised cases there is great pain, prostration, moderate pyrexia, and sometimes vomiting and diarrhœa. The patient presents a pitiable appearance, and, when the buccal mucous membrane is involved, even liquid food causes great pain; insomnia is a constant symptom, and the unfortunate sufferer, utterly exhausted, eventually lapses into the tremulous, maudlin state which heralds the approach of death.

Pathology. The bullæ are formed by the effusion of fluid, which collects sometimes beneath the horny layer, and sometimes beneath the whole epidermis. The fluid at first contains considerable numbers of eosinophil corpuscles, and later becomes turbid owing to the leucocytosis which results from secondary staphylococcal contamination. In the papillary layer of the skin there is inflammation with infiltration of leucocytes, many of which are eosinophil, and eosinophilia in the blood is often very pronounced. *Post-mortem* examinations have failed to reveal any constant morbid changes in the viscera.

Ætiology. Although true pemphigus may occur from childhood to old age, it is, perhaps, most frequently seen between the ages of forty and fifty. The two sexes are about equally affected. The Jewish race is particularly predisposed, whereas this is not true of dermatitis herpetiformis. It is generally believed that the disease is due to a specific infection, and various types of micro-organisms have been described and thought to be causal by different observers. Welsh has recently carried out exhaustive bacteriological investigations in seven cases, and claims to have isolated a specific strain of streptococcus, which he obtained in all cases from the nasopharynx, from the blood in five, and from blister-fluid once only. The organism is pleomorphic and Gram-positive.

Urbach and Wolfram have produced encephalomyelomeningitis in rabbits by subdural inoculation with the filtered contents of bullæ or of the blood serum in several cases of pemphigus and dermatitis herpetiformis. The animals suffered from paralysis or spastic paresis. By using a filtrate of the brain, transference from rabbit to rabbit was obtained. These experiments, which require confirmation, suggest that pemphigus and dermatitis herpetiformis are due to a specific filterable virus.

Diagnosis. The essential lesion of true pemphigus is the bulla, and the diagnosis is not usually difficult. The bullous variety of *Erythema multiforme* may lead to confusion, but the sites of predilection in this condition, the acute course, and the presence of the typical erythematous patches, should suffice to distinguish it from true pemphigus. *Dermatitis herpetiformis* in its bullous phase may be difficult to diagnose from pemphigus, but eventually the appearance of papules and small vesicles, the herpetiform grouping of the lesions, and the intense itching, will make the diagnosis clear. *Epidermolysis bullosa* may be distinguished by the localisation of the bullæ over points of pressure and friction and by the history. Confusion with bullous impetigo should not

occur. Sooner or later the phenomenon known as " Nikolsky's sign " is present. This consists of detaching the stratum corneum by the firm pressure of the finger. Moreover, at the site of pressure a bulla develops. This sign is also present in pemphigus foliaceus and in epidermolysis bullosa.

Prognosis. Probably pemphigus is invariably fatal. The patients may, however, survive for years, and may pass through periods of freedom from the eruption. In thirty cases analysed by Highman a fatal issue resulted in every one.

Treatment. The oral administration of arsenic may control the disease to some extent, but is not so effective as in dermatitis herpetiformis. A mixture containing quinine and hexamine is also of benefit in some cases. Intravenous injections of a solution of quinine (0·5 per cent.) and of salvarsan have given good results temporarily. Success has also been claimed by a method which consists of intravenous injections of iron cacodylate in the dosage of 1 grain, together with intramuscular injections of coagulen (1·5 c.c.), thrice weekly. Recently a new preparation—Germanin (Bayer)—has been extensively used, chiefly on the Continent. On the whole the reported results have been very favourable, except in patients in an advanced stage of the disease. The dosage advised is 0·5 to 1 gramme intravenously every three to five days. Toxic symptoms must be watched for, such as albuminuria and icterus. Autohæmotherapy and blood-transfusion from a suitable donor sometimes lead to striking temporary improvement, but more permanent results are likely to be obtained with Germanin than by any other known method of treatment.

The local treatment consists in keeping the skin as clean and comfortable as possible by means of boric baths, mild antiseptic creams and powders, etc. Lozenges containing cocaine and carbolic acid relieve the pain when the oral mucosa is involved. In the terminal stages morphia should be given freely.

Pemphigus foliaceus. This is a very rare and fatal form of pemphigus, in which the whole surface of the body is gradually involved. The blebs are flaccid and flat, never tense and hemispherical. Their contents are turbid, and when these escape an inflamed excoriated surface is left; to this the remains of the bullæ adhere, forming thin flakes, the under-surface of which is moist with an offensive secretion. If the flakes are removed there remains a red, raw, secreting surface, not unlike that of *Eczema rubrum.* When the whole surface is affected, it is mostly covered with the adherent epidermis, with raw patches at intervals; then also the occurrence of blebs is not easy to observe, as they form under the existing epidermis and soon rupture. The course is slow, with remissions and relapses, it may be with healing of the skin in parts; but eventually the disease is fatal by exhaustion or intercurrent disease.

Pemphigus vegetans is another rare variety, in which the mouth is first affected; then bullæ of ordinary type form on the skin, ulcerate, and remain unhealed for a long time. The characteristic feature is that in moist situations, like the axillæ, groins, and gluteal folds, fungating papillary growths form on the site of the ruptured blebs, project a quarter to half an inch above the surface, and secrete an offensive muco-purulent fluid. Severe prostration ensues, and the cases end fatally. Some relief may be obtained by local antiseptic applications. Many observers have isolated the *Bacillus pyocyaneus* from the lesions, and it is likely that the disease is true pemphigus complicated by secondary infection with this organism.

Epidermolysis bullosa. This very rare congenital and hereditary disease is one in which the skin is abnormally susceptible to trauma, so that even trivial mechanical injury results in the formation of bullæ. Two forms are recognised, the simple and the dystrophic, and the latter may be subdivided into three groups, each inherited in a different way and with differences in their clinical manifestations (**54**). In the simple form the bullæ heal without leaving scars, and the skin only is affected; in the dystrophic variety the mucous membranes may also be

involved, and scarring occurs. This difference depends upon the site of formation of the bullæ. In the simple form this is in the epidermis, either in the stratum corneum or rete, in the other between the epidermis and the corium.

Patients suffering from the simple form are usually otherwise normal without defects in the teeth, hair, and nails. The formation of bullæ is usually delayed until early childhood, and is rare in infancy. They occur on sites exposed to injury, *e.g.* the hands and feet, and where there is pressure from garters, suspenders or belts. The tendency often decreases or disappears at or after puberty.

In the dystrophic form, of which there is a dominant and recessive variety, the latter being the more severe, the bullæ may be present at birth or soon afterwards, and other ectodermal defects involving the teeth, hair, nails, and mucous membranes, occur, particularly in the recessive cases. The bullæ may be hæmorrhagic, scarring is severe, and a characteristic feature is the presence of milium cysts in the atrophic skin. In both the simple and dystrophic varieties hyperidrosis of the palms and soles is a common accompanying symptom.

Ætiology. The disorder is hereditary and familial, and details of many affected families have been described (**54**). A deficiency of the elastic tissue of the skin has been held to be the actual cause of the bullous formation, but in some cases no change in the elastic fibres has been found. Another view is that it is due to an inborn error of metabolism comparable to porphyrinuria congenita. No treatment is of any avail, except that protection from trauma should be ensured as far as possible. The bullæ, when formed, should be dressed with a mild antiseptic paste.

HYPERKERATOSES OF THE SKIN

CALLOSITIES AND CORNS

These are produced by friction and pressure.

A *callosity* consists of a hypertrophy of the horny layer of the epidermis, and is familiar on the ball of the great toe, the heel, the hands of the working man, of oarsmen and others, the tips of the fingers of those who play the violin, etc.

The *corn* (clavus) is a local thickening of the epidermis resulting in a conical downgrowth, which presses upon the subjacent papillæ, causes their atrophy, and sets up inflammation and hypertrophy in the surrounding papillæ. Corns are common, as is well known, on the toes, especially the outer side of the little toe, the dorsum and the sides of the other toes. The pain of the ordinary corn is largely due to the little plug being driven down on the cutis beneath, but spontaneous shooting pain is often present. When the corn lies between the toes and is kept constantly moist, the thickening is less marked; but the inflammation is more obvious, and the part is often extremely tender (*soft corn*). Occasionally corns will inflame and ulcerate, or a cyst or bursa forms under the corn, constituting a *bunion*.

Treatment. Corns may be cured, and almost entirely prevented, by the use of properly shaped boots. The sole should be as large as, or slightly larger than, the sole of the foot as it shapes itself in the standing position with the weight of the body upon it. If the boot sole is narrower than the sole of the foot, the upper leather will be in close contact with the edge of the foot in any movement, and constant friction will be the result. The inner edge of the sole should be straight, and pointed boots should be strictly avoided. If corns have formed, they must be treated by soaking in hot water, and shaving with a sharp knife or razor, when the dry white plug will be met with and can be removed. A corn plaster may then be worn, or the toe may be simply strapped with a good linen plaster, by which, with properly constructed boots, the friction will be reduced to a minimum. Soft corns may also be carefully shaved, and pressure removed by cotton wool between the toes, or by a turn or two of narrow strapping below

the corn. The thickened epidermis may also be removed by the application of salicylic acid, either as a 5 per cent. ointment, or as plaster, or in solution in collodion (℥j to ℥j). The tender part may be benefited by the use of alum or tannic acid lotions. But in all cases a sufficiently broad-toed boot, with a wide sole and a low heel, is the one requirement for permanent relief.

KERATOSIS

Keratosis, or increase of the horny layer of the epidermis, is an essential part of many of the forms of dermatitis already described, such as psoriasis, chronic eczema, and pityriasis rubra pilaris. Increase of the horny layer also results from arsenical poisoning. A rare congenital disease, in which enormous hypertrophy of the horny layer of the palms and soles occurs, is known as *keratosis* or *tylosis palmaris et plantaris*. It may occur through several generations and in members of the same family.

KERATOSIS PILARIS

This condition in its simplest form is extremely common, and may be regarded as a follicular variety of ichthyosis, in which abnormality it is, moreover, habitually present. As in ichthyosis, the parts of the skin affected are those in which the sebaceous and sweat glands are normally less developed and active, and which are consequently drier, namely, the extensor surfaces of the limbs, the calves, the flanks, and outer portions of the thighs. As a rule it is most evident on the extensor aspects of the upper arms and on the postero-external parts of the legs below the knees.

The lesions consist of follicular papules, due to the presence in the infundibular portions of the follicles of horny cones, which are very adherent. The lanugo hairs are atrophied, and traverse, coiled in spiral fashion, the cones. The colour of the affected areas may be normal, but keratosis pilaris is frequently seen in girls with acrocyanosis. In them, as a rule, there is excess of subcutaneous fat on the upper arms, thighs, and legs, and, owing to circulatory stasis, the skin of these parts, particularly on the extensor surfaces, is bluish-red, and studded with the horny plugs, around each of which is a bluish halo.

Keratosis pilaris may appear at an early age—two or three years—but is most marked in adolescence, tending to diminish or disappear in adult life. In the affected follicles the sebaceous glands and lanugo hairs ultimately atrophy completely, and the lesions are succeeded by punctiform scars.

Ætiology. Like ichthyosis, the condition is congenital and familial, and is by far the commonest variety of the inborn dyskeratoses.

Treatment. Thorough inunction with ℞. acidi salicylici gr. 15–25. glycerini amyli ℥ 2½, paraff. moll. alb. ℥ 2½, adip lanæ hyd. ad ℥ 1 will improve the roughened appearance and texture of the skin. Thyroid gland, with or without an active ovarian extract, is indicated in some cases.

Keratosis Pilaris Atrophicans. *Kératose Pilaire Rouge Atrophiante* (*Brocq*), *Ulerythema Ophryogenes* (*Taenzer*). A more severe form of keratosis has been variously labelled by different observers. It involves the eyebrows, particularly their outer halves, the centre of the forehead, the cheeks, and the scalp. The affected parts have a reddish tint, the plugged or atrophied follicular orifices being surrounded by a halo of hyperæmia. In severe cases the scalp may become almost completely bald, and the eyebrows and eyelashes are lost.

Ætiology. Like the ordinary form of ichthyosis and simple keratosis pilaris, the condition is congenital and often familial. Cases have been recorded in which one or other parent was ichthyotic.

Keratosis Follicularis (*Darier's Disease*). This rare condition, first described by Darier in 1889, is a form of dyskeratosis, characterised by a peculiar type of degeneration of the epithelial cells, which occurs chiefly in the upper

third of the pilo-sebaceous follicles and of the sweat ducts. The same kind of cellular degeneration is also seen in Paget's disease of the nipple, and the so-called pre-cancerous dermatosis of Bowen. Briefly, the essential lesions are papules, covered by brownish crusts, situated in the dilated orifices of the pilo-sebaceous follicles and sweat ducts, and on the intervening skin. The crusts tend to become confluent, and to form verrucose patches. In the folds and joint flexures there may be vegetations, which become moist, often periodically, and emit a foul smell.

Except in the very rare instances in which the eruption is unilateral and has a segmental distribution, like a nævus unius lateralis, the lesions are bilaterally symmetrical, and the sites of election are the face, particularly the temples and naso-labial folds, the scalp, the aural conchæ, the pre-sternal and interscapular regions, the waist-line, and joint-flexures, but other parts may be affected. On the dorsal surfaces of the extremities there may be lesions resembling flat-warts, and there is often a punctate keratosis of the palms and soles. The *mucous membranes* of the mouth, including the tongue, pharynx, œsophagus, and rectum may be involved.

As a rule the disease appears first in early life, but the onset may be delayed until middle-age or even later. It progresses rapidly for a while, and then remains stationary.

Ætiology. It is familial and hereditary in about 50 per cent. of cases, and may appear in two or more generations. Other defects, physical and mental, may coexist with it.

Morbid Anatomy. There is hyperkeratosis, and hypertrophy of the rete Malpighii. The characteristic dyskeratotic cells—" corps ronds " and " grains," —which Darier at first mistook for parasitic psorosperms, are seen in the rete and stratum corneum.

Treatment. Ointments or pastes containing keratolytics, such as salicylic acid and resorcin, are helpful. Striking improvement has been effected by the judicious use of the X-rays, and more recently by the Grenz-rays.

CORNU CUTANEUM

Horny growths, sometimes several inches in length, and generally twisted or bent, have in rare cases been seen. They are, as a rule, solitary. They consist of accumulated epidermic layers on a base of hypertrophied papillæ.

The **Treatment** consists of removal and cauterisation of the base.

ICHTHYOSIS

The term ichthyosis has been loosely applied to include a number of distinct conditions, all of which may be regarded as congenital dyskeratoses, but which differ as regards their distribution, severity, and mode of inheritance (**54**). Here only the common form (*Ichthyosis vulgaris, simplex*, or *nitida*) will be described. In this condition the skin is abnormally dry and covered with scales, which vary in size according to the severity of the abnormality. The parts chiefly affected are those in which the sebaceous and sweat glands are normally least active, namely, the extensor surfaces of the limbs, particularly the elbows and knees, and to a less extent the trunk, face, scalp, and extremities. The joint-flexures and natural folds, on the other hand, are hardly or not at all affected. The palms and soles have usually a characteristic appearance in that the finer lines are obliterated and the deeper ones much exaggerated. The nails are dry and brittle, the scalp is scaly, and the hair thin and lustreless. As might be expected the secretion of sebum and sweat is deficient on the affected areas, and many ichthyotics suffer considerable discomfort owing to their inability to perspire during vigorous exercise. Moreover, the lack of fat renders the ichthyotic skin extremely susceptible to the action of defatting agents, such as

alkaline soaps, soda, and hard water, so that chapping, fissuring, and eczematisation of the hands and wrists is very common in these subjects.

Although not apparent at birth, ichthyosis usually manifests itself in early infancy, and becomes more marked up to the age of about ten years. There may be some improvement at puberty, but it persists throughout life. It is frequently associated with the allergic triad of symptoms—infantile eczema, the prurigo of Besnier, and asthma. Cockayne suggests that ichthyosis and a liability to these allergic symptoms are due to independent genes lying in the same chromosome, and that there is linkage between them.

Morbid Anatomy. The horny layer is thickened and the rete Malpighii thinned. The stratum granulosum is diminished or absent. The sebaceous glands are few and small, but the arrectores pilorum are hypertrophied. Various changes in the sweat glands and ducts have been described.

Ætiology. Ichthyosis is hereditary and familial, but often skips a generation, and single cases are met with. Studies of the basal metabolic rate have not indicated hypothyroidism, but the therapeutic value of thyroid extract is incontestable.

Treatment. Alkaline soaps and other defatting agents should be avoided. Regular inunctions, at first daily and later two or three times a week, should be given with an ointment containing glycerine of starch, lanoline, and vaseline. Thyroid gland in suitable dosage should be given persistently over long periods with intervals of rest. Sunbathing has a remarkable effect on the ichthyotic skin, and may temporarily render it indistinguishable from the normal. Ichthyotics are almost invariably thin, and benefit from a dietary rich in the fat-soluble vitamins.

ATROPHIC AND DYSTROPHIC CONDITIONS OF THE SKIN

SCLERODERMIA

Sclerodermia may be diffused or circumscribed. In *diffused sclerodermia* there is a general hardening or induration of the skin, which begins most commonly about the face, neck, shoulders, chest, and arms, and may gradually extend to the lower part of the body. A similar condition may begin in the fingers, forming *sclerodactylia* or *acrosclerodermia* (*see* p. 310). There is at first no change in colour, but the skin is hard, rigid, inelastic, and cannot be pinched up into folds. As it progresses the movements of the limbs are hindered, the joints are more or less fixed, the chest is limited in its respiratory movements, and if the face is affected it loses its power of expression; the mouth can be opened with difficulty, but the eyelids often retain their mobility. Subsequently the skin becomes shiny and glossy, irregular patches of pigment appear, and here and there are areas of vascular dilatation, giving a pink or violet colour. The secretions of sweat and sebum are diminished. The course of the disease is slow, and it extends over years, eventually, in many cases, subsiding entirely. During this time the patient's health is practically unaffected, but rheumatism and cardiac troubles have been noted as occasional complications. In the skin itself eczema, erythema, and ulceration may occur.

In some cases, the disease begins with more thickening or œdema of the skin, and this, according to Crocker, tends to result in an atrophied, rigid, tight condition, which is much less liable to spontaneous recovery than the simply indurated forms.

Ætiology. The diffused form is commonly associated with Raynaud's disease. Localised forms have occasionally followed injury, and more general conditions have been attributed to chills, to worry, and to the specific fevers. In recent years it has been regarded by various authors as due to disorders,

whether of excess or defect, in the internal secretions, of the thyroid gland especially, but also of the suprarenals and of the pituitary body.

The disease occurs in young adults and middle-aged persons, less frequently in children, and hitherto not under the age of thirteen months (*see* Sclerema Neonatorum). It is more frequent in women than in men, but little is known of its causes (*see* Ætiology of Vitiligo).

In *circumscribed sclerodermia*, or *morphœa*, there is an asymmetrical patch of 2, 3, or more inches in diameter, frequently corresponding to the distribution of a nerve. For instance, a patch may occur over the distribution of the supraorbital nerve on the forehead; the trunk near the breast and the limbs are also common places for the eruption. The patches are irregular in shape, or may be in the form of bands round or along a limb. They are of a dead white ivory colour, surrounded by a violet or pink zone of dilated vessels. The skin is smooth and dry, and may often be pinched up; it may be level with the healthy skin, or below or above it. The disease lasts several years, and then subsides and disappears, or it may extend into the diffused form, or persist in an atrophic condition. Circumscribed sclerodermia is also more common in women than in men, and can sometimes be referred to local irritation as a cause.

Anatomy. The epidermis is unaffected except for some pigment in the rete; there is a considerable overgrowth of connective tissue in the corium and subcutaneous tissues; the deeper vessels are surrounded by numerous leucocytes, and the superficial vessels are often contracted and empty. Leucocytes also surround and may obstruct the sweat gland ducts, and the muscular fibres of the skin are hypertrophied.

Treatment. Very little can really be done in this disease. The patient should be kept warm at all times, and tonic remedies should be given. Locally emollient applications and friction, and shampooing to restore the circulation in the skin, and galvanism may be employed. The use of thyroid extract and the application of X-rays have been followed by improvement.

Sclerema Neonatorum. This is a peculiar induration of the skin, which is either congenital or appears shortly after birth in feeble infants with deficient circulation. It may begin in the lower extremities and spread to the rest of the body, or it occurs in scattered patches on the thighs, buttocks, trunk, arms, and cheeks. The affected parts feel quite hard and firm, suggesting that the subcutaneous tissue has been frozen. The patches have a well-defined edge, are slightly raised above the surface, and sometimes have a bluish-red colour. They only pit after very prolonged pressure. The children are cold and drowsy, with small pulse and feeble respiration. They often die from collapse or diarrhœa, but occasionally recover. The cause of the change is not well understood.

It may be confounded with a true *œdema*, which occurs in similar circumstances. Œdema affects mostly the dependent parts; the skin is blue and mottled, can be pinched up from underlying structures, and pits readily on pressure.

Treatment. The child should be kept warm and efficiently fed, by a nasal tube if necessary.

Besides senile atrophy, in which the skin becomes dry, inelastic, wrinkled and often pigmented, the following conditions may be described as atrophy of the skin.

Atrophodermia Neuritica. This, the "glossy skin" of Paget, follows upon neuritis and other lesions of the nervous system. It is especially well seen in the fingers, of which the skin becomes smooth, shining, dry, the colour pink or red, the whole finger tapering, and the nails curved longitudinally and transversely. With this is a severe and persistent burning pain.

STRIÆ ET MACULÆ ATROPHICÆ
(*Atrophodermia striata et maculata*)

Striæ atrophicæ are translucent, scar-like lines in parts of the body which have undergone considerable distension, such as the abdomen after pregnancy (*lineæ*

gravidarum, lineæ albicantes), the breasts after lactation, the abdomen, thighs, legs, and arms after extreme anasarca, and the shoulders, breasts, and thighs, from obesity or the presence of more localised fatty tumours. The lines are from 1 to 3 or 4 inches in length, tapering to a point at each end; they are slightly depressed below the surface of the healthy skin, but in the event of œdema or anasarca occurring in the part they project beyond it. A similar change may occur in the skin without any preceding distension, and this most commonly during some prolonged and prostrating illness, such as typhoid fever. It is then seen mostly about the buttocks, thighs, knees (*lineæ patellares*), and ankles; and the atrophic lines may be associated with circular spots, or *maculæ*, varying from $\frac{1}{8}$ inch to $\frac{1}{2}$ inch in diameter. In all these cases the skin is really atrophied, and the elastic tissue disappears; the epidermis is thinned, the papillæ are small or absent, and the subcutaneous tissue and glands are atrophied. But an early vascular, or inflammatory, or even hypertrophied, condition has been observed in the cases not related to distension; and in them the action of toxins is invoked as an explanation.

Xerodermia Pigmentosa (*Kaposi's Disease*). This is a remarkable and rare disease, which consists of combined atrophy of the skin, increased pigmentation, telangeiectasis and later the growth of malignant tumours. It occurs equally in males and females, and has a tendency to affect members of the same family without being actually hereditary. Although the racial incidence is wide, it is commonest in Jews, and in a high proportion of cases there is consanguinity of the parents (**54**). It begins in childhood, and generally in the summer-time, with pigment spots, or with erythematous spots, which soon fade into pigment. These form over the face, neck, scalp in the temporal region, outer side of the arm and forearm, and back of the hand. The pigment spots afterwards become atrophic, and patches of white, depressed, shrunken skin form among them. These white spots are slightly contracted, and difficult to pinch up; and subsequently sufficient tightening of the skin may occur to depress the eyelids, and set up conjunctivitis. On the atrophic area there occur pink spots of dilated vessels, which gradually enlarge. The disease may remain stationary for a long time, and may never spread to other parts of the body; but eventually warty growths develop out of either the dilated vessels or the pigment spots, and these subsequently grow into tumours of an epitheliomatous nature. These fungate, discharge or bleed; and, other tumours forming in remote parts of the body, the patient is carried off by exhaustion.

Treatment can do little for this disease. As it is thought that exposure to the sun has something to do with the development of the disease, it is advisable to protect the face by thick red veils or by local applications. New growths may be excised as they arise, or be treated with radium or X-rays.

Kaposi described a *xerodermia albidum* (atrophodermia albida, Crocker) affecting the leg from the thigh downwards, and sometimes the arm down to the hand, in which the skin is atrophied and then stretched. It begins in early childhood and remains stationary.

ALTERATIONS OF PIGMENT

Increase of pigmentation is a frequent result of intense or persistent hyperæmia, through which, no doubt, there is extravasation of hæmoglobin, but the links between this and the increase of the pigment naturally in the deepest layers of the epidermis are still obscure. The most familiar instance is exposure to the sun or to the wind; but in the foregoing sections it will have been noticed how frequently pigmentation is said to follow upon the different forms of dermatitis —for instance, eczema, erythema, pemphigus, lichen, and psoriasis; to these may be added erysipelas, syphilitic eruptions and ulcerations, and especially old-standing ulcers from varicose veins in the lower extremities. The application

of blisters and mustard plasters is often also followed by staining, a fact which should make one careful how one orders these counter-irritants to the neck or arms of ladies. Another common traumatic cause of increased pigmentation is the scratching which is indulged in to relieve pruritus, especially that which results from severe prurigo, or from the presence of pediculi.

Some disorders of the skin in which hyperæmia is not a marked feature are also accompanied by pigmentation, such as sclerodermia, Kaposi's xerodermia, and leucodermia, which will be described presently. As a result of internal disease, we see pigmentation of an extreme form in Addison's disease, to a less extent in some cases of lymphadenoma, in the carcinomatous cachexia, in malaria, in Graves' disease, in rheumatoid arthritis, and in some cases of tuberculosis, of diabetes, and of cirrhosis of the liver. Interference with the solar plexus has been suggested for its origin in lymphadenoma and in Addison's disease, but toxic causes are highly probable in many of the above and in some other disorders, such as chloasma uterinum; and pigmentation is well known as a result of the internal use of arsenic. It is not common to employ any special name, but the terms *melanodermia*, *melasma* (melasma suprarenale) and *chloasma* (from χλοάζω, I am pale green) have been used in different instances. In all the cases which are due to a removable cause, the pigmentation will, in its absence, eventually disappear; on the other hand, it persists in incurable cases like Addison's disease, and increased pigmentation coming on in old age does not, of course, undergo any improvement. Local collections of pigment occur, as pigment moles and pigmented warts. The special forms to be here described are lentigo or ephelis, chloasma uterinum, and ochronosis.

Deficiencies of pigmentation are seen in albinism and leucodermia.

LENTIGO

(*Ephelis, Freckles*)

Yellow, orange, or yellowish-brown maculæ appear on the face, neck, forearms, and backs of the hands, from exposure to the sun under certain conditions. They are most marked during the summer-time, and fade or entirely disappear during the winter; they are first seen about the age of late childhood, and rarely in advanced life; and they affect especially people with fair hair and blue eyes (xanthochroic type).

Treatment. As a rule freckles are better left alone; they can, however, be removed by touching them with pure carbolic acid on a sharpened match-stick.

CHLOASMA UTERINUM

The pregnant state, as is well known, is commonly accompanied by an increased pigmentation of the nipples, axillæ, and the line between the umbilicus and the pubes. In some women, in these circumstances, a broad band of pigment forms on each side of the forehead, just below, but not touching, the margin of the scalp. It is narrower in the middle line, widens out as it reaches the temple, and may extend over the zygoma on to the cheek; it is continuous, or broken into separate small patches. The colour is yellow or brown. With it may be associated the familiar dark ring round the eyes. This frontal chloasma sometimes recurs with each successive pregnancy, and disappears with delivery. It may be due to other uterine disturbances—*e.g.* dysmenorrhœa—and sometimes no cause can be traced.

Treatment. Mercury perchloride has been most used locally, in a solution of the strength of 1 or 2 grains to an ounce of almond emulsion, applied twice daily until the skin is reddened. Zinc ointment may then be applied. Solutions of citric acid, carbolic acid, and other mild caustics, by which the epidermis is removed, and with it the pigment, have also been used. But the colour is likely

to recur. Crocker recommended salicylic acid paste, or plaster, or a saturated solution of the acid in alcohol kept on for some hours.

Ochronosis. Virchow gave this name to a rare condition, in which there is a black pigmentation of the skin, cartilages, and sclerotics; but whereas in these cases the cartilages have been constantly stained, the skin has been affected in only a few instances. The face is of coal-black or dark brown colour, darker than that of Addison's disease; the hands may present bluish-black areas, and patches have been seen on the mucous membrane of the lips. A black patch is seen in the sclerotics on each side of the cornea, midway between it and the canthus. The change in the cartilages is clinically observable in the ears, which have a bluish-grey colour, due to the blackened cartilage being seen through the thin skin; but *post mortem* the rib cartilages and the intervertebral, sterno-clavicular, laryngeal, and tracheal cartilages have been found of jet-black or inky black colour.

Some tendons have been smoky brown in colour, and the cardiac valves and chordæ tendineæ discoloured in patches. The pigment is deposited in the matrix of the cartilages and in the fibrous tissue of the corium of the skin.

Some of the cases have been associated with *alkaptonuria* (*see* p. 510), and a few with carboluria after the constant application of carbolic acid to chronic ulcers for many years.

Albinism. This is a congenital deficiency of colour, not only in the skin, but also in the hair and in the iris and choroid. It is at once recognised by the white hair and the pink eyes; and there is commonly intolerance of light (*photophobia*), and it may be nystagmus, from the want of pigment in the fundus of the eye. It occurs in dark races as well as in the pale-faced, and in various animals—cats, mice, and others.

VITILIGO (*See Plate 65, C*)

(*Leucodermia*)

Vitiligo is an affection of the skin characterised by the depigmentation of certain areas and increased pigmentation of the zones immediately surrounding them. It is acquired, and must be distinguished from congenital leuco-melanodermia, which is nævoid in origin. The depigmented areas are milk-white in colour, oval or irregular in shape, and of varying size; their margins are sharply demarcated from the neighbouring hyperpigmented parts, the colour of which is usually of greater intensity at the edges of the white patches, fading off gradually at the periphery into the normal skin. The hairs covering the white patches may be also depigmented, or of normal colour. The pigmentary change is preceded by a transient erythema, such as is also seen in alopecia areata and circumscribed scleroderma.

The *Distribution* tends to be markedly symmetrical, and the backs of the hands, wrists, forearms, face and neck, the loins and genital organs are most frequently affected. The *evolution* appears to vary in different cases. The onset may be sudden or gradual, and the pigmentary change may slowly extend or remain stationary for years. Sunlight renders it more obvious by causing increased pigmentation of the dark areas, and thus accentuating the contrast. Partial recovery is common, but complete restoration of the skin to normal is rare. Sometimes the depigmentation becomes almost generalised.

Ætiology. Vitiligo is rare in very young children, and is seen chiefly in youth and middle age; it is commoner in the female sex. It is associated with Graves' disease, alopecia areata, scleroderma, or circumscribed prurigo in a considerable percentage of cases, and also with organic diseases of the nervous system, such as tabes, syphilitic meningo-myelitis, subacute combined degeneration of the cord, and involvement of the spinal cord or nerve-roots secondary to tuberculous caries, osteoarthritis of the vertebral joints, and spina bifida. A

familial incidence is not uncommon, as in alopecia areata. There would appear to be no doubt that both these conditions and scleroderma are dependent on involvement of the sympathetic nervous system; this view, which is supported by experimental evidence, explains the frequency of their association with Graves' disease, and the influence of shock and worry as provoking factors. The sympathetic may be involved by organic central nervous disease, or more commonly by acute or chronic infection. During the war the writer (**28**) observed several cases in which vitiligo was apparently provoked by pediculosis corporis; and the leucodermic patches tended to appear first on the sites of election of pediculosis, viz., the shoulders, sacral region and thighs. Whether the venom of the lice or the long-standing peripheral irritation was responsible is uncertain. Vitiligo is usually seen in persons who have several pigmented moles of varying size. The moles are often surrounded by a halo of depigmentation (leucoderma acquisatum centrifugum (**62**)).

Anatomy. Histological examination shows absence of pigment in the white patches, whereas there is excess in the epidermis and dermis of the surrounding dark areas.

Treatment. This must necessarily depend on complete investigation of each individual case. A search should be made for evidence of organic nervous disease, of syphilis, and of chronic focal infection. It has been shown that repeated exposures of the affected skin over a long period to sunlight or the carbon arc light rays will gradually restore pigment to the white areas, particularly if certain essential oils, such as oil of bergamot, which sensitise the skin to light, be previously applied.

Acanthosis Nigricans. This rare condition is of importance owing to the fact that in the majority (about two-thirds) of cases it is associated with abdominal cancer. It is characterised by: (1) diffuse papillomatosis, chiefly of the natural folds of the skin; (2) the occurrence of scattered warty lesions, which may be discrete or confluent; (3) increased pigmentation, most evident in the folds and flexures. The sites principally involved are the axillæ, the neck, the groins and internatal cleft, the umbilicus, the antecubital fossæ and popliteal spaces, the areolæ of the nipples, the submammary and hypogastric folds, the face, and the backs of the hands and feet. Diffuse warty lesions may occur on the vermilion borders of the lips, on the eyelids, in the external auditory meatuses, and on the vulva and vagina, and scattered papillomata, closely resembling ordinary warts, may be present almost anywhere on the surface of the skin. The papillæ of the palms and soles are also hypertrophied, and the tongue may have a villous appearance from a similar change. The skin as a whole may be darkened from increased pigmentation, but this is most intense in the joint-flexures and natural folds. In contrast with Addison's disease, the mucous membranes are not pigmented. Changes in the nails and alopecia may occur. The patients usually complain of itching, which may be intense.

Morbid Anatomy. Histologically there is seen papillomatosis with acanthosis, and increase of pigment, varying in degree according to the site.

Ætiology. Two types of the disorder are recognised—the adult and the juvenile. The fully developed form in adults is probably always due to malignant disease, but the writer has seen what may be called a *forme fruste* after shock or a long period of worry. In the malignant cases there is usually extensive involvement of the abdominal viscera and peritoneum. The primary growth is probably more often in the stomach than elsewhere, and the writer has seen three cases in which it was of the "leather-bottle" type. But it may be in the intestine, breast, uterus or elsewhere. In one case the condition disappeared after the removal of a deciduoma malignum. It has been suggested that it is direct involvement of the abdominal sympathetic and suprarenal glands by malignant growth that brings about the peculiar changes in the skin, but it is also possible that cancer cells produce a toxin which acts on the endocrine-sympathetic

system. In the juvenile form the symptoms are less marked and tend to remain stationary. They would appear to be due to suprarenal dysfunction, and other endocrine disorders may be present. Cases have been described in association with obesity, and this association may be familial. In other familial cases there has been a syndrome of acanthosis nigricans, severe diabetes mellitus, infantilism, imbecility, hypertrichosis lanuginosa, and cutis verticis gyrata, thus indicating multiple abnormalities of the endocrine glands.

Treatment. Nothing, as a rule, can be done for the adult cases, since the malignant disease is usually far advanced and inoperable. Improvement has been noted in some juvenile cases under thyroid medication.

AFFECTIONS OF THE SWEAT GLANDS

ANOMALIES OF SECRETION

Anidrosis, or deficiency of perspiration, is seen in fevers, in diabetes and in some diseases of the skin—*e.g.* ichthyosis and pityriasis rubra.

Hyperidrosis, or excess of perspiration, may be general or local. General sweating results from dilatation of cutaneous blood vessels, as after exercise, or from emotional causes. Sometimes, on the other hand, it occurs with contracted vessels, as in conditions of collapse or fear. General perspiration has been mentioned in connection with malaria, phthisis, pyæmia, and the crisis of acute illnesses. Local excess of sweating occurs from emotional causes and in rickets. A very troublesome form of excessive sweating is found about the hands and feet, axillæ, and genitals in some persons without any adequate cause. Some such sufferers are in deficient general health, but others are perfectly well.

The local application of belladonna liniment or the use of atropine of belladonna internally should be tried. A drop dose of liquor atropinæ will sometimes stop the sweating of phthisis for two or three successive nights. Profuse local sweating of the axillæ, and palms of the hands, has been successfully treated by the Röntgen rays. It may be also treated by the methods used for the next complaint.

Bromidrosis. This is often associated with hyperidrosis—that is, the sweat is both offensive and excessive. The experiments of Benians suggest that the odour, which resembles that of atrophic rhinitis, is due to the decomposition of keratin by staphylococci in alkaline sweat. A similar odour can be produced *in vitro* by incubating staphylococci with horn-shavings in an alkaline medium. It is not uncommon in young men or young women of the domestic class, and it may be quite independent of the general health. Thin has described a bacterium in connection with it—*Bacterium fœtidum*. It is essential to wash the feet thoroughly and frequently, and use astringents and antiseptics. The socks may be dusted inside with finely powdered boric acid, and should be frequently changed, or with a mixture of salicylic acid 3 parts, starch power 10, and talc 87 parts ; or the feet may be painted with a 5 per cent. solution of chromic acid, or smeared with a salicylic ointment of 2 per cent. strength, or an ichthyol ointment of 5 per cent. strength. It has been also recommended to spread glycerine or a solution of glucose over the soles of the feet, and over the toes, before the socks are put on in the morning, and to repeat this every morning as long as required. A cure may take place in three days (Benians). The rationale of this method is that the staphylococci produce acids when growing in glycerine or glucose, and the acid medium thus created prevents the decomposition of keratin.

Chromidrosis (*Coloured sweating*). Many of the reported cases are suspect, the discoloration being sometimes feigned and sometimes due to dye dissolved out from a garment by the sweat. Some apparently authentic cases have, however, been recorded. Blue coloration has been ascribed to pyocyanine, derived from the active growth of the *B. pyocyaneus*, and to indican. Red coloration, which is seen principally in the axillæ, is usually, at any rate, due to lepothrix (q.v.).

Hæmatidrosis, or sweating of blood, is of very doubtful occurrence.

Uridrosis is the name given to some cases in which the sweat has crystallised on the surface, and the crystals have been found to contain urea and salts.

MILIARIA

This name is given to rashes determined by profuse secretion of sweat, such that it is unable to escape by the ducts, and either raises small vesicles in the epidermis or sets up a local inflammation.

Miliaria crystallina or ***Sudamina.*** In this form there are small transparent vesicles, not larger than a pin's head, due to the elevation of the most superficial layer of the epidermis by accumulated sweat. They are found most abundantly on the chest and abdomen, but from their perfect transparency may be better felt than seen. The vesicles dry up, and leave a few branny scales, the remains of the detached epidermis. They are most common in phthisis and in enteric fever.

In ***miliaria rubra*** (q.v.), there are vesicles produced in the same way, but accompanied by inflammation. They are surrounded by a red areola, and contain a yellow, turbid alkaline fluid or actual pus.

AFFECTIONS OF THE SEBACEOUS GLANDS

Milium. This is a small bright, white, round tumour, the size of a pin's head or slightly larger, which results from dilatation either of the sweat-ducts or of the pilo-sebaceous follicles. Such little tumours are seen on the forehead, eyelids, cheeks, and genitals. Occurring in children, they were formerly called *strophulus albidus*. Sometimes they are met with in great numbers on thin cicatrices, especially those of epidermolysis bullosa. The contents are cholesterin and fatty material. When occurring in scars, they are of the nature of retention-cysts ; in other cases they are cystic nævi. They can be treated by puncturing the skin and squeezing out the contents.

Adenoma Sebaceum. This is really a mixed tumour, consisting partly of an overgrowth of the sebaceous glands and partly of vascular new growth (angioma). The tumours are of small size, being seldom larger than a pea. They occur chiefly on the nose, especially the alæ, on the adjacent portions of the cheeks, on the centre of the forehead and upper lip, and more rarely as isolated lesions on the scalp and neck. As a rule their distribution is symmetrical. Their colour varies from brown to light red, according to whether the sebaceous or the vascular overgrowth predominates. Frequently sebaceous adenomas are associated with pigmented moles, telangiectases, and patches of pigment on other parts of the body, and they occur most frequently, but not always, in persons of defective mental development, epileptics, and idiots. Though of congenital origin, the tumours do not as a rule appear until some years after birth.

Treatment. The tumours can be removed by the cautery or electrolysis, and the larger ones may, if necessary, be excised or curetted out.

SEBACEOUS CYSTS

(*Wens*)

These are retention cysts arising from obstruction to the ducts of the sebaceous follicles. They are most common on the scalp, but occur on the eyebrows, face, or neck, and more rarely on the trunk or limbs. In size they vary from that of a pea to that of a nut or an orange. They are hemispherical, or more globular, uniform and smooth. The skin looks thin, and often presents well-marked vessels ramifying over it. The contents are semi-fluid or pasty, and consist of animal fats, albumin, epidermic cells, cholesterin, and earthy salts enclosed in a capsule made up of layers of epithelial cells and fibrous tissue.

The **Treatment** consists in incising the cyst, squeezing out the contents, and tearing out, or dissecting out, the cyst wall entirely; or the interior may be swabbed with pure carbolic acid.

AFFECTIONS OF THE HAIR AND HAIR FOLLICLES

Excessive development of hair—hirsuties or hypertrichosis—is common and is the cause of much distress in some women. It may be a congenital or familial characteristic, but in females may result from adenoma of the suprarenal cortex or basophil adenoma of the pituitary, or be one of the symptoms of virilism induced by a hypernephroma. In the latter case successful removal of the tumour is curative. For a full discussion of the ætiology and treatment of hirsuties reference should be made to special text-books. Deficiency or falling of the hair, known as *alopecia*, is exceedingly common. The following three conditions are quite rare: *trichorrhexis nodosa*, in which some of the hairs are found to present little nodules or thickenings due to the splitting up of the cortical fibres; it is usually caused by the defatting action of alkaline soaps and spirit shampoos; *monilethrix*, in which the hair looks beaded, and breaks readily at the internodes, so that it is only 2 or 3 inches long all over the head; and *lepothrix*, in which the hairs of the axilla, scrotum and perineum are brittle, and present irregular masses on and around them, consisting of clumps of bacteria enmeshed in a homogeneous viscid substance.

The most common *change of colour* in the hair is that known as *canities:* the hair gets successively grey and white. This is a senile change which may occur prematurely. But occasionally sudden whitening of the hair occurs after fright, intense emotion, or in consequence of neuralgia, and localised or even more or less generalised calvities may be part of vitiligo or a sequel to alopecia areata. The decoloration of the hairs has been ascribed to the presence of air-bubbles in the hair-shaft, but is probably due, as a rule, to the absence in the hair-roots of the ferment responsible for the production of pigment. The colour sometimes returns spontaneously, but nothing can be done for it.

Of the above ailments *alopecia* will be more fully described.

ALOPECIA

In dermatology the word *alopecia* is employed indiscriminately to designate fall of hair (defluvium), from whatever cause arising, the denuded areas that result from it, and even congenital absence of hair. It is derived from ἀλώπηξ, a fox, probably owing to the loss of hair in patches that occurs in this animal during the seasonal change of coat.

The following classification is arranged on an ætiological basis:—

Alopecia universalis. (*a*) Congenital.
(*b*) Acquired (generalised form of alopecia areata).

Regional and Diffuse Alopecia

I. Congenital forms.
II. Acquired forms.

(1) *Traumatic, e.g.*, from friction, and from pulling of the hair (trichotillomania).
(2) *Alopecia symptomatica.*
(*a*) After acute infections, *e.g.*, erysipelas, typhoid fever, pneumonia, influenza, tonsillitis, eruptive fevers, etc.; and in the secondary stage of syphilis.
(*b*) After surgical operations, childbirth, severe accidents, shock, and anxiety.

(*c*) In association with chronic diseases, *e.g.*, anæmia, diabetes, cancer, leukæmia, mycosis fungoides, tuberculosis, and other chronic infections; endocrine disorders, *e.g.*, myxœdema, Graves' disease, ovarian diseases, the menopause, and castration in the female.

(*d*) After the administration of chemical poisons, particularly thallium acetate; and metallic salts, *e.g.*, of gold, arsenic, and bismuth.

(*e*) In association with certain skin diseases, *e.g.*, generalised exfoliative dermatitis, eczema, widespread ringworm.

(*f*) Senile alopecia.

(*g*) After the application of X-rays.

(3) *Calvities* or *Alopecia prematura idiopathica* (male or seborrhœic form of alopecia).

(4) *Diffuse Alopecia Areata.*

Circumscribed Alopecia.

I. *Non-cicatrical.*

(1) *Alopecia areata.*
(2) *Localised traumatic alopecia.*
(3) *Alopecia following pyogenic infection*—impetigo, boils, carbuncle.
(4) *Ringworm* (non-suppurative).

II. Cicatricial.

(1) *From injuries, burns, etc.*
(2) *Favus and suppurating ringworm* (Kerion).
(3) *Lupus erythematosus.*
(4) *Lupus vulgaris.*
(5) *Tertiary syphilis.*
(6) *Herpes zoster.*
(7) *Scleroderma.*
(8) *Alopecia cicatrisata* (Pseudo-pelade of Brocq).
(9) *Folliculitis decalvans* (L'acné décalvante of Quinquaud).
(10) *Alopecia in association with Lichen Planus and Lichen Spinulosus.*
(11) *Keratosis pilaris atrophicans.*

Traumatic Alopecia. Alopecia areata, resulting from traumatism, will be described later.

Trichotillomania. By this is meant a morbid impulse to pull out the hair on the scalp, eyebrows, beard, or elsewhere. The hairs may be pulled out entire, leaving bald areas, or may be broken off at various distances along their shafts. It is a neurosis, and may be met with both in children and adults of both sexes. In hysterical girls it may be associated with dermatitis artefacta elsewhere. The denuded or partially denuded areas may be mistaken for alopecia areata or ringworm, but the differential diagnosis is easy. Cases are sometimes met with in which the hair is cut with scissors instead of being pulled. Psycho-analysis and psycho-therapy are, of course, necessary to achieve a cure of this neurosis.

Alopecia Symptomatica. A sudden diffuse loss of hair is most frequently caused by an acute pyrexial disease. Erysipelas in particular, with or without involvement of the scalp, is likely to be followed by a very severe fall, resulting sometimes in almost complete, though temporary, alopecia. In certain epidemics of influenza, such a loss has been a striking sequela (l'alopécie grippale), and a very large number of cases were met with and studied in those of 1918–19.

Apart from acute infections, child-birth, severe accidents, and major operations are often succeeded by a similar type of alopecia. There is an interval of about two to two and a half months (fifty-six to eighty days) between the causative event and the onset of the alopecia. Sabouraud insists that in post-infectional alopecia the temperature must have attained 103° F. or higher during several days, but he does not consider that the pyrexia itself is the direct cause of the

death of the affected hairs. It is probable that an infection of sufficient severity, like child-birth, shock, severe accidents or surgical operations, affects the sympathetic nerve-supply of the hair, and that it is upon this disturbance that the fall of hair depends.

In erysipelas, if the scalp is directly involved, the hair will fall over the affected area in about a fortnight, whereas elsewhere there will be the usual interval of about seventy days before the loss is manifest.

The prognosis in this variety of symptomatic alopecia is uniformly good, and as a rule a complete re-growth of hair occurs.

Syphilis. Syphilitic alopecia may be considered as a variety of that caused by acute infections, but it may present certain features that are pathognomonic. It occurs as a rule during the third month of the disease, corresponding in point of time to the appearance of the roseola ; its onset may be delayed till the fourth and even, it is said, until the sixth month. The fall of hair is sudden and at first diffuse, but small areas almost completely denuded, quickly arise, particularly over the temples and occipital regions, which give to the scalp a " moth-eaten " appearance. This is the " *alopécie en clairières* " of the French, and is characteristic of syphilis. It is probable that these denuded areas correspond to the sites of pre-existing roseolar macules.

The severity of the alopecia varies ; rarely it is so intense as to resemble at first sight a rapidly-spreading alopecia areata, but in this condition there are always present older patches of considerable size, sharply defined and completely bald, such as never occur in syphilitic alopecia.

The fall continues for three weeks, and then declines. Even if the patient remains untreated, spontaneous re-growth of the hair always takes place. Accompanying the alopecia of the scalp, a similar and characteristic fall of hair from the eyebrows is usually seen. As Sabouraud remarks, the appearances are as if the hair had been snipped irregularly with scissors. They are quite distinct from those seen in post-infectional alopecia or in alopecia areata.

Calvities (*Alopecia seborrhœica vel præmatura*). This form of alopecia affects the majority of males sooner or later, and occurs to a less degree and far less commonly in women. A great deal of confusion still exists as to its ætiology, which for the sake of convenience will be considered first.

Ætiology. Calvities must be considered as a secondary sex-characteristic. It may be said that the most virile type of man tends to lose his hair on the vertex of the scalp at the time of sexual maturity, while that on the face and certain parts of the body and limbs grows vigorously. In this connection it is of interest that the ancients represented the satyrs as bald on the head and very hairy on the body. On the other hand it is characteristic of the female to possess a massive growth of hair on the scalp, but (apart, of course, from lanugo hair) none on the face, nor on the body limbs except in the axillæ and pubic region. Between these two extreme types—the most virile man and the most feminine woman—there are many intermediates. It is well known that the effeminate type of man usually has luxuriant hair on the head, a relatively feeble growth on the face, and a smooth hairless skin on the body ; whereas masculine woman tends to develop coarse hair on the face and body, and to have a scanty growth on the scalp. Moreover, at the menopause, when the ovarian secretion diminishes, it is the rule for the scalp to become thinned and for coarse hair to appear on the moustache and beard regions.

This influence of the sexual glands on the growth and distribution of the hair is illustrated by the fact that, as Sabouraud's enquiries revealed, *eunuchs never develop calvities*, a fact that was known to Aristotle, and by cases of virilism occurring in women with suprarenal cortical tumours. In a case of this kind observed by the writer, there occurred amenorrhœa, a rapid growth of a beard and moustache, and a loss of hair on the scalp exactly resembling the usual male type of baldness. After removal of the tumour, normal menstruation was

established, the hair on the face fell off, and a complete regrowth of that on the scalp took place. Unfortunately the growth recurred, and the signs of virilism returned before death.

Association with seborrhœa. Premature baldness in both sexes is associated with seborrhœa, although the converse is not necessarily true. It is therefore common in patients with commencing calvities to find the scalp heavily infected with pityrosporon and consequently scurfy, and the pilo-sebaceous follicles invaded by the acne bacillus. But neither of these organisms is the *cause* of the alopecia. It is true that vigorous local treatment of the scalp in these cases may diminish for a while the loss of hair, but it will never arrest it. A male, whose calvities begins at the age of seventeen, will be inevitably more or less " bald on the top " by the age of thirty, for the earlier the onset the more complete the baldness. After the age of thirty the progress of calvities is much less rapid, consequently, a man, who at thirty still has a considerable quantity of hair on the vertex, is unlikely ever to develop complete calvities.

Heredity. That there is in many cases an hereditary predisposition both to seborrhœa and to calvities is unquestionable. Conversely, certain families appear to be almost immune. Fantham has published the pedigree of a family in which all the males had calvities and transmitted it to all their sons. Cockayne suggests that in the tendency to seborrhœic manifestations the genetic factor is one that determines the development of large and active sebaceous glands, and that it is probably a simple dominant.

Symptoms and Evolution. As already pointed out, the age of onset in seborrhœic alopecia varies, and this is true of both sexes. The following description applies to a male in which it is precocious and severe. In such a case simple dry dandruff (pityriasis simplex) is usually present at the age of eleven ; at thirteen or fourteen seborrhœa is manifest and consequently the scurf becomes greasy (*pityriasis steatoides*), and acne is likely to develop. At seventeen the hair on the scalp begins to fall, while that on the face, body, and limbs tends to grow long and coarse. There is usually sexual precocity and the boy appears older than his years. The fall of hair on the scalp is limited to the vertex, chiefly the temporo-frontal regions and the tonsure. It occurs in paroxysms, followed by periods during which it is much less, but it is always progressive. After a while it will be observed that the denuded temporo-frontal areas tend to extend backwards, separated by a central zone where the hair remains relatively long, and between them and the tonsure is another similar zone crossing the scalp transversely.

With the fall of the long hair a regrowth of new downy hairs appears, but these fall to be replaced by even more delicate and shorter ones, until eventually the affected areas become completely bald. Later, the same process involves the zones which at first were to some extent spared, so that in time the calvities is fully established, the whole of the vertex from the forehead to the occipital region becoming denuded.

During the development of seborrhœic alopecia it will be observed that the pilo-sebaceous follicles of the scalp are enlarged, so as to be visible to the naked eye, and that they are plugged with inspissated sebum, which forms the seborrhœic " cocoons," containing myriads of acne bacilli. As might be expected, comedones often develop on the bald areas.

In women with severe seborrhœa of the scalp a similar loss of hair may occur, but with certain differences of evolution. The loss is more diffuse, although, as in men, it is most evident on the vertex. The occipital region, however, is never affected. Moreover, however severe the fall may be, complete calvities never develops, and some long hair remains all over the scalp. Sabouraud has pointed out that in the later stages, more often in females than in males, a follicular sclerosis may take place, so that many follicles become obliterated.

It will be understood that the foregoing is a description of the evolution of

calvities as seen in severe cases, and that all degrees may be met with according to the individual and to the age. In many men, for example, it may not begin until late middle age, and in women until the menopause.

Treatment. This is most unsatisfactory in both sexes. It is based on an attempt to check the accompanying seborrhœa, but the results are at best only partial and never permanent. At first ointments containing sulphur, oil of cade, salicylic acid, and in dark-haired persons resorcin should be employed, *e.g.*, ℞. Sulphur præcip. gr. 30, Acidi Salicylici gr. 15, Vaselini Alb. ʒ 2, Ol. Cocois Nuciferæ ad. ℥i, Perfume q.s. (Resorcin gr. 10 may be added), or R. Olei Cadini ʒ 2, Sulphur. præcip. gr. 30, Acidi Salicylici gr. 15, Paraffini duri q.s., Ol Cocois Nuciferæ ad. ℥i, Perfume q.s. The ointment should be thoroughly rubbed into the whole scalp on three nights a week, and washed out on the following mornings. Every morning a salicylic lotion should be well brushed in :—℞. Acidi Salicylici gr. 10, Ol. Lavandulæ ♏ 3, Ol. Ricini q.s., Acetoni ʒ 1, Spt. Vini Meth. indust. ad. ℥i. To this Resorcin gr. 10, may be added in dark-haired persons, or euresol pro capillis in others. At the end of a month's treatment, the use of the ointment may be discontinued and a lotion containing perchloride of mercury used daily, *e.g.* ℞. Hydrarg. perchlor. gr. $\frac{1}{6}$, Acidi Salicylici gr. 10, Resorcin (or euresol) gr. 10, Ol. Lavand., ♏ 3, Ol. Ricini q.s., Spt. Vini Meth. indust. ad. ℥i.

Local applications of ultra-violet light to the scalp also have considerable vogue, and may have a temporary effect in stimulating new hair-growth, but their value is certainly greater in alopecia areata. In the writer's opinion no treatment, however assiduously carried out, will prevent the gradual progress of calvities, particularly when it begins in early life.

Alopecia Areata. (***See Plate 59, C, p. 878.***) (*Area Celsi*). This form of alopecia usually begins by the sudden appearance of a bald patch on the scalp, which gradually increases in size. Frequently other patches are discovered soon afterwards either near to or at a distance from the original patch, and by coalescence large areas of baldness may result, or less commonly the hair of the whole scalp is lost. Other hairy parts may be affected, particularly the eyebrows, and the beard region in males, but the disease usually, though not always, attacks the scalp first. Recent patches of alopecia areata are pinker than the surrounding scalp, and on them the orifices of the empty follicles, often filled with sebaceous matter, are clearly visible. Older patches become pale, absolutely smooth, and depressed below the level of the unaffected parts of the scalp owing to the atrophy of the hair. At the edges of a patch, and sometimes all over it, are seen the characteristic "exclamation mark" hairs. These are from $\frac{1}{16}$ to $\frac{1}{2}$ inch in length, and their distal end is frayed out and appears thickened, while the proximal part is very thin and devoid of pigment. On extracting such a hair it will be found to come out entire and without a bulb; *i.e.* it has left its papilla and is in the process of being shed. These "exclamation mark" hairs may sometimes be seen after X-ray treatment has been given for ringworm of the scalp or after the internal administration of thallium acetate for the same purpose, but otherwise they are characteristic of alopecia areata; when, however, the fall of hair has ceased, they may, of course, be entirely absent, and their presence at the edges of the patches is evidence that the disease is still progressing. After a while new hair begins to make its appearance, as a rule in the central older parts of the patches; at first it is fair and downy, but in time it acquires the normal colouring, although in some cases it may return quite white and remain so indefinitely. As a rule, complete regrowth of hair takes place eventually, but there may be a partial return, associated with persistent baldness in certain areas, lasting for years; recurrent attacks of alopecia areata are far from uncommon, and occasionally the hair is permanently lost over part or the whole of the scalp and other hairy regions. The disease is apt to be most persistent in those cases in which a complete band of baldness is formed around the lower and posterior part of the scalp (ophiasis of Celsus).

Alopecia areata may be associated with dystrophy and atrophy of the nails, and also with leucomelanoderma (vitiligo). It also occurs in Graves' disease more frequently than can be explained by mere coincidence. Acute infections such as influenza, erysipelas, scarlet fever, and follicular tonsillitis may not only be followed by a general fall of hair, but also by typical alopecia areata.

Ætiology. At one time alopecia areata was considered to be of parasitic origin and even contagious like ringworm. Jacquet was a staunch opponent of this view, and sought to disprove it by numerous experimental inoculations on himself and others, including those already affected by the disease and therefore presumably predisposed. In not a single instance was an inoculation successful. He championed the trophoneurotic theory, and ascribed the cause in many cases to reflex irritation of the nerves supplying the affected areas by erupting or carious teeth, alveolitis, sinusitis, and chronic naso-pharyngeal infection in persons with an hereditary or constitutional predisposition to the disease. The reported epidemics in schools and institutions, which at first sight appeared to support the parasitic theory, can be explained partly, as Sabouraud pointed out, owing to an error in diagnosis between the bald patches following contagious impetigo and true alopecia areata, and partly owing to the occurrence in institutions or schools of one or a few cases of the latter, and the unconscious or deliberate production of bald patches by pulling out the hair on the part of other children, in order to excite the interest, and perhaps obtain the exemption from work accorded to the genuine cases, as in the epidemics reported by Haldin-Davis.

In discussing the ætiology of alopecia areata the relationship of the disease to vitiligo and scleroderma must be emphasised. The three conditions in fact form a closely-linked triad, since they not only occur together with some frequency, particularly alopecia areata and vitiligo, but because all three are often met with in association with disturbances of the endocrine-sympathetic system—for example, Graves' disease. The following points of similarity should also be noted: (1) All three may occur in a localised or in a generalised form. (2) They may all be seen with the so-called " band " distribution. (3) In the ætiology of all three conditions, one or more of the three factors that are known to affect the endocrine-autonomic system—namely, acute or chronic infections, reflex irritation, and psychical disturbances—appear to be of paramount importance.

The various ætiological factors that appear to be operative in the production of alopecia areata will now be considered.

Heredity. Sabouraud found that 22 per cent. of eighty-one cases stated that other members of their families were affected, and it is certainly quite common to obtain a history of an inherited or familial tendency to the disease. In a family recorded by Poynton, two brothers, a sister, and an aunt all had complete alopecia. Cockayne suggest that there are two factors—an hereditary liability and an environmental one; the former is inherited as a dominant. Dark-haired persons are affected far more frequently than fair, and, according to Cockayne, the genes for the tendency to the disease and the genes for dark pigmentation of the hair are probably carried by the same chromosome.

Age of Incidence. It is rare before the age of three years and after the age of sixty. Sabouraud states that twenty years ago its maximum incidence was between the ages of twelve and fifteen, but that now it is between twenty-two and twenty-four. In women there is a rise in incidence between forty and fifty (*pelade de la ménopause*), and several cases have been recorded after ovariotomy, and in men after castration. *Sex Incidence.* Statistics show that males are affected more often than females in the familial cases, but apart from these, the incidence is about equal in the two sexes. *Syphilis.* Sabouraud in particular has emphasised the importance of syphilis—hereditary more often than acquired—as an ætiological factor. It is in the variety already described as *ophiasis* in childhood and adult life that an inherited syphilitic taint should be suspected. Sabouraud has published many cases in which indisputable stigmata of congenital

syphilis were present, or in which the family history indicated its presence. In some of these, vigorous antisyphilitic treatment was successful in curing a long-standing alopecia. No doubt syphilis may be responsible for some instances of familial alopecia, and, in view of the profound influence that the congenital form of the disease may exert on the endocrine-autonomic system and on epithelial structures, it is to be expected that it should be a factor in some cases.

Immediate Provoking Factors. These may be tentatively classified as follows: (1) *Peripheral irritation.* In this connection the views of Jacquet have already been mentioned. Whitfield published many years ago a series of adult cases, associated with *eyestrain* and headaches, in which correction of the error of refraction led to rapid recovery. The writer believes this to be a rare but established cause. Dore has noted a group of cases in which severe and long-standing irritation from pediculosis capitis preceded the onset of alopecia areata, and these are probably comparable to cases in which *vitiligo* was apparently provoked by pediculosis corporis in the war. (2) *Traumatism.* An occasional cause is an injury to the face or head, of which many cases have been recorded in France. The alopecia usually appears within a few days of the injury, but its onset may be delayed for two months, rarely longer. In one of the writer's cases, a woman who had received a severe scalp injury, the interval was eight days. Another group of post-traumatic cases is of particular interest. The alopecia is a sequel to severe and often multiple injuries to one or more limbs, with fractures and damage to the muscles and nerves, and followed by permanent changes due to involvement of the sympathetic nerve-supply—"glossy-skin," hyperidrosis, and vascular disturbances. In these cases the alopecia does not occur until several months or years after the injury, and this long interval may be explained by attributing the alopecia to an ascending nerve-degeneration, which eventually reaches the sympathetic nerve-centres concerned in the spinal-cord. (3) *Psychical disturbances.* There is no doubt that nervous shock, or a period of acute anxiety and worry are frequent predisposing causes. One of the writer's patients had three separate attacks of alopecia, the first after her mother's death, the second two years later when her father died, and the third after the death of her sister. There was a great increase in the incidence of alopecia areata during the war, both among soldiers on active service and among civilians during the air-raids ("alopecia *air-raider*," as a wag put it). In many cases following a severe shock the alopecia is of the generalised type. The latent period is very short, sometimes only a few days. Symptoms of endocrine-sympathetic disturbance indicative of hyperthyroidism ("basedowism") often accompany the alopecia in patients in which shock or long-continued worry are responsible. Lévy-Frankel and Juster recognise two kinds of alopecia areata; one, endocrine-sympathetic, with altered basal metabolism; the other, vascular-sympathetic, with normal basal metabolism. The former includes the cases in which the alopecia occurs in association with Graves' disease, latent or manifest, and those following shock or psychical disturbances; the latter the true post-traumatic cases. (4) *Acute or focal infections.* Apart from the usual diffuse post-infectional alopecia, already described, alopecia areata may be a sequel to an acute infection, such as erysipelas, influenza, pneumonia, mastoiditis, &c. Many cases have also been recorded in which a long-standing alopecia areata has yielded to the removal of chronic foci of infection in the teeth, nasopharynx or nasal-sinuses. In view of the influence of acute or chronic infections on the autonomic nervous system and endocrine glands—particularly the adrenals and thyroid—one might expect them to be a frequent factor in the ætiology of the disease.

It will be clear from what has been said that alopecia areata must be regarded as a non-specific disease in the ætiology of which various factors may be operative. The writer considers that it should be classed among the allergic group of diseases, with one or other of which it is indeed often associated. As in alopecia areata, a

local or general disturbance of the autonomic nervous system is concerned in the production of all of them, and the same hereditary or familial predisposition is apparent.

Diagnosis. The chief diagnostic features of a patch of alopecia areata are as follows: (1) Its sudden appearance; (2) The great majority of the hairs fall out completely, thus leaving the patch smooth and bald; (3) The presence of exclamation-mark hairs; (4) The absence of cicatrical atrophy.

From *ringworm* it may thus be distinguished by the fact that in the common microsporon infection of the scalp the surface of the patch is scaly, the affected hairs break off but do not fall out, so that the patch is not actually bald, and the hair-stumps are quite different in appearance from exclamation-mark hairs; microscopical examination of them will reveal the characteristic "moth-eaten" appearance, the frayed ends, and the fungus elements. Moreover, examination of the scalp under Wood's light in a dark room will demonstrate the bright green fluorescence of the infected hairs. In endothrix infection of the scalp ("black-dot" ringworm) the diagnosis is more difficult; there is no scaliness and many of the infected hairs break off at the mouth of the follicle and appear as black points, similar to those sometimes seen in alopecia areata. Microscopical examination of the extracted stumps will, however, show the large spores arranged in chains inside the shaft of the hair. From *syphilitic alopecia* the points of differential diagnosis have already been indicated. In the small patches of alopecia that temporarily surround the site of *furunculosis* of the scalp, the presence of the central scar left by the boil is sufficient. In the temporary patches following *impetigo* of the scalp the history of the infection, the presence of a few remaining crusts, and the absence of exclamation-mark hairs will aid the diagnosis. From *post-traumatic scars*, *lupus erythematosus*, *favus*, *pseudo-pelade*, and *folliculitis decalvans* the cicatricial atrophy suffices to exclude alopecia areata.

Prognosis. The majority of cases of alopecia areata recover spontaneously, but relapse is very common. Of grave prognosis are those in which rapid spread occurs until the whole or greater part of the scalp, the face, and the other hairy parts become involved. Nevertheless patients who have had complete or almost complete alopecia for many years occasionally recover.

Treatment. *General.* The treatment to be adopted in a case of alopecia areata must necessarily depend upon a complete investigation of the patient, and on a consideration of the most likely factor or factors responsible. The possibility of an inherited or even acquired syphilitic infection must always be borne in mind. Eyestrain, and the presence of a focal infection in the teeth, nasopharynx and nasal sinuses must be excluded. In many cases enquiry and an examination of the patient will reveal evidence of nervous exhaustion from shock, anxiety, a preceding acute infection, insomnia, or overwork. For these an initial complete rest followed by an outdoor holiday, a generous dietary with extra milk, sedatives, and sometimes judicious psychotherapy are indicated. Small doses of bromide with the glycerophosphates are often of value, *e.g.* ℞. Sodii Bromidi, gr. 5–7, Syr. Glycerophosph. Co. ℥ 1–2, Aq. Chloroformi, ad. ℥ss t.d.s., p.c. ex aqua, or luminal, gr. ¼ t.d.s., may be given instead of bromide. In some cases phosphoric acid and strychnine are more effective in overcoming the feeling of exhaustion of which these patients complain. In women who develop alopecia at the menopause active preparations of ovarian extract by mouth or by injection are worth a trial.

Local. It is very doubtful whether any local measures check the spread of a patch of alopecia, but there is some evidence that irritants which produce hyperæmia stimulate re-growth of the hair. Many such are employed, such as liq. epispasticus, carbolic acid, tincture of iodine, or tincture of cantharides and ammonia. The following is useful: ℞. Acidi Carbolici 1, Acidi Lactici 4. It should be painted on the patch daily until a reaction is produced, and resumed when this has subsided. Ultra-violet light, however, is admittedly more effica-

cious, and local applications, sufficient to provoke erythematous reactions on the patches, should be combined with total light-baths. For resistant patches small stimulating doses of X-rays are sometimes remarkably effective.

NEW GROWTHS IN THE SKIN

Only a small number of these will be here described. For *nævi*, *epithelioma* and *sarcoma* the reader is referred to works on surgery.

FIBROMA MOLLUSCUM

This is a soft, flaccid, wrinkled, often pendulous tumour, consisting of a covering of scarcely altered cutis and epidermis, containing a fibrous meshwork with a variable proportion of round cells and albuminous fluid. The tumours may be very few, or exceedingly numerous; they vary in size from a pin's head to the head of a man, and they occur especially on the trunk. They may apparently be congenital, but are generally first seen in early childhood. According to von Recklinghausen, they are really neuro-fibromas, starting from the fibrous sheaths of the smaller cutaneous nerves, and thence invading the fibrous structures of the vessels, the sweat glands, and the hair follicles. In an allied condition there are no separate tumours, but the skin is thickened and overgrown, or lies in large, loose, overlapping folds (*dermatolysis*). In von Recklinghausen's disease there are multiple neuro-fibromas which may be associated with diffuse pigmentation and pigmented nævoid patches varying in size from mere freckles upwards. The pigmented patches may be present alone. Very occasionally the neuro-fibromas spring from the spinal nerve roots (*see* Plate 65, A and B, p. 968).

Treatment. Removal by the knife is the only possible treatment; but if the tumours are very numerous, only such growths can be removed as are in specially inconvenient positions.

CHELOID

Cheloid is a growth of the skin and subcutaneous tissue, consisting chiefly of dense bands of fibrous tissue, containing in its earlier stages numerous spindle cells. Its more common sites are on the chest, over the sternum, on the mammæ, on the neck, back, lobules of the ears, and on the limbs. It is usually single. It begins as a flat, smooth, pink nodule, which extends laterally to a considerable size and becomes paler in the centre, while the skin around is more or less reddened. After a time bands and ridges, separated by furrows, develop, running in various directions across the tumour and into the surrounding skin. By the slow contraction of these bands much deformity may be caused, and movements of adjacent joints may be seriously restricted. The growth of the tumour is often accompanied by considerable pain and tenderness.

Similar growths not infrequently develop on former scars, such as those of cuts, burns, acne, varicella, vaccination, or small-pox. These have been called false cheloid, but it does not seem that they are essentially different. Cheloid grows slowly, and rarely disappears spontaneously. If removed by a knife or caustic, it almost inevitably returns; but it always remains a strictly local disease, invading neither lymph glands nor viscera.

Treatment. Cure has been obtained by the use of Röntgen rays, and by radium. Small cheloids may be successfully removed by repeated freezing with carbon dioxide snow.

MYOMA, NEUROMA, LYMPHANGEIOMA

These occasionally occur as cutaneous affections.

Myoma occurs in rare cases as multiple small, hard nodules, from the size of a pin's head to that of a pea or bean, on the face, trunk, or limbs. Each is a small

tumour in the corium, consisting of smooth muscular fibres (*leiomyoma*), related, apparently, in some cases to the arrectores pilorum.

Neuroma forms multiple, painful small growths in the course of the nerve fibres of both trunk and limbs.

Lymphangeioma is a rare growth, due to dilatation of lymphatic vessels into visible cysts and overgrowth of the intervening connective tissue. It has been seen in association with ordinary vascular nævi.

XANTHOMA

(*Xanthelasma, Vitiligoidea*)

First described by Rayer as " plaques jaunâtres des paupières " in 1836, this disease was called Vitiligoidea by Addison and Gull, Xanthelasma by Erasmus Wilson, and Xanthoma by W. F. Smith. Three varieties are now recognised, viz., Xanthoma palpebrarum vel planum, to which the term Xanthelasma is by some restricted, Xanthoma tuberosum multiplex, and Xanthoma diabeticorum.

The first is by far the commonest, and occurs, as a rule, in middle life. The lesions consist of sharply defined, yellow patches, resembling chamois-leather, and situated most frequently on the upper lids near the inner canthi. Others may appear on both lids, and by extension may rarely encircle the eyes in confluent sheets. Occasionally the nose, malar regions, the ears, and the nucha may become involved. Increased pigmentation of the eyelids and sometimes elsewhere is usually an associated symptom. Hutchinson noted the frequency of migraine in patients with xanthelasma, and cholelithiasis or more rarely hepatic cirrhosis may be present.

In xanthoma multiplex the lesions are far more widespread, and occur as papules, nodules, infiltrated plaques, striæ, or tumours of considerable size. They are yellow or yellowish-red in colour. Their surfaces may be smooth, furrowed or lobulated. The sites most commonly affected are the joints, particularly on the extensor surfaces of the knees and elbows and on the dorsal and lateral surfaces of the finger-joints. Symmetrical tumours may also occur in the sheaths of the Achilles tendons. On the palms and soles striæ, involving the natural creases and joint-folds, are often seen, and on the buttocks large tumours are not uncommon. It would appear that this distribution corresponds to parts most liable to pressure and friction, but large numbers of lesions of varying size may be widely scattered over the face, neck, trunk and limbs. Apart from the skin, xanthomatosis may affect the mucous membranes of the conjunctiva, mouth, pharynx, larynx, trachea, bronchi, œsophagus, and stomach. Death may result from obstruction of the trachea or main bronchi. The liver may be enlarged as a result of its involvement by xanthomata, and there may be a secondary cirrhosis; the lesions have also been found in the peritoneum, pericardium, and in the spleen, heart, and large vessels. Mitral and aortic incompetence may be caused by endocardial xanthomatosis, and familial instances of this have been described. Diabetes insipidus has been present in some cases, and attributed to xanthomatosis of the pituitary gland.

Xanthoma diabeticorum is a rare form which occurs usually in those who have glycosuria. It appears as yellow conical spots surrounded by a red raised area; these are seen first on the extensor surfaces of the arms, and at the lower part of the back and abdomen, and subsequently in other parts. They often subside rapidly.

Ætiology. Numerous instances of an hereditary and familial tendency to xanthomatosis have been described. Whereas xanthoma palpebrarum occurs rarely before middle-life, the other two varieties may be met with in young children. The cholesterol-content of the blood is usually raised, and the figure may be very high in xanthoma multiplex. It has been shown (**63**), however,

that the formation of xanthomatous deposits depends rather upon an abnormal ratio between free cholesterin and cholesterin-ester, or upon an alteration in the concentration of the phosphatides. These disturbances are revealed by tolerance tests, a cholesterin-fat mixture (5 grms. of cholesterin in 100 grms. of olive oil) being administered, and the quantities of free cholesterin, cholesterin-ester, phosphatides, and of total fat being afterwards estimated in the blood at intervals.

In xanthoma diabeticorum there is usually glycosuria with hyperglycæmia and hypercholesterinæmia.

Morbid Anatomy. In the flat patches the corium shows a newly formed connective tissue, with large round or fusiform cells, often multinucleated, filled with fat granules and closely aggregated fat drops (*xanthoma cells*). The nodules have a similar structure, but the fibrous tissue is more abundant.

Treatment. The smaller lesions of xanthoma palpebrarum may be successfully treated by electrolysis, but large deposits should be excised. Both in this condition and in xanthoma multiplex a low-fat dietary, with exclusion of cholesterol-containing foods, has been prescribed, but the results in the writer's experience have not been encouraging. In xanthoma diabeticorum, however, disappearance of the lesions has resulted under the influence of a suitable diet and injections of insulin.

MYCOSIS FUNGOIDES

In this rare disease, the skin is affected by a number of tumours, the appearance of which is often preceded, sometimes for years, by erythematous, eczematous, or urticarial patches. The tumours vary from the size of a bean to that of an orange, or larger. They are round, oval, or lobulated; the skin is stretched over them, tense and shining; the skin around them is often infiltrated. After a long duration some of them may shrink and disappear, others ulcerate on the surface and form fungating masses, discharging a clear watery serum. In this stage they are generally painless and free from itching or smarting. The disease lasts months or years, but ultimately the health fails, and the results have almost invariably been fatal. The view has been held that the disease is an infective granuloma rather than a sarcoma or a lympho-sarcoma; but no organisms have been found, and the tumours consist of lymphoid cells in a fine stroma of connective tissue. (*Vide also* Premycosic Erythrodermia.)

Treatment. Great improvement, though sometimes only temporary, has been recorded from the use of Röntgen rays.

REFERENCES

1	U. J. Wile and L. B. Kingery ..	1919	*Journ. Amer. Med. Assoc.*, 970.
2	C. Levaditi, P. Harvier and S. Nicolau	1922	*Ann. Inst. Past.*, **36**, 63, 105.
3	R. T. Brain	1936	*Brit. Journ. Derm. and Syph.*, **48**, 21.
4	R. T. Brain	1933	*Brit. Journ. Exper. Path.*, **14**, 67.
5	H. Head and A. W. Campbell ..	1900	" Brain," **28**, 353, 523.
6	T. Lewis	1927	" The Blood Vessels of the Human Skin and their Responses," London, 213.
7	R. Sabouraud	1913	*Entrétiens Dermatologiques*, Paris, 28.
8	H. Haxthausen	1927	*Ann de Derm. et de Syph.*, **8**, 201.
9	J. V. Cooke	1926	*Arch. Derm. and Syph.*, **14**, 539.
10	T. H. C. Benians	1915	*Brit. Journ. Derm. and Syph.*, **27**, 394.
11	T. H. C. Benians and B. H. Jones	1929	*The Lancet*, **i.**, 174.
12	R. Sabouraud	1928	*Pyodermites et Eczémas*, Paris, 224.
13	H. Radcliffe-Crocker	1888	" Diseases of the Skin," 1st Edition, London, p. 128.
14	H. W. Barber and J. W. H. Eyre	1927	*Brit. Journ. Derm. and Syph.*, **39**, 485.
15	D. Krestin	1927	*Quart. Journ. Med.*, **21**, 177.
16	R. Sabouraud	1904	*Pityriasis et Alopécies Pelliculaires*, Paris.
17	J. M. H. MacLeod and G. B. Dowling	1928	*Brit. Journ. Derm. and Syph.* **40**, 139.
18	W. N. Goldsmith	1925	*Arch. f. Derm. u. Syph.*, **149**, 575.
19	J. Darier	1928	*Précis de Dermatologie*, 4th Edition, Paris, p. 104.
20	A. Civatte	1924	*Brit. Journ. Derm. and Syph.*, **36**, 461.
21	H. W. Barber, G. L. Attwater and G. Marshall	1921	*Brit. Journ. Derm. and Syph.*, **33**, 154.
22	H. W. Barber and G. B. Dowling	1926	*Proc. Roy. Soc. Med.*, **19**, 33.
23	G. M. MacKee and M. B. Sulzberger	1935	*Arch. Derm. and Syph.*, **31**, 159.
	U. J. Wile and F. H. Graner ..	1935	*Ibid.*, 174.
24	J. Schaumann	1924	*Brit. Journ. Derm. and Syph.*, **36**, 515.
25	J. V. Klauder	1934	*Derm. Wchnschr.*, **98**, 613.
26	E. Bruusgaard	1922	*Brit. Journ. Derm. and Syph.*, **34**, 150.
27	B. Shelmire	1925	*Arch. Derm. and Syph.*, **13**, 788.
28	H. W. Barber	1929	*The Lancet*, **ii.**, 591.
29	E. Ramel	1930	*Brit. Journ. Derm. and Syph.*, **42**, 1.
30	R. Hallam and J. W. Edington	1933	*Brit. Journ. Derm. and Syph.*, **45**, 133.
31	H. W. Barber	1921	*Guy's Hosp. Rep.*, 385.
32	L. Landouzy	1913	*Presse Méd.*, **21**, 1045.
33	H. W. Barber and L. Forman ..	1933	*Brit. Journ. Derm. and Syph.*, **45**, 4.
34	L. Forman and G. P. B. Whitwell	1934	*Guy's Hosp. Rep.*, **74**, 213.
	G. P. B. Whitwell	1934	*Ibid.*, **75**, 227.
35	A. B. Cannon and G. G. Ornstein	1925	*Arch. Derm. and Syph.*, **12**, 691.
36	H. W. Barber	1929	*The Lancet*, **ii.**, 483.
37	S. Shone and G. P. B. Whitwell	1934	*The Lancet*, **ii.**, 11.
38	T. Wingate Todd	1933	" Behaviour Patterns of the Alimentary Tract," Baltimore, p. 79.
39	T. Lewis	1927	" The Blood Vessels of the Human Skin and their Responses," London, p. 81.
40	A. E. Boycott	1912–13	*Journ. Path. and Bact.*, **17**, 110.
41	J. H. Stokes	1914	*Journ. Cut. Dis.*, **32**, 751, 830.
42	B. Bloch	1929	*Arch. Derm. and Syph.*, **19**, 175.
43	A. Civatte	1926	*Ann. de Derm. et de Syph.*, **7**, 142.
44	J. V. Klauder and H. Brown ..	1927	*Arch. Derm. and Syph.*, **15**, 1.
45	R. Hallam	1927	*Brit. Journ. Derm. and Syph.*, **39**, 95.
46	W. Brack	1926	*Zeitsch. f. ges. experiment. Med.*, **51**, 525 ; and *Klin. Woch.*, 1925, **4**, 1109.
47	C. H. Rogerson	1934	*Brit. Journ. Derm. and Syph.*, **46**, 368.

48	H. W. Barber and G. H. Oriel..	1928	*The Lancet*, **ii.**, 1009, 1064.
49	H. G. Adamson	1906	*Brit. Journ. Derm.*, **18**, 125.
50	H. W. Barber and F. D. Howitt	1926	*Guy's Hosp. Rep.*, **76**, 314.
51	R. Cranston Low	1924	"Anaphylaxis and Sensitisation," Edinburgh, p. 74.
52	N. Walker	1925	"An Introduction to Dermatology," 8th Edition, Edinburgh, p. 83.
53	A. Garrod and G. Evans ..	1924	*Quart. Journ. Med.*, **17**, 171.
54	E. A. Cockayne..	1933	"Inherited Abnormalities of the Skin and its Appendages," London.
55	H. G. Adamson	1920	*Brit. Journ. Derm. and Syph.*, **32**, 183.
56	O. Grütz	1934	*Deutsche. Med. Wchnschr.*, **60**, 1039.
57	H. W. Barber	1930	*Brit. Journ. Derm. and Syph.*, **42**, 500.
58	S. E. Dore	1928	*Brit. Journ. Derm. and Syph.*, **40**, 12.
59	G. C. Andrews, F. W. Birkman and R. J. Kelly	1934	*Arch. Derm. and Syph.*, **29**, 548.
60	H. D. Rolleston	1924	*Brit. Journ. Derm. and Syph.*, **36**, 407.
61	H. W. Barber	1926	*Brit. Journ. Derm. and Syph.*, **38**, 143.
62	R. L. Sutton	1916	*Journ. Cut. Dis.*, **34**, 797.
63	J. C. Michael and H. O. Nicholas	1934	*Arch. Derm. and Syph.*, **29**, 228.

DISEASES OF THE TROPICS

INTRODUCTION

MANY diseases such as trypanosomiasis, yaws, kala-azar and yellow fever are essentially tropical or sub-tropical in distribution and no one would seriously question their tropical status, but other diseases now found almost exclusively in warm climates at one time occurred extensively in temperate zones. Relapsing fever, typhus, malaria, plague, leprosy and hydrophobia were prevalent in England in the past but have now ceased to be endemic mainly as a result of applied hygiene and the improved standard of living in the community. Official figures show that from 1850–1860 the incidence of malaria at St. Thomas' Hospital, London, varied from 12 to 60 per 1,000 patients. (1) Facts such as these are not sufficiently realised and indicate that hygienic rather than climatic conditions are responsible for the high incidence of many so-called tropical diseases in tropical communities.

Another interesting aspect of this problem is the modified incidence of ordinary disease in tropical countries. Cirrhosis of the liver, for example, is ten times more frequent in the native population of the Dutch East Indies, which does not indulge in alcohol, than in Europe. Again, the type of cancer occurring in a community may be determined by local custom or disease. The habit of chewing betel-nut in Southern India has led to much buccal cancer there, while in Egypt carcinoma of the bladder and penis are frequent owing to the irritation set up by deposits of schistosome eggs in these tissues. Primary carcinoma of the liver is more prevalent in China than in other parts of the world. Again, pigment gall stones are more commonly encountered in the tropics, probably owing to hyperbilirubinæmia resulting from chronic malarial and blackwater fever, while urinary calculi are also abnormally frequent in certain parts of India. The ordinary venereal diseases—syphilis, gonorrhœa and chancroid—are common in the tropics. Two other venereal diseases, ulcerating granuloma of the pudenda and climatic bubo, also occur. Sailors visiting tropical ports may contract climatic bubo from native women, and the disease is now gradually becoming established in Europe.

Respiratory diseases, such as influenza, tuberculosis and measles, have been introduced by Europeans and have caused a high mortality amongst native races possessing little or no immunity against them. This is exemplified amongst the Polynesians where the severe ravages of these diseases have led to an appalling mortality in certain of the Pacific islands. Similarly, the stone-age aboriginals of Australia have not been able to overcome European-introduced diseases and are rapidly disappearing. Tuberculosis is also an increasing menace in India and especially in Africa (2). The primitive races of the "Dark Continent," not previously exposed to tuberculosis, tend to develop the infantile type of infection with glandular involvement and generalised dissemination which is often rapidly fatal (see p. 87). Serious responsibility lies with the white man who introduces incidentally with his culture, infections which, if uncontrolled, may lead to depopulation of vast areas of country or even to racial extermination.

The European and his Tropical Environment. Tropical countries are inhabited by oriental and native races of varying physique and character, scattered amongst whom are a limited number of Europeans and people of mixed European blood,

often possessing little immunity to the infections which are rife amongst the local inhabitants. Blood-sucking insects, arthropod vectors, flies, food and water are the usual means of transmission. The chronic carrier, especially amongst servants, proves a most potent source of danger to the European in the tropics. Where there is no densely infected native population, as in Northern Tropical Australia, the expectancy of life in European adults and children compares favourably with that encountered in temperate zones.

The difficulty of obtaining a pure water supply and a balanced dietary is another disadvantage of tropical environment. Milk is usually grossly contaminated, and if obtained from the buffalo has an unduly high fat content. Red meat may be of poor quality, and vegetables and fruit difficult to obtain. Under these circumstances vitamin reinforcement of the diet becomes essential if the effects of avitaminosis are to be avoided. The monotony of life, limitations of social intercourse and the prolonged effects of hot or moist warm climate which has little variation enervate the white man and often lead to an irritable mental state, sleeplessness and loss of concentration—a syndrome which alcohol aggravates rather than alleviates.

CLINICAL EXAMINATION OF THE TROPICAL PATIENT

A careful clinical history and physical examination of the whole patient is of primary importance in the investigation of any case from the tropics. The previous geographical habitat often affords a clue to diagnosis. Attention should be directed to the spleen, liver, colon and bases of the lungs. Amongst isolated African negroes suffering from tuberculosis, 52 per cent. showed only basal and midzonal lesions.(2) In Europeans and natives the base of the right lung must receive special attention owing to the frequency with which physical signs indicative of pulmonary congestion, collapse, consolidation or of pleural effusion occur in this situation as a complication of amœbic abscess of the liver. Similar features may accompany hydatid of the liver, but the general tendency is for the cyst to develop downwards, whereas an amœbic abscess generally progresses towards the diaphragm. Both lesions involve the right side of the liver in approximately 80 per cent. of cases.

Where any single system is implicated a particular group of diseases needs consideration in the differential diagnosis. Thus, neurological manifestations may be attributable to cerebral malaria, trypanosomiasis, cysticercosis, bilharzial granuloma of the brain or even lathyrism, while peripheral neuritis may be due to leprosy, pellagra or beri-beri. It is interesting to note that sub-acute combined degeneration of the cord, so frequently associated with pernicious anæmia, rarely, if ever, complicates tropical sprue, although megalocytic anæmia is common to both diseases. Similar examples might be cited in regard to other systems. In the endemic hæmoptysis of Japan, for example, the sputum contains not tubercle bacilli but the eggs of a pulmonary fluke, *Paragonimus westermanii*. In Egypt and other parts of Africa hæmaturia is regularly caused by bilharzial disease of the bladder (*Schistosoma hæmatobium*). Enough, however, has been said to indicate the special knowledge necessary in the clinical approach to cases from the tropics.

Laboratory Diagnosis. A wide range of infective agents produce disease in the tropics. Amongst these agents are filterable viruses, Rickettsial bodies, bacteria, fungi, spirochætes, protozoa and helminths. The demonstration of a causal organism can be made with a frequency that is often impossible in the diseases of colder climates. Latency is a characteristic of many tropical diseases, especially those of protozoal and helminthic origin. Multiple infection is not unusual. The blood and fæces of every patient coming from the tropics should be examined for parasites as a routine procedure in addition to the usual urinary examination.

Serological methods such as the Weil-Felix reactions in typhus, the agglutina-

tion reactions for the enteric and undulant fevers and the complement fixation reactions in schistosmiasis, hydatid and *Loa loa* infestations, confirm the clinical diagnosis. Biochemical estimations are of great assistance in blackwater fever and sprue. Megalocytic anæmia occurs in tropical macrocytic anæmia, Oroya fever and sprue, and these, with other types of anæmia encountered in the tropics, call for modern hæmatological investigation.

Special Investigations. Radiological evidence is of great value in suspected liver abscess; immobility and elevation of the diaphragm, or definite upward pointing may confirm the provisional diagnosis. Similar help may be forthcoming in pulmonary amœbiasis and in hydatid disease of the liver or lungs. Calcification in the adventitia of an old hydatid cyst or in the wall of an amœbic abscess may be revealed by X-ray examination and contraindicates operative interference. Similar deposition of lime salts in other parasites may lead to typical shadows, such as calcified filarial nodules, the convoluted, moniliform outline of calcified guinea worms, the elongated, oval shadows produced by calcified cystercerci in muscle, or the multiple, oval umbilicated shadows occasioned by calcified *Porocephalus armillatus* encysted in the mesentery, liver and lungs of men. In the alimentary tract, bilharzial papillomata due to *Schistosoma mansoni* may be demonstrated in the colon by the opaque enema. In urinary schistosomiasis various complications, including papillomata, calculi, stricture of the ureter, hydronephrosis and pyonephrosis may only be evident after ascending or descending pyelography.

Sigmoidoscopy is of great importance in any tropical case with blood and mucus in the stools. It is of great value in excluding carcinoma and ulcerative colitis and in recognising the chronic types of tropical colitis due to *Balantidium coli*, amœbic ulceration or bilharzial involvement of the colon. It is, however, rarely necessary or advisable in acute bacillary dysentery. In the material obtained by gently curetting suitable lesions may be found ciliated balantidiæ, motile vegetative amœbæ containing ingested red corpuscles or lateral spined ova of *Schistosoma mansoni*.

Cystoscopy is of assistance in vesical schistosomiasis. The early lesions consist of shallow ulcers or of yellowish, round, submucous nodules or bilharzial pseudo-tubercles which become china-white when the ova are dead; later sandy patches, vesical papilloma or even carcinoma may be demonstrable. In filarial chyluria milky fluid may be seen exuding from the ruptured and dilated lymphatic varix in the base or walls of the bladder, while if of renal origin the affected kidney may be ascertained by ureteric catheterisation.

SPECIAL THERAPY IN TROPICAL DISEASE

Specific drug therapy is specially applicable to spirochætal, protozoal and helminthic diseases. Dramatic cure follows accurate diagnosis and treatment in suitable cases. The assistance that can be thus given to a patient demands and justifies the detailed clinical and laboratory investigation of any obscure disease originating in the tropics or sub-tropics. The spirochætal diseases which occur in the tropics respond to salvarsan preparations, amœbiasis to emetine, malaria to quinine, atebrin and plasmoquin, Kala-azar to the pentavalent antimony compounds and trypanosomiasis to tryparsamide and Bayer 205. Certain trivalent antimony compounds exert a specific lethal effect on schistosomes. Carbon tetrachloride and other organic preparations are very useful in eradicating certain intestinal helminthic infestations.

As in temperate climates drugs have little or no effect on the course of bacterial infections, but a valuable antidysenteric serum is available for Shiga dysentery. Potent monovalent or polyvalent antivenenes are procurable in an increasing number of countries for their indigenous venomous snakes. In Upper Egypt the mortality rate amongst children from scorpion bites has been greatly reduced by the intravenous injection of anti-scorpion serum.

HEAT-STROKE AND ALLIED MALADIES

(Sunstroke, Heat Apoplexy, Thermic Fever, Heat Exhaustion, Sun Traumatism.)

In the tropics, during periods of unusually hot weather in temperate climates, and under conditions such as are sometimes experienced by stokers and miners when the atmospheric temperature and humidity become unduly high, a series of maladies may arise which include heat exhaustion, heat hyperpyrexia (heat-stroke, sun-stroke) and heat cramp. The tragedy of the Black Hole of Calcutta in the hot, sultry June of 1756, where 123 out of 146 British prisoners succumbed, is a classical example of heat-stroke in Army history.

Ætiology. It has been shown (**3**) that, in a climate where shade temperatures approximate to those of the skin, a man performing hard manual work would need to evaporate a litre of sweat per hour from his skin to maintain his temperature balance. This is impossible unless the clothes worn are very thin and wet and a corresponding quantity of water be imbibed. Furthermore, the naked body exposed to the sun may absorb 3,420 small calories per minute, or three times its resting heat production; this is the equivalent of the extra heat that a man would produce walking at the rate of three and a half miles on the flat. Strenuous work in conventional European clothing under tropical conditions, direct exposure to the heat rays of a tropical sun, a shade temperature approximating to 110° F., a high humidity and lack of air movement are the factors leading to heat exhaustion and heat hyperpyrexia. Debilitated or alcoholic patients and those suffering from malaria, typhoid and other fevers are particularly susceptible.

Pathology. Hyperæmia and œdema of the brain and meninges, and excess of cerebrospinal fluid are found. Degeneration of nerve cells may be present. Petechiæ involving the skin and mucous membrane are common, the blood is fluid, the organs congested and the right side of the heart dilated. The myocardium, liver and kidneys show cloudy swelling. In non-sweating laboratory animals (**4**) hyperthermia is accompanied by a rise in the blood lactic acid and a fall in the plasma bicarbonate; in addition in sweating man there is a fall in blood chloride. It has been suggested (**5**) that hypochloræmia itself is responsible for the anhidrosis which can only be relieved by the administration of salt as well as water.

There are four means (**6**) by which a final breakdown in the thermal equilibrium between man and his environment may be brought about: (1) hyperpyrexia due to derangement of the central nervous system involving the mechanism controlling heat production and heat loss; (2) circulatory failure secondary to dilatation of peripheral vessels; (3) dehydration from fluid loss; (4) heat cramp due to chloride depletion. Unfortunately, it is impossible to forecast how any individual will react to given atmospheric conditions of heat, and the clinical picture which results may be complex and not always accurately fit into the clinical types below.

Symptoms. 1. *Heat Exhaustion.* This generally comes on suddenly with giddiness, weakness and faintness. Constipation is common. In severe cases cramps may occur. The temperature is 102° to 103° F. and lasts a few days, the pulse is rapid and weak and cardiac failure may supervene. If not appropriately treated, anhidrosis, anuria and hyperpyrexia may set in, so there is no inseparable line of demarcation between severe heat exhaustion and heat-stroke. 2. *Heat Hyperpyrexia.* The onset is often sudden, with pyrexia, convulsions and coma. In other cases the patient feels restless, giddy and dyspnœic and may suffer from nausea and vomiting. There is often frequency of micturition and sometimes urethral discomfort. Sweating diminishes or ceases altogether. Soon after these premonitory symptoms the patient became unconscious, the breathing laboured and stertorous, and the pulse rapid. Fibrillary muscular twitching and Cheyne-Stokes' breathing may develop. The skin feels hot, is

absolutely dry and may show petechial hæmorrhages. The face and conjunctivæ appear congested and cyanosis may be marked. The urine often contains albumin and indican and sometimes ketone bodies. Violent convulsions may occur frequently associated with incontinence of the urine and fæces. At this stage the rectal temperature may rise to 108° to 112° F. Knee jerks are absent. The untreated patient dies in coma with a weakening pulse and respiratory failure; if appropriately treated he may rapidly regain consciousness, though fever may persist for a few days. Convalescence is gradually established, but for some weeks great care must be taken to avoid exposure to high temperature conditions. Complications and sequelæ include persistent headache, anarthria, neuritis, chronic mental disorders and cardiac dilatation. 3. *Gastro-intestinal Type.* A gastric and also a choleraic type of heat-stroke with collapse and watery diarrhœa usually terminating fatally in three to four days have been described. 4. *Heat Cramps.* This condition, due to hypotonicity of tissue fluid secondary to loss of chloride and total base, not infrequently affects people like stokers and engineers who are doing hard muscular work in very hot atmospheres. The spasms are very painful, invôlve the muscles of the extremities and abdomen and may last twenty-four hours or longer.

Prognosis. The prognosis of heat-stroke depends almost entirely on the rapidity with which treatment is started. In the choleraic type and in comatose patients with temperatures over 110° F. the outlook is always grave, and even after the temperature has been reduced debilitated patients may die from collapse and heart failure.

Prevention. Protection from the heat rays of the sun by suitable topees and spinal pads, light clothing, adequate water and salt intake, the avoidance of excessive exertion at temperatures approximating to 110° F. and abstinence from alcohol before sunset are important prophylactic measures. Fever cases in the hot season should be treated in artificially cooled wards and receive several pints of citrated lemonade daily.

Treatment. The patient suffering from *heat exhaustion* is put to bed in a cooled room, purged and treated for shock when necessary. Citrates, sodium bicarbonate, sodium chloride and glucose may with benefit be added to the drinks; but, if repeated vomiting occurs, 1 to 1½ pints of normal saline (0·9 per cent.) containing 2 per cent. bicarbonate of soda should be given intravenously and repeated when thought advisable. In *heat hyperpyrexia* it is essential to reduce the temperature, and for this purpose artificially cooled heat-stroke wards have been recently constructed in the tropics. Hydrotherapy is essential. The patient is stripped naked, placed under a fan on a rush or wire mattress, and sprayed with ice-cold water. Ice is also applied to the head and nape of the neck. The rectal temperature must be taken every few minutes to control the effects of treatment, and hydrotherapy is stopped when the temperature reaches 102° F. If congestive features or convulsions are present venesection of 1 pint of blood is indicated. Iced saline enemata containing bicarbonate (2 drachms to 1 pint) should be given. Morphia or chloroform inhalations may be necessary when the fits are severe. Where circulatory failure ensues the blood volume is decreased and the blood appears viscid; intravenous injections of isotonic saline, with or without bicarbonate of soda, must be given. Collapse with low temperature should be treated by hot-water bottles and strychnine, and cardiac failure by digitalin and pituitary extract. Blood smears should invariably be made and examined for malarial parasites, and in any case where doubt exists or if the high temperature does not respond to hydrotherapy, quinine bihydrochloride (10 grains) should be injected intravenously and quinine or atebrin subsequently given *per os.* *Heat cramp* responds to intravenous injections of hypertonic saline (sodium chloride, 120 grains; potassium chloride, 6 grains; calcium chloride, 4 grains; water, 1 pint), or normal saline containing 5 per cent. glucose. It is best prevented by increasing the daily consumption of salt.

FOOD POISONING AND DIET DEFICIENCIES

Food poisoning due to infection of food with organisms of the salmonella group or *Proteus vulgaris* are more common in hot than in cold countries. Undercooked meat, fish, unboiled milk and ice-cream are the usual sources of infection. This question is dealt with on p. 367. Poisonous fungi are sometimes mistaken for edible mushrooms, and their poisonous constituents may lead to severe gastro-enteritis, collapse, hepatic or even renal failure and death. *Amanita phalloides* is the only one that certainly kills. It resembles an ordinary mushroom, but is coloured olive-green on top of the cap, has white gills underneath and a cup at the base of the stem. It produces acute colicky pain, vomiting, diarrhœa and collapse followed by temporary improvement; subsequently jaundice and acute yellow atrophy of the liver may ensue. The orange or bright red coloured fungus, *Amanita muscaria*, leads to serious gastro-intestinal features, but is rarely if ever fatal. Ergotism is an example of food intoxication with a fungus which contaminates rye. Poisonous fish of the genus *Tetrodon* (Japan) contain poison in the gonads, and the roe of such fish may prove fatal in a few hours if eaten. Many other species of poisonous fish are found in tropical waters. Some, like the barracuda which are usually edible, become poisonous at certain times of the year, possibly as a result of feeding on poisonous vegetable or animal foods. Certain specific food intoxications of tropical interest will be considered in more detail.

Lathyrism. Lathyrism is a form of spastic paraplegia resulting from eating the seeds of *Vicia sativa* and possibly other closely related vetches.

Ætiology. The disease is particularly common in India, occurring mainly in the central plateau, North Behar and the United Provinces, but it occurs in France, Italy, Algeria and Persia. It occurs particularly amongst young male adults during famine periods when bread is often made from a mixture of chick pea and wheat flour. *Vicia sativa* or "akta," as it is called in India, contains a toxic glucoside base "vicine" and when fed to ducks and monkeys produces a syndrome suggestive of lathyrism (7). *Lathyrus sativus* or "khesardal" is harmless, but may be adulterated with the seeds of *Vicia sativa*. Before this was realised it was erroneously regarded as the cause of the paralysis.

Pathology. Sclerosis of the pestero-lateral columns of the spinal cord are found, probably resulting from toxic spasm and thrombosis of arteries supplying its dorsal region.

Symptoms. The early symptoms include backache and burning pains in the lower extremities. The feet and legs become stiff, weak and tremulous, soon the thighs are involved and within ten days walking without the aid of a stick may be impossible. A peculiar spastic gait develops with adductor spasm, and in India these unfortunate people may be seen progressing laboriously along by means of a two-handed staff. When recumbent the thighs can be separated and adductor spasm ceases. Sensation is not affected, so the knee jerks are markedly increased and ankle clonus is present. Sexual impotence and incontinence of the urine and even of fæces may occur. Occasionally, in bed-ridden patients, cystitis develops.

Diagnosis. Milder cases at the beginning of an outbreak may not be recognised, but later the appearance of multiple cases with spinal features and a history of eating bread made from chick peas will confirm the diagnosis. Sporadic cases need to be differentiated from syphilitic and other forms of paraplegia.

Prognosis. The disease is not generally fatal, but improvement can only be expected in early stages before the cord has been permanently damaged.

Treatment. Varieties of chick pea including "khesari dal" must be excluded from the diet, which should be rich in proteins and vitamins. Damp and wet conditions must be avoided. Treatment of the paraplegia by massage, electricity and postural measures is useful, especially in early cases.

Ackee Poisoning. (*Vomiting Sickness of Jamaica.*) A disease caused by eating the arilla of unripe ackee fruit (*Blighia sapida*). (8) It frequently affects children, is often fatal and is characterised by gastro-intestinal and nervous symptoms. The ackee is found in the West Indies and the West African coast. The ripe fruit is harmless, but soup prepared from the unripe fruit is particularly poisonous.

Pathology. Visceral hæmorrhages, congestion of the meninges, and fatty degeneration in the liver are characteristic. Degenerative changes in the heart, kidneys and brain cells are also described.

Symptoms. The onset is sudden; some two hours after the child has eaten the unripe fruit, nausea, vomiting and abdominal discomfort develop. This persists for three or four hours and is often followed by a quiescent period preceding the onset of muscular twitchings, cerebral vomiting, convulsions and coma.

Prognosis. The illness is invariably fatal once nervous features have supervened, death occurring in about twelve hours.

Treatment. Scott decreased the mortality in school children from 90 to 27 per cent. by the rapid administration of rum or ether and ammonia. Alcohol precipitates the poison both *in vitro* and in the stomach.

Atriplicism. This disease occurs in North China amongst the poor who eat the shoots of the weed *Atriplex littoralis*, in times of famine. Some say the disease is caused by small insects on the plants. After twelve to eighteen hours from eating the shoots there is tingling of the fingers followed by local œdema and itching of the hands, forearms and face, which may last a week or more. Anæsthesia of the digits may develop and heat sensation is increased. Vesicles and skin ulceration may follow. The disease may be confused with Raynaud's disease or erythromelalgia. Medication consists of saline purgatives.

Favism. This disease, which is not completely understood, is said to follow the ingestion of fresh beans of *Vicia fava* or even exposure to the flowering plant. The illness develops only when the beans are ripening. Personal idiosyncrasy is marked as everyone exposed is not affected. Cases have been reported from Italy, Greece, Mesopotamia and elsewhere.

Symptoms. Shortly after ingesting the beans, fever develops with hæmolytic anæmia, jaundice, hæmoglobinæmia and hæmoglobinuria. The red blood corpuscles may decrease rapidly to 2,000,000 per c.mm. with an even greater fall in hæmoglobin. Renal involvement may follow. Recovery is the rule with adults, but the disease may be rapidly fatal in children.

Treatment. Purgation when the beans have been recently ingested, abundant fluids by mouth and rectum, the administration of citrates and sodium bicarbonate per os and blood transfusion when signs of anoxæmia develop, appear rational procedures.

The various vitamin deficiency diseases such as pellagra, beri-beri and epidemic dropsy encountered in the tropics and sub-tropics are considered, pp. 569 *et seq.*

TROPICAL MACROCYTIC ANÆMIA

(*Tropical Megalocytic Anæmia, Tropical Anæmia of Pregnancy.*)

A severe megalocytic, hyperchromic anæmia of nutritional origin especially affecting pregnant native women in the tropics; it responds specifically to the administration of marmite and liver extract with a reticulocyte response and rapid blood regeneration.

Ætiology. Though not unknown amongst males the disease mainly occurs in pregnant women and has been reported in native populations resident in India, the Malay States, China and the West Coast of Africa, where the diets are known to be unsatisfactory. The age incidence is generally between fifteen and thirty years, and whites are rarely affected. Marmite, which is an autolysed

extract of brewers' yeast, cures the condition, and it (9) has recently been shown that vitamin B_1, B_2 and B_4 are not responsible for the therapeutic response and that the curative factor probably arises from protein breakdown during autolysis. The morbid anatomy has not been satisfactorily investigated.

Symptoms. Signs and symptoms, mainly due to the anæmia, consist of weakness, palpitation, shortness of breath, pallor, low blood pressure and cardiac murmurs. Fever, œdema of the feet and puffiness of the face are frequent. Sore tongue, vomiting, diarrhœa and enlargement of the liver and spleen may also occur, but intercurrent infection with malaria, amœbiasis and ankylostomiasis may be responsible for certain of these features.

The red cell picture and Price-Jones curves resemble pernicious anæmia. Often the erythrocytes are reduced below 1,000,000 per c.mm., but the hæmoglobin is not correspondingly reduced, so the colour index generally exceeds unity. Anisocytosis and megalocytosis are marked and both normoblasts and megaloblasts may be present. The serum bilirubin, however, is not increased in uncomplicated cases. Free hydrochloric acid is usually present in the gastric juice.

Diagnosis. The presence of megalocytic anæmia in pregnant white women will generally suggest sprue or pernicious anæmia, but these diseases rarely occur in the native populations under consideration.

Prognosis. Liver treatment has lowered the mortality from 40 per cent. to 33 per cent. and the recent introduction of marmite has caused a further reduction.

Treatment. Prevention depends on the institution of a balanced diet adequate in vitamins. Once the disease has developed, rest in bed, and the administration of marmite in a dosage of 1 teaspoonful four times daily, is indicated. In a favourable case a rapid reticulocyte response occurs about the fifth to seventh day and rapid blood regeneration follows. Intercurrent infections require appropriate treatment.

TROPICAL DYSFUNCTION OF THE GASTRO-INTESTINAL TRACT

TROPICAL SPRUE

(*Psilosis ; Cochin-China Diarrhœa ; Diarrhœa alba.*)

Tropical sprue generally affects adult Europeans or those of mixed European stock after some years of residence in endemic areas. Hot, damp, coastal climates favour its development and it is especially common in India, Ceylon, the Federated Malay States, Java, Cochin-China and Porto Rica. It may directly follow on hill diarrhœa and is not infrequently preceded by a history of dysentery or of chronic malaria necessitating prolonged quinine administration. Children in the first decade are not affected and, Porto Rica excepted, native populations rarely develop the disease. Peculiar features are its patchy geographical distribution, its absence from Africa and its occasional onset in tropical patients after many years of residence in Europe. Ashford (1915) regarded it as a moniliasis of the digestive tract engrafted on an unbalanced dietary. Scott (1923) postulated parathyroid deficiency, while Elders (1919) regarded it as a primary deficiency disease due to lack of vitamin A and B and amino acid. Castle and Strauss (1932) recently suggested its classification along with pernicious anæmia as a conditional deficiency; they regarded vitamin B_2 as the source of intrinsic factor

Sprue arises as a metabolic breakdown of the gastro-intestine in which there is generally defective secretion of Castle's intrinsic factor, and malabsorption of fat, calcium and glucose in the small intestine. The possible factors under-

lying this breakdown are (1) unbalanced dietary; (2) preceding tropical infections, some of which have been already proved to depress gastric secretion; (3) prolonged residence in a humid climate which involves an increased distribution of blood to the skin at the expense of the alimentary tract. A diet rich in fat and carbohydrate and poor in first-class protein, which is the main source of extrinsic factor, is known to precipitate relapses in sprue and may possibly prove the most potent single factor in the initiation of the disease.

Pathology. No primary pathological lesions are found in the stomach and small intestine. The characteristic findings are disappearance of subcutaneous fat and wasting of muscles, a smooth atrophic tongue, thinning of the intestine, a small heart showing brown atrophy, decrease in the size of the spleen, liver and other viscera and megaloblastic hypertrophy of the red marrow similar to but generally less extensive than that seen in pernicious anæmia. Intestinal ulceration and occasional perforation with peritonitis may be encountered as complications.

Symptoms. Early features of onset may include (1) sore tongue and buccal aphthæ; (2) dyspepsia, abdominal distension and intestinal flatulence; (3) morning diarrhœa: typically, several pale, bulky, fatty, gaseous stools are passed before noon, after which the patient often enjoys relative comfort. The lingual features may precede or follow the bowel condition but in some cases of recurrent sprue they may not appear for many years. As the disease progresses marked loss of weight, asthenia and anæmia of megalocytic type develop. Apyrexia is the rule, the temperature generally being subnormal. Fever, however, may be present for the first day or two in the initial attack, but its recurrence at a later date or during relapses should arouse suspicion of intercurrent infection or some complication such as intestinal ulceration.

The well-established case of sprue presents a definite clinical picture. Emaciation is marked. The skin is dry, wrinkled and often of a parchment-like consistency and patchy pigmentation may appear over the forehead, malar eminences, buttocks and elsewhere. The mucous membranes are pale and the nails are rigid and brittle. The appearance of the tongue varies from time to time: it is invariably clean and in the early stages may show prominent papillæ, painful, red, inflamed patches, fissures and apthous ulcers; later the papillæ disappear and the tongue becomes smooth, pale and atrophic. Distension of the abdomen is an outstanding feature, and its walls are often so thinned that peristaltic movements in the distended coils of intestine are obvious on inspection. Unlike pernicious anæmia the spleen is not palpable in uncomplicated sprue, while the liver usually appears decreased in size on percussion. The systolic blood pressure is low, not infrequently being less than 100 mm. Hg.; hæmic murmurs sometimes develop. The knee jerks and other tendon reflexes may be decreased or absent. Paræsthesia and blunted sensation may result from peripheral nerve changes, while in cases complicated by tetany, excessive muscular irritability is readily disclosed by Trousseau's and Chvostek's signs.

The total fæcal fat is increased from 25 to 70 per cent., but the fat itself is split normally, while the glucose tolerance test often shows a flat or low curve, or a delayed rise indicative of defective absorption. The excessive bulk of the stool in sprue is due to its large fat residue, while its acid and gaseous characters are attributable to fermentation of glucose which has been inadequately absorbed; the pale colour is dependent on the high fat content as well as on the transformation of the normal fæcal pigment—stercobilin—into a colourless derivative—leucobilin. Hypochlorhydria and achlorhydria are common, but acid secretion follows the injection of histamine in at least 70 per cent. of cases, a test which may prove of value in differentiating sprue from pernicious anæmia; hyperbilirubinæmia is also less marked in sprue. Hypocalcæmia is often observed, and where the blood calcium falls below 7 mg. per 100 c.c., tetany supervenes.

Sprue anæmia is megalocytic in type, and though it is not as severe as in

pernicious anæmia in the primary attack, it may become so later in relapses. The Price-Jones curve is asymmetrical, shows displacement to the right, with broadening of the base; there is an increase in the average diameter of the corpuscle.

Course. Though sprue may occasionally prove fatal within six months of onset, it generally runs a very chronic course with spontaneous remission and relapses, which may be brought on by indiscretions of diet containing an excess of fat, carboyhydrate or condiments, or by chill, respiratory infection and other intercurrent disease. There is a tendency to natural cure provided the patient leaves the tropics, and it is well to remember that many cases of sprue recovered with alimentary rest in a cool climate prior to the introduction of liver extract therapy; in this respect sprue again differs fundamentally from pernicious anæmia.

Complications include anal fissure, hæmorrhoids, femoral and other thromboses, neuritis, eczema, intestinal ulceration and rarely perforation of the small or large intestine.

Diagnosis. Other megalocytic anæmias, especially those associated with tropical macrocytic anæmia, pernicious anæmia, gastro-jejuno-colic fistula, intestinal ulceration with stricture and tuberculous ulceration with fistulæ may lead to confusion. Diseases giving rise to fatty diarrhœa such as idiopathic steatorrhœa, abdominal lymph-adenoma and tuberculous adenitis involving the mesenteric glands and causing lymphatic obstruction, and interstitial pancreatitis may occasionally need differentiation. In the diagnosis of atypical sprue clinical experience combined with a careful case history, physical examination and detailed laboratory and X-ray investigation may prove essential.

Prognosis. With modern treatment the patient is generally convalescent and the blood restored to normal within two months. Return to the tropics can be permitted with reasonable safety after six months' freedom from symptoms in those under fifty-five years of age; relapses, however, may occur even after many years of good health.

Treatment. The patient with sprue must be put to bed on an appropriate diet for a period of five to eight weeks and receive liver extract in full dosage if anæmic. On admission oleum ricini (2 drachms) is given, and where the diarrhœa is severe, pulv. bataviæ co. (½ to 1 drachms t.d.s.) may be prescribed. Bed rest is essential as it halves the calorie requirements of the patient and permits alimentary rest which is of fundamental importance in recovery. Several different diets have been advocated empirically, including the fruit diet of van der Burg, the milk diet of Manson and the red meat diet of Cantlie. On the basis of the biochemical findings a graded series of high protein diets low in fat and carbohydrate have been introduced successfully, the ratio of these different constituents being 1·0 of protein : 0·3 of fat : 1·3 of carbohydrate instead of the usual 1·0 : 1·0 : 4·0 (**10**). The energy value of the first diet = 600 calories, that of the last = 3,000 calories, and the dietary is gradually increased as the diarrhœa and other alimentary features improve. Lean red meat is the main source of protein, but a defatted high protein milk powder (sprulac) (**11**) is also available. A convalescent high protein diet and vegetables can generally be allowed about the fifth week, and thereafter the quantity of fat and carbohydrate is gradually increased.

The anæmia is almost invariably of megalocytic type and generally it is hyperchromic. Provided the diarrhœa be controlled by suitable dietary, as indicated above, liver extract by mouth is adequately absorbed and reticulocytosis and rapid blood regeneration follow as in pernicious anæmia. Liver extract should be given in a dosage equivalent to 1½ lb. of whole liver daily for the first month, in a dosage equalling 1 lb. for the second month, and in a dosage of ½ lb. for the third month or until such time as the blood picture has attained complete normality. In severe chronic cases a maintenance dose for

several months or even one year is occasionally advisable. Occasionally refractory cases are encountered where reticulocytosis is submaximal and improvement inadequate; here oral treatment should be reinforced or replaced by large doses of liver preparations given parenterally, such as Campolon 6 c.c. daily for fourteen days. In those rarer cases where hypochromia is present and the colour index is low, or where there is an undue lag in the production of hæmoglobin following liver extract therapy, complications or intercurrent disease should be suspected. Iron in the form of freshly made Blaud's pills (5 grains) should be prescribed, commencing with two and working up to four pills thrice daily after food, or, alternatively, ferri et ammon. cit. (30 grains) may be given thrice daily after meals. When the secretion of HCl is found defective acid hydrochlor. dil. (B.P.) in doses of 1 drachm should be administered in orange juice thrice daily after food.

Tetany with hypocalcæmia calls for calcium salts such as calcium lactate, 40 grains, thrice daily, and in addition a diet low in fat is essential since calcium cannot be satisfactorily absorbed while there is an excess of fat in the stools.

Once well, the sprue patient must continue with a well-balanced diet adequate in vitamins and first-class protein, and avoid rich, spiced and sugary food and condiments. Aperients should be taken with caution and chill and respiratory infections guarded against as far as possible.

Hill Diarrhœa. A disease of high altitudes affecting Europeans who have gone to hill stations during the hot weather.

Ætiology. It occurs during the rainy season at heights over 6,000 feet in hill stations, in India, Ceylon and South America; it probably results from a physiological breakdown of the gastro-intestinal tract under conditions of low barometric pressure and high humidity. Europeans of all ages and both sexes are susceptible, and during particularly wet seasons epidemics have occurred in which a large proportion of the hill population have been affected. Nothing authoritative is known of the pathology, or of its clinical biochemistry.

Symptoms. Diarrhœa commences about 4 to 6 a.m. and is followed by three to six urgent actions of the bowels before mid-day, after which the patient is generally comfortable. The stools are copious, pale, like pipe-clay and of a frothy, fluid consistence. Some state there is an excess of fatty acid, soaps, undigested food and yeasts. Flatulence, borborygmi and abdominal distension are troublesome and if the condition persists, anorexia, dyspepsia and considerable loss of weight ensue. Lingual features are absent.

Prognosis. The condition is never fatal, but it may be very distressing and necessitates a return to lower altitudes. A certain number of cases develop into typical sprue after returning to the Plains.

Treatment. Rest in bed, warm clothing, the avoidance of chill and a milk diet are advised. Oleum ricini (½ ounce) should be given at onset and acid hydrochlor. dil. B.P. (1 drachm) after food. From its resemblance to sprue a high protein, low fat, low carbohydrate diet, such as sprulac, would appear preferable to a milk diet liable to contain an excess of fat.

INFECTIOUS DISEASES OF THE TROPICS

Diseases due to Filterable Viruses

There are a number of predominantly tropical diseases such as hydrophobia, yellow fever, dengue, sand-fly fever, Rift Valley fever and climatic bubo which fall into this category. The outstanding characteristics of the viruses are firstly, that they are ultramicroscopic, measuring less than 250 $\mu\mu$ in size and so fail to be resolved by the ordinary microscope, and secondly, that they pass through filters which are usually impervious to bacteria. Some of these diseases like yellow fever, dengue and sand-fly fever are insect borne, others are transmitted

directly; climatic bubo for instance is acquired during coitus, and hydrophobia by the bite of an infected canine. Complement fixing and protective antibodies may be found in the serum. In distemper and yellow fever, immunisation by means of virus and antiserum has been introduced. With the exception of rabies, however, killed virus produces little or no immunity. For small-pox, see p. 28.

HYDROPHOBIA

(*Rabies, Lyssa*)

An infective disease occurring as an epizootic amongst canines due to a filterable virus which is present in the salivary glands and central nervous system. It is generally transmitted to man and other warm-blooded animals by the bite of an infected dog or by its licking a freshly abraded skin surface; jackals and wolves also transmit the disease in the East. In Central and South America, the transmission to man and stock by infected blood-lapping bats has been recently demonstrated. The disease itself has been known from ancient times, reference being made to it in the writings of both Aristotle and Celsus.

In dogs there are two forms—"furious" and "dumb" rabies—but neither is ever accompanied by the hydrophobic syndrome observed in man The first indication of disease generally appears some three to six weeks after the bite and consists of a decisive change in temperament, while later signs of irritation or vicious fury develop with staring coat and a tendency to bite wildly at living or even inanimate objects. Ordinary food may be refused, while earth, straw, clothes, etc., are eaten with avidity. This stage lasts from a few hours to two or three days. Later, difficulty in swallowing develops, leading to dribbling of saliva and a peculiar bark, change in the note of which is often erroneously attributed to a "bone in the throat"; futile and dangerous attempts may be made to remove it. As the disease progresses the lower jaw drops, the hind limbs and tail become paralysed, the gait unsteady, and finally, the animal collapses and dies with asphyxia two to five days after the onset of symptoms. In "dumb" rabies there is no stage of fury or excitation, paralysis setting in early.

Ætiology. Pasteur in 1881 discovered that the virus of rabies could be transferred from one animal to another in series by direct brain inoculation. During this process in rabbits it was noted that after some twenty passages the incubation period of street virus which varies from eight to sixty days was reduced to seven days. This is known as virus fixé or fixed virus, and, despite its enhanced virulence for rabbits when inoculated directly *viâ* the brain, it fails to produce the disease in either experimental animals or man on subcutaneous injection. Street virus is transmitted *viâ* the peripheral nerves to the central nervous sytem and is present in emulsions of the parotid and submaxillary glands as well as in the milk of lactating women. Brain emulsions are not filterable, but salivary virus passes readily through Chamberland F. filters. The infectivity of saliva is much greater than that of the brain or spinal cord.

Morbid Anatomy. Post-mortem examination reveals injection of the pia arachnoid, a few petechial hæmorrhages and an excess of cerebro-spinal fluid, while microscopic examination shows leucocytic infiltration of the perivascular lymph spaces and Negri bodies within the cytoplasm of the nerve cells. These important structures, described by Negri in 1903, are globular or oval in shape, of very variable diameter (0·5 to 25 μ) and commonly located in the hippocampus and the Purkinje cells of the cerebellum. Though demonstrable in 97 per cent. of dogs with street rabies they are never found in the salivary glands. By some they are regarded as of protozoal nature, but more probably they originate as pathological degenerations or cell inclusions.

Symptoms. The incubation period generally varies from four to eight weeks, the limits being eleven days to a year or longer. As the virus travels

viâ the nerves, face, head and neck, bites have a shorter incubation period than those involving the arm, and arm bites a shorter incubation than those implicating the leg.

The onset is generally sudden, but prodromal features may be noted for a day or two and include local pain in the scar, fever, anxiety, restlessness, insomnia, irregular and sighing respiration and phases of rushed speaking.

The hydrophobic syndrome itself consists of sudden spasmodic attacks involving the muscles of the pharynx, larynx and, indeed, the whole respiratory tract. In the early stages such an attack may be induced by offering the patient a drink. As the glass is lifted to the mouth the head is retracted in a series of spasmodic jerks accompanied by gasping respirations, and any water reaching the mouth is expelled. During the attack the shoulders are raised, the chest expanded and the sternomastoid and platysma muscles contracted. Later, even the suggestion or thought of drinking suffices to bring on a paroxysm, while external stimuli such as sudden sounds, a draught of cool air, flashes of light and strange smells have the same action. The voice becomes altered and raucous, and, owing to the dysphagia, tenacious mucus and frothy saliva collect in the throat and on the lips, and during paroxysms are flung about the room. Feelings of terror or accesses of fury may accompany the attacks, but in the intervals the patient generally lies quietly at rest and the mentality is clear. Extension to the general musculature leads to rigidity and arching of the body, and respiratory spasm may result in sudden death from over-distension of the right heart. During this stage of excitation the temperature is raised, the face flushed, vomiting is common and exhaustion and emaciation marked. The reflexes are increased and glycosuria not uncommon. Near the end, the spasms may ameliorate or cease entirely.

Should the patient survive this excitation, depression very occasionally ensues with various paralyses, including paraplegia, hemiplegia and Landry's ascending paralysis, followed by fatal coma.

Diagnosis. This generally presents little difficulty, especially if the disease in the dog has been confirmed. Typhus fever may be accompanied by hiccup, pharyngeal spasm, dysphagia, neuro-muscular excitability, lymphocytosis and increase of globulin in the cerebro-spinal fluid; here the clinical history, the absence of rash and negative Weil-Felix reaction will assist. Lyssaphobia, which is an hysterical manifestation unaccompanied by fever, generally develops well within ten days of the dog bite, while the absence of trismus and the presence of dysphagia should distinguish rabies from tetanus. Bulbar paralysis from any cause and cases of datura and other forms of poisoning in India have occcsionally caused difficulty. The disease in the vector can be confirmed by demonstrating Negri bodies or by subdural inoculation of rabbits with brain emulsion.

Prognosis. The death rate in untreated cases is variously estimated as from 5 to 33 per cent., while in those having early anti-rabic inoculation it is considerably lower—about 1 per cent. The mortality varies with the location of the bite—it is highest in face bites—the number of tooth marks, the depth and degree of tissue laceration, the interposition of clothing and the rapidity and type of local treatment adopted (**12**). The earlier anti-rabic vaccine is inoculated, the better the prognosis.

Prevention. The prevention of rabies in England has been carried out by (1) the muzzling order; (2) restricting the movement of dogs; (3) strict quarantine of all imported dogs. In endemic areas all bites from canines should receive prompt local treatment. A suspected dog should never be destroyed; it should be muzzled and kept under observation for ten days. If alive and well at the end of this period the bitten person cannot have been infected and does not require treatment. This rule, adopted at all Pasteur Institutes, is based on the observations that the saliva of a rabid dog is never infective more than four days before the onset and that an infected animal never survives longer than six days after

symptoms appear. In definitely bitten cases it is safer to commence treatment at once, especially in face and neck bites, and to discontinue if the dog survives. The virus of rabies does not pass through the intact skin, so the question of inoculating a person licked by a suspected dog only arises if recent abrasions be present. Should the person be seen at this time the abrasion should be washed with permanganate solution and cauterised; in these circumstances anti-rabic inoculation need be given only when there are face or neck abrasions or the animal develops symptoms, dies or has escaped.

Treatment. (1) *Local.* If seen within half-an-hour of the bite, a ligature to facilitate bleeding by stopping venous return, should be applied and the parts washed with permanganate solution. Each tooth-mark should be probed and cauterised. Wounds, especially those of the face, must not be sutured for at least three days. (2) *Anti-Rabic Vaccine.* The principle is to immunise the patient against the disease before the virus implanted in the wound reaches the central nervous system; the longer incubation period of the street virus makes this possible. Five vaccines are in use. During the period of inoculation the patient is instructed to rest and to avoid alcohol. The Pasteur vaccine is the attenuated virus prepared by drying, for varying periods at 22° C. under potash, the cords of rabbits sub-durally inoculated with infected brain emulsions. Eighteen injections are given of emulsions of cords dried from fourteen to three days. With Högye's method the virus is attenuated by dilution; saline suspension of fresh medulla, 1/10,000, is first used and gradually increased to 1/100. Semple's carbolised vaccine consists of a 1/200 brain suspension in 0·25 per cent. phenol and 0·85 per cent. saline; a full course of treatment is fourteen daily subcutaneous injections of 5 c.c. Etherised vaccines may cause more severe local reactions, though paralytic sequelæ are less frequent than after carbolised ones. The most potent vaccine, now used in India, consists of a 5 per cent. carbolised emulsion of sheep brain infected with Paris virus. In mild cases 2 c.c. of this vaccine is given daily for seven days, in the average case 5 c.c. for fourteen days, while in severe cases such as children bitten on the bare skin, in face and neck bites and in jackal and wolf bites, an intensive course of fourteen daily injections of 10 c.c. each is advised. Cutaneous reactions take the form of itching, tender swellings surrounding the inoculation site and appearing about the eleventh day. Paralytic accidents are, fortunately, infrequent though their incidence is the same after either living or dead vaccines. Facial neuritis, dorso-lumbar myelitis and an ascending paralysis of Landry's type which has a mortality of 30 per cent. may be encountered (**13**).

Treatment of Paroxysms. Neither chemotherapy nor specific anti-rabic serum is of value and all that can be done is to alleviate the suffering of the patient by good nursing and sedative treatment. Morphia, hyoscine, chloral, chloroform inhalations, atropine and even curare have been employed. Intravenous barbiturates may find a sphere of utility here. Tetrado-toxin, ½ to 1 c.c. every four hours, has been used extensively in India for the relief of spasms.

YELLOW FEVER

(Yellow Jack, Black Vomit, Typhus Icteroides, etc.)

An acute infectious disease occurring mainly in West Africa and parts of tropical America, caused by a filterable virus which is transmitted by the bite of the tiger-banded mosquito, *Aëdes ægypti* (*Stegomyia fasciata*).

Ætiology. The disease is widely endemic in West Africa and like intestinal schistosomiasis (*S. mansoni*) was probably transmitted to the Americans by the slave traffic. It was known to sailors as Yellow Jack—that much-dreaded and mysterious disease which caused such great loss of life amongst the crews of ships visiting ports in endemic areas. No race is immune; the disease affects all ages and both sexes, though children are less severely affected. In 1900, Carroll

showed that the mosquito vector was *Aëdes ægypti*, and that it became infective to man after a period of twelve days provided it was fed on a patient during the first three days of fever; small quantities of blood collected during this period also produced infection on injection into man, and after filtration the serum was still infective. The West African Yellow Fever Commission in 1928 found that Rhesus monkeys (*Macaca mulatta*) were very suspectible to yellow fever, that human sera derived from patients who had suffered from yellow fever protected monkeys, and that the virus would penetrate the intact skin. The virus passes through Berkefeld filters V and N, but not W. Infected blood is very dangerous, and Stokes, Noguchi, Young and others acquired fatal infections in this manner. Many species of mosquito other than *Aëdes ægypti* are experimentally capable of transmitting the disease.

It has been shown (**14**) that the inoculation and subsequent passage of the ordinary viscerotrophic virus through the brains of mice converts it into a neurotrophic virus with fixed characters, which can immunise against the viscerotrophic virus without producing yellow fever. Subcutaneous injection of immune serum is given before the neurotrophic virus in prophylactic immunisation in man. This is regarded as safe and many have now been immunised. The fact that active immune bodies persist permanently in recovered yellow fever cases has been utilised to determine the endemic incidence of the disease. Mice are used because of the expense of Rhesus monkeys. The protection test (**15**) consists of an intra-cerebral inoculation of starch solution, followed by an intraperitonal injection of serum and virus into mice. If immune bodies be absent from the serum the virus localises in the brain, producing encephalitis and death within fourteen days; if they are present this does not occur. Protection tests afford an index not only of past epidemics but also of acquired immunity following inoculation.

Pathology. The skin and serous membranes may show hæmorrhages and jaundice. Rigor mortis is well marked. The liver is yellow coloured and greasy on section; the gall bladder contains dark, thick bile. Midzonal fatty degeneration and hæmorrhages are frequent and acidophil intra-nuclear inclusion bodies may be present. The kidneys show congestion and cloudy swelling. The heart muscle is pale and flabby; hyaline or granular degeneration of the muscle elements is common and bradycardia due to involvement of the A.V. bundle occurs. Erosions and petechial hæmorrhages involving the stomach and duodenum are frequently found. Death generally occurs on the fifth or sixth day of the disease, by which time the blood has lost its power to infect *viâ* the skin. The biochemical changes in yellow fever can be mainly interpreted as resulting from loss of liver function and, as its name implies, jaundice is generally present though not necessarily intense. Renal dysfunction is less in evidence. The direct van den Bergh reaction is delayed or biphasic, while a positive indirect varying from 2 to 6 units is generally found. Extreme hypoglycæmia may be encountered before death. Bile pigment and bile salts may appear in the urine which is acid in reaction and contains albumin, copious red cells and casts. In the later stages the blood urea may be increased and occasionally anuria supervenes. The cerebro-spinal fluid is under increased pressure and globulin and chlorides are said to be increased.

Symptoms. The incubation period is from three to five days, though occasionally and in contact infection through the skin it may be as long as ten days. Three clinical types are encountered. 1. *Mild or Larval Types.* These, occurring in epidemics or quiescent periods in endemic areas, are characterised by headache, vomiting and transient fever lasting one to four days. Albuminuria is generally present and mild jaundice may ensue. 2. *Ordinary Type.* Three phases are present: *Sthenic Stage.* The onset is sudden with chill or a rigor, and the temperature rises rapidly to 103° or 104° F. The patient complains of frontal headache, backache, pains in the limbs and photophobia. The

face is flushed, the conjunctivæ injected, the tongue thickly furred with bright-red edges and epigastric pain, nausea and vomiting often ensue. Prostration is severe. Albuminuria occurs on the second day and steadily increases, but bile pigments are not found till later. A rapid, high tension pulse is found at first, but with involvement of the A.V. bundle it slows to 60 to 70 per minute on the third day despite the elevated temperature (Faget's sign); it remains slow during the secondary rise of fever. *Stage of Remission.* This stage is transient and by no means invariably present. It is observed about the third or fourth day, is indicated by a drop in the temperature to 100° F. or lower with amelioration of symptoms, and may terminate in recovery or in recurrence of fever. *Asthenic Stage.* The temperature rises again, but generally does not persist longer than three days. Epigastric discomfort and hiccup may occur. The liver is enlarged and tender and jaundice appears. Petechiæ, melæna and black vomit are not infrequent and there is hypotension and bradycardia. Oliguria is the rule and anuria may ensue in fatal cases. 3. *Fulminating Type.* This is rapidly fatal and is characterised by high fever, petechial or purpuric skin hæmorrhages, oozing from the gums, epistaxis, black vomit, melæna, jaundice, oliguria and anuria. Severe hiccup, muscular tremor and delirium are marked and the patient dies on the third or fourth day from overwhelming toxæmia.

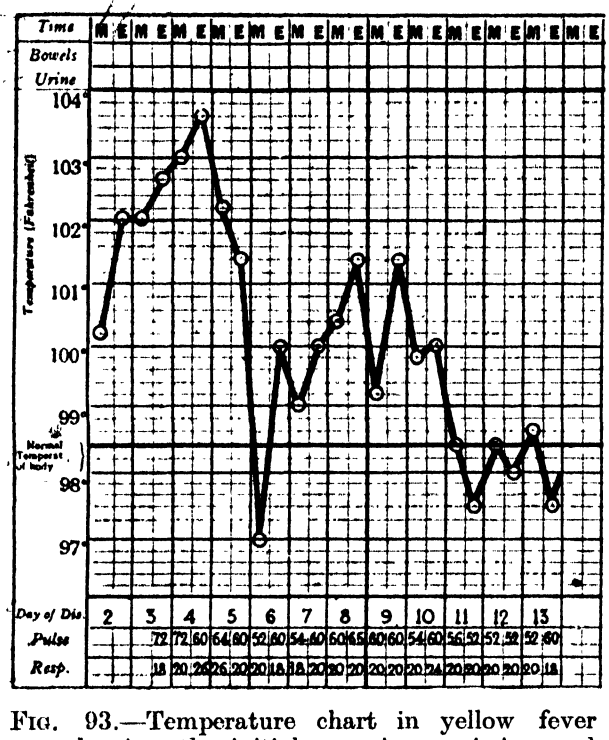


FIG. 93.—Temperature chart in yellow fever showing the initial pyrexia, remission and secondary rise.

Relapses are rare, and as a rule the disease does not last more than ten days; once a normal temperature has been reached a steady progress towards recovery ensues. Complications are not common, but boils, abscesses and jaundice may appear during convalescence.

Diagnosis. The mild cases are difficult to recognise. The inoculation into a susceptible animal of blood collected during the first three days of illness or the demonstration by the mouse protection test of immune bodies in the serum during convalescence enables a diagnosis to be made. In cases of average severity, the early albuminuria, excessive prostration, bradycardia and jaundice about the fourth day associated with a tender, enlarged liver, suggest the diagnosis. In both bilious remittent fever and blackwater fever the jaundice is earlier, splenomegaly is marked and malarial parasites may be present. Hæmoglobinuria is of course characteristic of blackwater. Weil's disease is very similar to yellow fever. Clinically, pain and muscular tenderness are more pronounced, Faget's sign is absent, the jaundice is much more severe and there is a history of occupational or other relationship to rats. It was the confusion of Weil's disease with yellow fever in 1918 which led Noguchi erroneously to attribute the cause of the latter disease to a Leptospira. In relapsing fever with jaundice there is splenomegaly and spirochætes are readily found in the peripheral blood. In dengue there is no albuminuria; leucopenia with lymphocytosis is characteristic, as is the eruption after the third day; jaundice is rarely if ever observed.

Prognosis. In cases of average severity the mortality rate approximates

to 20 per cent. Many mild unrecognised cases, however, occur in every epidemic and these would lessen the apparent mortality. Deep jaundice, severe hæmorrhages, anuria, intractable hiccup and severe nervous manifestations are of grave import.

Prevention. Cases should be treated in mosquito-proof wards, and anti-mosquito measures instituted. Owing to the danger of direct skin infection, doctors and nurses should use rubber gloves when collecting blood from all febrile cases in endemic areas. Vaccination with neurotrophic virus and immune serum results in the production of immune bodies of high titre in the blood and appears safe, though severe reactions may result. Convalescent serum confers only temporary protection.

Treatment. Absolute rest and skilful nursing are essential. Copious fluids are given, but no food is allowed during the acute phases. Glucose and sodium bicarbonate are added to the drinks or given *per rectum*. In severe cases 1 to 2 pints of intravenous glucose (5 per cent.) may be given daily with benefit. Immune serum does not affect the course of the disease once fever has developed. Symptomatic treatment is often necessary. Cold sponging is indicated where the temperature exceeds 103° F., vomiting may be helped by champagne or tincture of iodine *per os*, hiccup by mustard plaster to the epigastrium, and anuria by cupping to the loins and intravenous glucose injections.

DENGUE

(Break-bone Fever, Dandy Fever)

A specific disease, lasting not more than seven days, caused by a filterable virus which is transmitted by the mosquito *Aëdes ægypti*.

Ætiology. Dengue occurs chiefly in tropical countries and to some extent in temperate climates; often it appears in epidemic form but sporadic cases may be encountered. All ages and both sexes are susceptible. The virus is present in the circulating blood during the first three days of fever, and *Aëdes ægypti* feeding on such blood become infected for life, though seven to eleven days must elapse before the bite is infective. One attack does not always confer immunity.

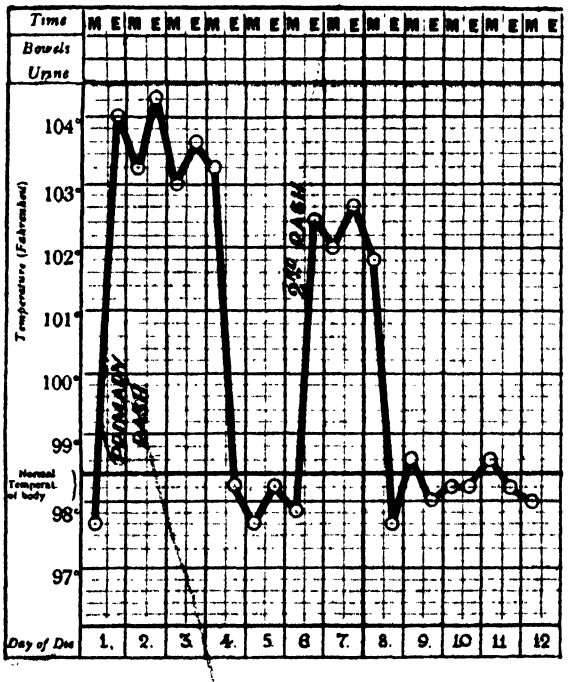


FIG. 94.—Temperature chart in dengue showing the two-phase type of fever.

Symptoms. The incubation period is three to seven days. The onset is sudden with chilly feelings, headache, aching eyeballs and rapidly developing fever (103° to 104° F.). Excruciating pain is often experienced in the back and around the joints; signs of peri-articular inflammation such as redness and swelling are, however, uncommon. The tongue is furred and red at the margin and the throat and conjunctivæ are congested. Within twenty-four to forty-eight hours the skin over the face, neck and chest not infrequently becomes flushed and reddened—the so-called primary rash. Restlessness and insomnia are characteristic, and anorexia, vomiting and constipation may be present. Enlargement of the cervical and epitrochlear glands are features of some epidemics.

The pulse, at first accelerated, soon slows and by the third or fourth day there is a critical fall of temperature to 100° F., or lower, accompanied by sweating and occasionally by diarrhœa or epistaxis. The patient often feels better, but after a period, from a few hours to three days, the temperature rises again and the typical saddle-back chart results. Pains in the limbs and mental depression reappear, and a measly or scarlatiniform rash, which fades on pressure, may implicate the limbs and sometimes the trunk. Desquamation and itching may follow. This so-called secondary rash usually appears from the fourth to the sixth day or earlier and lasts from a few hours to three days. A leucopenia with relative lymphocytosis is very characteristic. The secondary bout of fever generally subsides within two or three days and convalescence is as a rule uneventful. Complications are rare, but hyperpyrexia culminating in heat-stroke may supervene in very hot weather. Mental depression, insomnia and troublesome peri-articular joint pains are occasional sequelæ. Epidemics vary considerably in their clinical manifestations, as do individual cases in the same epidemic. Eruptions are by no means always present, pains in the limbs may not be prominent and considerable variation in the type of fever may be encountered. Occasionally the fever is short, lasting only three days (one-phase type); or it may be continuous for six to seven days, but as a rule there is a terminal rise. In the two-phase type the fever is completely interrupted, thus differing from the typical saddle-back chart in which there is no apyrexial period (**16**). In children, epistaxis and convulsions are more common and the mortality is higher.

Diagnosis. Diagnosis is generally easy during an epidemic; but considerable difficulty may be encountered in differentiating sporadic dengue from sand-fly fever and influenza. The typhus group of fevers and the exanthemata may need consideration, while yellow fever is distinguished by the early albuminuria, profound prostration, jaundice and absence of leucopenia.

Prognosis. The mortality rate is very low, varying from 0·1 to 0·5 per cent. in different epidemics. Deaths are confined to debilitated aged people and young children.

Prevention in dengue consists in the institution of anti-mosquito measures.

Treatment. The patient is kept in bed on a liquid diet. An aperient should be given at the onset and a diaphoretic mixture during the course of the disease. Cold sponging is beneficial where the temperature exceeds 103° F. Aspirin, phenacetin and caffein citrate often relieve the joint pains, but in severe cases morphia may be required. During convalescence a change of climate, liberal diet and tonic treatment are advisable.

SAND-FLY FEVER

(*Phlebotomus Fever, Papataci Fever*)

Sand-fly fever is caused by a filterable virus and transmitted by *Phlebotomus papataci*.

Ætiology. The virus is present in the blood only during the first and second days of the disease, and after the phlebotomus feeds on such blood it cannot transmit the disease until seven days or more have elapsed. This is the period of maturation of the virus in the sand-fly vector which possibly also conveys the virus to its offspring. Sand flies mainly breed under the bark of trees, in the crevices of wood or stony walls and in rockeries, rubbish or rubble surrounding human habitation The disease occurs either in sporadic form or severe epidemics in tropical and sub-tropical countries; it has also been recorded during the hot weather in temperate climates such as Central Europe. At times 90 per cent. of the population may be affected, people of all ages and both sexes being susceptible. After one attack the immunity is said to be more lasting than in the case of dengue.

Symptoms. The incubation period varies from two to seven days and is generally from three to five days. The onset is sudden with chill, headache, fever and pains in the back and limbs. The face and neck are flushed and the conjunctivæ injected, while vomiting, bradycardia and leucopenia with relative lymphocytosis may occur. Actually the clinical picture is indistinguishable from the primary pyrexia of dengue, but secondary rise of temperature and

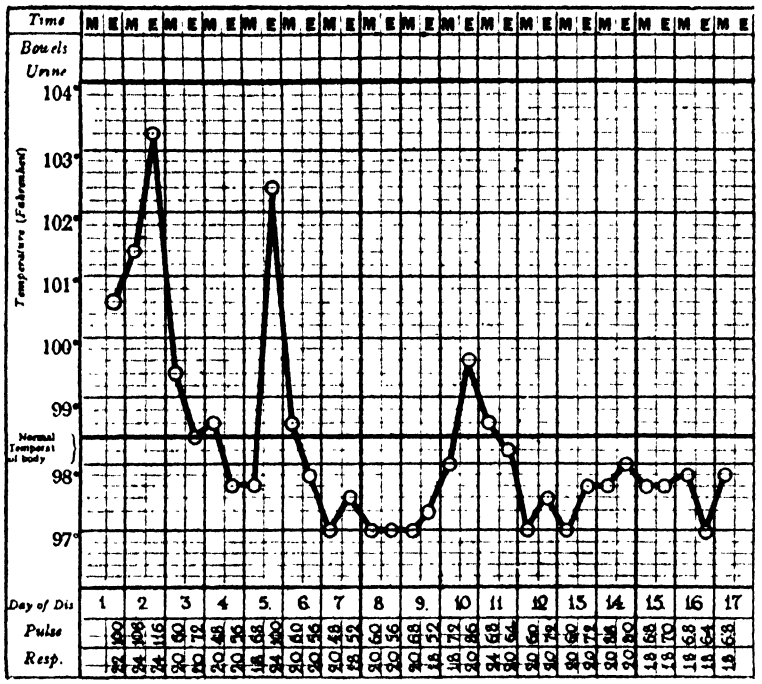


FIG. 95.—Temperature chart in Rift Valley fever showing initial pyrexia and two relapses.

rashes are very uncommon. Complications are rare, convalescence rapid, but mental depression may persist for several days after cessation of fever.

Prevention. The disease is best prevented by destroying the insect vector in its breeding places, spraying lower storey rooms with formalin or " Flit " and using a very fine mesh net at night ; the ordinary mosquito net will not suffice. The *treatment* is identical with that outlined for dengue which in many respects is closely related to sand-fly fever.

Rift Valley Fever. (*Enzootic Hepatitis.*) This is a specific fever of short duration due to a filterable virus occurring in stock in Kenya Colony (**17**) and probably other parts of the tropics. Human beings may acquire the infection by direct contact with infected animals or from handling the virus in the laboratory. In man, jaundice is absent. The fever lasts one to three days but relapses may occur. The only recorded fatal human case died with multiple venous thromboses.

CLIMATIC BUBO

(*Tropical Bulbo, Lymphogranuloma Inguinale*)

A venereal disease caused by a filterable virus.

Ætiology. It affects particularly adult males and is contracted in the tropics from native women. Surgeons have contracted axillary buboes from infection of the fingers when operating on these cases. It is found on the east and west coast of Africa, in China and Japan, and an increasing number of cases are now being recognised in England and on the Continent, where it has been transmitted by white women. The pus is bacteria-free and produces large buboes on subcutaneous injection into guinea-pigs. The virus passes through a

Berkefeld filter and can be transmitted to both mice and monkeys on intracerebral injection.

Pathology. The glands are matted together and on section show a reddish tinge; softening and suppuration frequently occur and cavities may be found filled with muco-pus of a greenish or grey colour. Microscopic examination reveals granulomatous tissue composed of fibroblasts, epithelioid cells which often present a palisade arrangement, polymorphonuclear leucocytes and occasionally giant cells.

Symptoms. The incubation period varies from a few days to three weeks, the primary lesion consisting of small herpetiform ulcers on the penis. Unilateral or bilateral swelling of the median group of inguinal glands follows in from one to six weeks' time. Discomfort, tenderness and possibly pain in the groin, accompanied by fever, first direct attention to the condition. The conglomerated glands are slightly tender and very hard to the touch, being covered by skin which is first red and later bluish-violet. As suppuration advances fluctuation is demonstrable and sinuses result in about 50 per cent. of cases. The iliac glands are frequently palpable as a hard mass above Poupart's ligament, but here extensive suppuration never supervenes.

The general features include fever which is generally of remittent type, anorexia and loss of weight; skin eruptions resembling erythema nodosum are described. The temperature may last many weeks or only a few days, while healing of the glands may be complete within two months or be delayed to one and a half years. Other rare conditions found in women, such as chronic elephantiasis and ulceration of the vulva and inflammatory stricture of the rectum, are ascribed to an infection with the same virus; Frei's intradermal test is said to be positive in these cases (**18**).

Diagnosis. The history of coitus with native women is important. Herpes genitalis resemble the primary lesions, while filarial, septic and tuberculous adenitis, the venereal buboes due to chancroid, gonorrhœa and syphilis, and buboes due to plague, rat-bite fever and tularæmia may need differentiation. Laboratory investigations including culture and section of material obtained at biopsy and Frei's intradermal test may be of great assistance. The latter is regarded as a specific allergic reaction, and is performed by injecting the sterilised diluted pus into the dermis, observations being made in 48 hours. A reddish infiltrated papule of from 7·5 to 20 mm. diameter is required as positive and indicative of infection with the virus of climatic bubo.

Prognosis. Cases are rarely fatal, but in some instances the disease runs a chronic course and lesions may take eighteen months to heal.

Treatment. The patient is rested in bed and given a nutritious diet and tonic treatment. X-ray irradiation may be applied locally to the bubo. Non-specific protein shock therapy is well worthy of trial and is best given as T.A.B. vaccine, commencing with 50 million and increasing to 300 million bacilli in a series of six graded intravenous injections at intervals of three to four days. Early excision may give excellent results, but the femoral chain of glands should be left intact. Where fluctuation is demonstrable the pus should be aspirated under aseptic conditions, the needle being inserted into healthy skin at some distance from the bubo. Excision at this stage may result in secondary infection.

Diseases due to Rickettsia

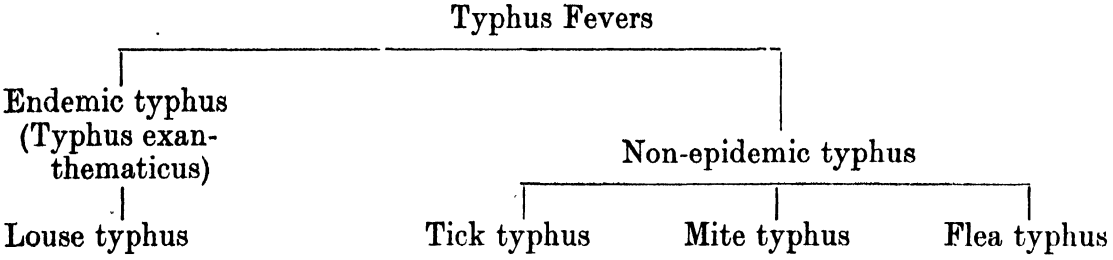
Rickettsia infections only occur in diseases having an arthropod vector and were first described in 1909 by Rickets in Rocky Mountain spotted fever; since then they have been recognised in epidemic typhus, trench fever, Japanese River fever, Brill's disease, tropical typhus affecting man and in heart-water in cattle.

Rickettsia bodies are Gram-negative, bacteria-like organisms of small size

(0·2 μ — 0·5 μ × 0·3 μ), showing a marked tendency to pleomorphism. They are found both in the epithelium of the gut and excreta of the arthropod vectors as well as in the blood and endothelial and other cells in human tissues where they have an intracellular location.

The great importance of Rickettsia bodies lies in their causal relationship to the rapidly expanding typhus group of fevers. Ordinary typhus is transmitted directly from man to man by lice, while the non-epidemic forms are primarily diseases of rodents, being transmitted to man by fleas, ticks and mites.

The classification of this group is at present best based on the insect vector as suggested by Megaw (**19**).



The Weil-Felix Reaction (20). This serological reaction is of considerable value in recognising both the epidemic and the non-epidemic forms of typhus, and depends on the fact that certain coliform organisms of the Proteus group are agglutinated by the sera of typhus patients. Two strains of organism are now being used, *B. proteus* X19 and *B. proteus* XK ; agglutination reactions of 1/100 are diagnostic and generally become evident during the second week of the disease. The titre may rise as high as 1/30,000 during convalescence and the reaction may remain positive for several months. A strong positive reaction to X19 suggests louse or flea typhus and a strong positive to XK favours mite typhus, while a negative or weak response to both strains fourteen days from the onset of a typhus-like fever supports the diagnosis of tick typhus.

LOUSE TYPHUS

(*Endemic Typhus ; Typhus Exanthematicus ; Jail Fever*)

Typhus fever is a louse-borne disease occurring in epidemic form and probably caused by *Rickettsia prowazeki.*

Ætiology. This is the only form of typhus which occurs in epidemic form, and until 1837 it was not differentiated from typhoid fever. It was not uncommon last century in England, Scotland and Wales ; it is now no longer encountered. During the Great War there were extensive outbreaks in Russia and Germany. It may occur at any time in the colder climates of Europe or during the cool weather in hot countries such as Egypt and Palestine ; in India it is only found in the Himalayas and in North-West plains, but not further South in the tropics proper, as lice do not survive such heat. There is no racial immunity, people of any age may be attacked and one attack generally confers immunity. Filthy surroundings, over-crowding, under-feeding and famine conditions favour its spread. Human blood collected during the febrile period is infective to monkeys, but the infective agent does not pass through Berkefeld filters. Nicolle and Conseil demonstrated the transmission of typhus by infected lice, but it is probable that human infection actually takes place by the rubbing of the excreta through abrasions in the skin rather than directly by biting. Lice become infected five to ten days after feeding on typhus blood and once infected remain so for life ; in the epithelial cells lining their alimentary tract *Rickettsia prowazeki* is found. Rickettsia is also demonstrable in the endothelial cells of the smaller blood vessels in human cases.

Pathology. The spleen is soft and possibly enlarged in the early stages,

while the liver and kidneys show cloudy swelling and the heart muscle is degenerated. Broncho-pneumonia is not infrequently terminal. The characteristic lesions which were described by Fraenkel in 1914 consist of proliferation of the endothelial lining of the arterial and capillary walls, followed by necrosis and perhaps perivascular infiltration with lymphocytes and plasma cells. Typhus pseudo-tubercles are thus produced and may be found in the skin, viscera and brain, where they especially involve the basal ganglia, medulla and cortex. Thrombosis of the smaller skin vessels accounts for the petechial eruption.

Symptoms. The incubation period is generally from eight to twelve days, the extremes being five to twenty days. Prodromata include general malaise, nausea and anorexia. The onset is frequently sudden with chilly feelings or shivering, fever, frontal headache, pains in the back and limbs, and, more rarely, vomiting and epigastric pain. Drowsiness and apathy are marked even early

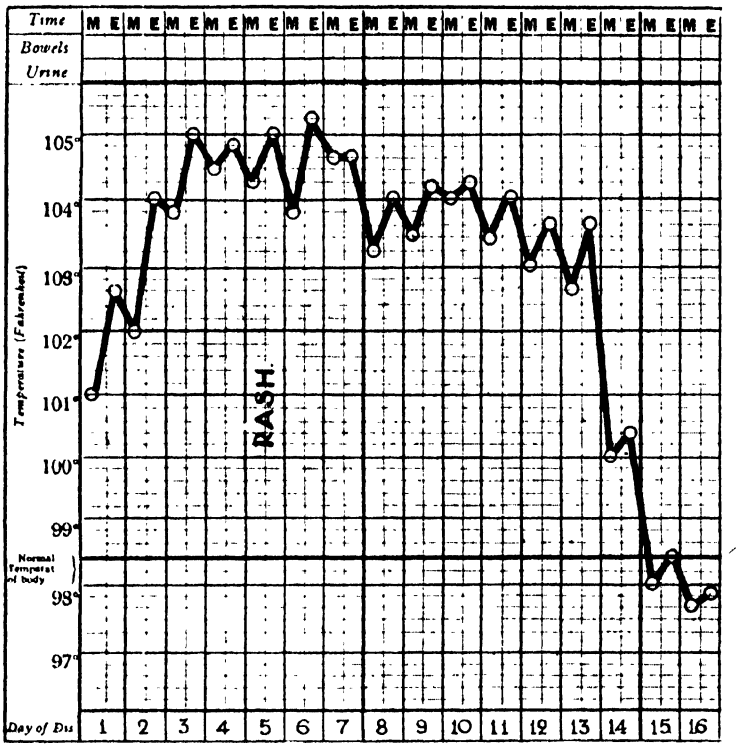


FIG. 96.—Temperature chart in louse typhus showing continuous fever with fall by crisis on the thirteenth day.

in the disease. The mentality is dulled, the face is flushed, the conjunctivæ congested and the tongue coated; constipation is marked. The temperature usually reaches its fastigium about the third day, and for the next eight to twelve days continuous fever is the rule (Chart IV.). Then remissions occur, and the temperature finally reaches normal by rapid lysis or crisis some twelve to sixteen days from the onset. Occasionally the temperature is of remittent type from an early stage in the disease. About the fourth or fifth day the rash appears as a rose-red macular or papular eruption which at first fades on pressure, but later frequently becomes petechial. It is often first seen in the axillæ and loins and later involves the whole trunk and generally the legs and arms, but not the face. In fulminating cases purpuric patches appear. The rash itself lasts a variable period from several days to two weeks. Toxic manifestations become established early and stupor may give place to a typhoid state with or without delirium as early as the fifth day; symptoms of meningismus with neck retraction may be superadded and simulate meningitis. As the disease progresses the tongue dries and sometimes becomes black in colour, sordes develops on the teeth, the pulse becomes more rapid and weak, cardiac sounds are distant

and the blood pressure low. Myocardial failure may supervene, while cough accompanied by moist sounds at the bases of the lungs are not infrequent during the second week. Constipation is a marked feature of the disease, but diarrhœa occasionally replaces it in severe cases.

Laboratory investigations may be of value. Little change is noted in the red cell count, but a mild leucocytosis with neutrophilia is not infrequent. The cerebro-spinal fluid is under increased pressure and shows an excess of lymphocytes and globulin. Most important of all, during the second week the serum almost invariably agglutinates *B. proteus* X19.

Complications are by no means infrequent and include bronchitis, broncho-pneumonia, thrombophlebitis of the femoral and other veins, arterial thromboses with gangrene of the extremities, particularly of the toes and feet, parotitis, otitis media, deafness and bed sores.

Diagnosis. During epidemics little difficulty is experienced, while in sporadic cases the stigmata of intoxication, the temperature chart and the rash will suggest the diagnosis which should receive serological confirmation later.

Prognosis. The death rate, which varies in different epidemics from 10 to 30 per cent., is particularly high in the aged and low in children. An early typhoidal state, a purpuric eruption and complications like broncho-pneumonia and thrombosis are of serious significance.

Prevention consists in the destruction of body lice and preventing skin contact with these infected arthropods.

Treatment. The patient must be nursed in the recumbent position and allowed plenty of fresh air and fluids. Particular care should be taken of the hygiene of the mouth, constipation should be controlled by enemata and bed sores prevented. A fluid diet including fruit juices, glucose, milk and broths should be administered and the fluid intake reinforced where necessary by nutrient enemata and intravenous glucose solution (5 per cent.). Cool sponging is advisable both to lower the temperature and for sleeplessness and other nervous manifestations; brandy and sedatives like morphia, chloral and hyoscine may also be necessary. The withdrawal of cerebro-spinal fluid by lumbar puncture may relieve the meningismus and is a rational procedure, while in adults convalescent serum should be given if available.

Tick Typhus. The best known form of tick typhus is Rocky Mountain or spotted fever which occurs in North America, but other typhus-like fevers transmitted by ticks are encountered in India, South Africa, Kenya, Nigeria and the Mediterranean coast. The Weil-Felix agglutination reaction does not appear to be of the same value in this group of diseases, as it is so frequently negative or only positive in low titre.

ROCKY MOUNTAIN FEVER

(*Spotted Fever; Black Fever; Blue Disease*)

The disease has a limited geographical distribution in Northern America, mainly occurring in the Rocky Mountain regions at 3,000 to 4,000 feet. The infective agent is a Rickettsia organism (*Dermacentroxenus rickettsi*) which has been found in infected ticks of the species *Dermacentor andersoni* or *venustus* as well as in infected human beings. The natural hosts are wild rodents, including ground and mountain squirrels and chipmunks. The disease can be experimentally inoculated into guinea-pigs which give a positive Pinkerton-Mooser reaction characterised by septicæmia, orchitis and an effusion into the tunica vaginalis containing Rickettsia bodies. One attack of the disease confers immunity, but not to louse typhus.

Pathology. The morbid anatomy is similar to louse typhus, but proliferation of vascular epithelium more often leads to thrombosis and gangrene.

Symptoms. The incubation period varies from four to twelve days, and the

general course and clinical picture is similar to louse typhus. The rash, however, is more conspicuous and appears from the second to the fifth day on the wrists, ankles and back, subsequently extending to the face, palms and soles, which is not the case in louse typhus. The spleen also is commonly enlarged, epistaxis and jaundice are not infrequent, while the fever tends to be more prolonged, and to show more conspicuous remissions during the fastigium; often an intermittent type of fever develops a few days before lysis. Early albuminuria and a leucocytosis with an increase in monocytes are found.

Gangrene of the scrotum, prepuce, fingers, toes and tonsils may occur even in mild cases; broncho-pneumonia is less frequent than in louse typhus, but otherwise the complications are similar in the two diseases.

Diagnosis. The diagnosis may be confirmed by a positive Pinkerton-Mooser reaction in an inoculated guinea-pig. The Weil-Felix reaction to X19 and XK is at most only weakly positive. Cerebro-spinal fever may be differentiated by examination of the spinal fluid.

Prognosis. The mortality varies markedly in different regions.

Treatment. The avoidance of tick bites in infected regions and cauterisation with carbolic acid when they are known to occur are the best prophylactic measures. Medicinal treatment follows the lines outlined for louse typhus.

TICK TYPHUS IN INDIA

A fever of the typhus group resembling Rocky Mountain fever in many respects and probably transmitted from wild rodents by ticks.

Ætiology. The disease is endemic in the central plateau of India in the cold season at a height of 1,500 feet and in the Himalayas at an altitude of 4,000 feet during the summer and autumn. Most of the recorded cases have been in Europeans. The usual vector appears to be *Rhipicephalus sanguineus* (**21**), but this has not been proved.

Symptoms. The incubation period is generally seven to twelve days. There is the usual rapid onset with a step-like rise in temperature and fever lasting ten to sixteen days; the rash appears on the third to the fifth day and consists of rose-red macules or papules fading on pressure. As with other forms of typhus the spits become dark red, then brown and then no longer fade on pressure; brown staining may persist for some weeks. The arms and legs are first involved and subsequently the palms and soles as well as the trunk and face. Petechiæ and purpuric eruptions may be encountered. Nervous prostration is marked, but jaundice is rare. The Weil-Felix is negative or only slightly positive (1/80 to 1/100) to proteus X19; there is a moderate leucocytosis with increase in the mononuclears, but unlike Rocky Mountain fever, guinea-pigs do not appear susceptible to experimental inoculation.

Diagnosis. The occurrence of a typhus-like fever in endemic areas will suggest the diagnosis.

Prognosis. The disease is less severe than Rocky Mountain fever, the probable mortality being about 5 per cent.

Treatment. This is similar to that outlined for louse typhus.

Mite Typhus. Originally the type of typhus fever known as tsutsugamushi or Japanese River fever, transmitted by the bite of larval mites, was thought to have a geographical distribution restricted to certain rivers in Northern Japan, but later it was found in Formosa and Korea. It is now known to occur in other places in the Far East, including the Federated Malay States and Sumatra, and probably in China and Australia as well. Not all cases of mite typhus, however, conform to the clinical picture of Japanese River fever, and probably there are a number of different though allied diseases in this group. For example, in the scrub typhus of Malay no primary sore or lymphangitis is encountered, while the pseudo-typhus of Sumatra has a much lower mortality

rate ; in addition, both these diseases are transmitted by the *Trombicula deliensis*, whereas in Japanese River fever the arthropod vector is *Trombicula akumushi*.

JAPANESE RIVER FEVER

(*Tsutsugamushi ; Kedani Mite Disease ; Flood Fever ; Akumushi Disease*)

This disease affects both sexes of all ages and is particularly common in hemp harvesters in the island of Nippon, in Japan, in Korea and Formosa. *Rickettsia nipponica* is the probable cause and is transmitted by the larval mite *Trobicula akumushi*, which often attaches itself to the skin for two or three days ; local necrosis and ulceration ensue, followed by tender enlargement of the related lymphatic glands.

Pathology. Myocardial softening, pulmonary congestion, bronchitis and splenomegaly, in addition to local ulcers and adenitis, have been described.

Symptoms. Some five to fourteen days after a mite bite the patient develops a shiver associated with headache, giddiness and fever which is at first of continous and later of remittent type, lasting two to three weeks. Locally, a small ulcer is found associated with a dark areola, lymphangitis and tender enlargement of the corresponding lymph glands. The rash appears from the fifth to the seventh day and consists of red macules and papules about 0·5 cm. in diameter. The arms, legs, trunk, face, palms and soles may all be involved. Petechiæ rarely, if ever, occur. The spleen may be enlarged and the usual cardiac, pulmonary and nervous manifestations common to the typhus group of fevers occur. There is a leucopenia associated with a decrease in the neutrophils, and the Weil-Felix reaction is strongly positive to *B. proteus* XK but not to X19.

Prognosis. The mortality varies from 5 to 60 per cent. in different areas.

Treatment. The destruction of field rodents, and the prevention of mite bites by suitable clothing, daily bathing and the removal of mites are important preventive measures. Medical treatment follows the lines outlined for louse typhus.

Flea Typhus. There are two main recognised types of typhus transmitted by fleas—Brills' disease in the United States of America, and the urban form of tropical typhus in Malaya affecting people working in stores ; the reservoir of infection is probably the rat in both instances and the vector the rat flea, *Xenopsylla cheopis*. The sera in both diseases give strongly positive Weil-Felix agglutination reactions to *B. proteus* X19.

Both are non-epidemic in type, while clinically they are allied to mild cases of louse typhus, the mortality is low and does not exceed 2 per cent. In Brills' disease there is a rapid onset of continuous fever with a maculo-papular eruption about the fifth day, which rarely if ever becomes purpuric ; the fever terminates by crisis about the fourteenth day. Frontal headache, apathy and prostration are marked as in louse typhus.

Nicolle regards marine typhus occurring in the crews of French warships as being transmitted by rat fleas from infected rats, and Megaw points out that certain of the typhus-like fevers occurring along the Mediterranean coast and in the Far East and Australia may ultimately be found to fall into this category.

Bacterial Diseases

A number of bacterial diseases occurring commonly in the tropics are also found in Europe, and one important group, the enteric fevers which include typhoid and the paratyphoid fevers, has been dealt with in another section (p. 71).

BACILLARY DYSENTERY

Bacillary dysentery is an acute specific colitis caused by various dysentery bacilli which can be isolated from the stools.

Ætiology. The organisms causing dysentery are the Shiga-Kruse bacillus

isolated in 1897, which does not ferment mannite, and the mannite-fermenting Flexner Y bacilli, of which there are five serological strains known as V, W, X, Y and Z. In addition there is Sonne's bacillus which is a late lactose fermenter.

All ages, races and both sexes are susceptible, but the disease is much more frequently encountered in the tropics and sub-tropics than in temperate climates. Outbreaks of Flexner dysentery, however, do occur from time to time in military barracks, prisons and asylums in Europe, and organisms of this type are responsible for many cases of summer diarrhœa in children. The mode of spread is by fæcal contamination of food and water from an infected individual or by house-flies. Overcrowding, deficient diet and malnutrition predispose to infection. In the tropics its greater incidence is in the early summer, autumn and the rainy season. During the South African War the troops were decimated with this disease, and in the Eastern theatres of the World War, dysentery in epidemic form occurred, as in Gallipoli, with serious consequences.

Pathology. In bacillary dysentery there is an acute fibrinous colitis, the rectum, sigmoid flexure and cæcum being most intensely involved, while in the most severe cases the lower 2 or 3 feet of the ileum may also be implicated. The liver is congested and enlarged, the mesenteric glands reddened and swollen and emaciation marked. Outstanding features are the superficial nature of the inflammation and the fact that the mucous membrane is uniformly involved. At first, the mucosa appears red and congested; sometimes it shows petechial hæmorrhages and is often covered with muco-sanguineous exudate; in acute fulminating Shiga infections large areas of colonic mucosa may be rapidly converted into a green, gangrenous membrane. As the inflammation progresses the mucosa becomes infiltrated with fibrin and a patchy coagulation necrosis results; exfoliation produces transverse or irregular, serpiginous ulcers situated for the most part on the swollen mucosal folds, which are separated by thickened, œdematous, congested mucous membrane. When recovery ensues healing takes place without scarring. Occasionally cases of chronic dysentery have been described showing thickening and rigidity of the bowel wall and a granular bleeding mucosa with isolated ulcers. Such a condition is indistinguishable from chronic ulcerative colitis of temperate climates which a minority opinion also attributes to infection with dysentery bacilli.

Symptoms. The clinical features vary within wide limits according to the resistance of the patient and the virulence and type of the causative organism. Some infections are often mild, Flexner Y of moderate severity, and Shiga most grave. As in cholera, toxæmia and dehydration may each play an important *rôle* in the production of the clinical picture.

The *typical* case presents a sudden onset with fever, possibly preceded by a chill and generally followed by headache, nausea and vomiting. Colicky abdominal pain, the frequent passage of small, muco-sanguineous stools and tenesmus due to sphincteric spasm are characteristic. The bowels may be open four to fifty times in the twenty-four hours and Manson's descriptive phase, "glued to the commode," not inappropriately describes the condition. As toxæmia increases, the cheeks become flushed, the expression anxious, the fever greater, the pulse more rapid and the tongue coated and yellow. Restlessness, mental confusion, sleeplessness and delirium may develop. With dehydration there is an increase in these nervous symptoms associated with thirst, pinched features, sunken eyes, a dry brown tongue, oliguria, urea retention, collapse of the peripheral veins, muscular cramps, a feeble, rapid pulse and low blood pressure, and in infants depression of the fontanelles. Where acidosis develops the breathing becomes deeper, more rapid and even irregular. The severest cases may simulate cholera and die in a state of collapse with sub-normal temperature, shrivelled skin and cold, blue extremities. Mild catarrhal cases, on the other hand, may be afebrile and be mistaken for simple diarrhœa, culture being necessary to demonstrate the true nature of the infection.

The appearance of the *stools* varies with the severity and stage of the disease. Early, they may be of fluid consistency, brownish or brownish-red in colour and soon contain glassy mucus ; alternatively they may be frankly muco-sanguineous from onset. Later they become muco-purulent and only as the inflammation subsides do they assume fæculent characters ; finally, solid stools with a mucous coating are passed. Microscopic examination shows that the exudate contains red blood corpuscles, numerous polymorphonuclear leucocytes, desquamated columnar epithelial cells and large macrophage cells which resemble non-motile amœbæ and are often mistaken for *E. histolytica.*

If cultures are to be successful, specimens must be collected as soon after the onset of fever as possible. Martin and Williams (**22**) found that 68 per cent. were positive when specimens were examined within the first five days of the disease, 17·4 per cent. in the second five days, and only 6·3 per cent. in the third five-day period. Furthermore, stools sent to the laboratory for investigation must contain mucus, for it is from such exudate that the bacilli are cultured ; finally, the specimen must be absolutely fresh and uncontaminated by urine or antiseptic, otherwise growth is impeded or impossible.

Examination of the patient in the early stages may reveal rigidity of the abdominal muscles, but localised pain and tenderness are infrequent owing to the absence of peritoneal involvement. Later the contracted sigmoid may be palpable. The temperature is remittent at first and sometimes intermittent subsequently, but with proper treatment generally subsides within seven to fourteen days. Continued fever implies persisting infection, either with dysenteric organisms or secondary invaders.

In *entero-dysentery,* where the small intestine is involved, the rectum and sigmoid may escape ; in these circumstances tenesmus is absent and the stools are not so typically colonic in type. The onset is sudden, toxic features, including vomiting, are marked ; the temperature is high, the mouth covered with sordes, while a typhoidal state may rapidly supervene. In the most severe cases choleraic-like stools are passed and the patient may die quite early with collapse symptoms.

Complications. Since the dysentery bacilli only invade the superficial lining of the gut, local complications such as perforation and stricture are not encountered ; septicæmia rarely, if ever, occurs, and hæmoculture is negative. A toxic arthritis involving the large joints such as knees, ankles, elbows, shoulders and wrists is not infrequent ; it takes the form of effusions into the joints and peri-arthritis, and especially occurs during convalescence from Shiga infections. Its onset, which is generally within the first three or four weeks, may be longer delayed ; it lasts a variable time, but rarely leads to permanent deformity. The aspirated fluid is almost invariably sterile on culture, though in very rare cases Shiga bacilli have been isolated. Acute conjunctivitis, iridocyclitis and iritis are also uncommon. They are of toxic origin and usually clear up without leaving any permanent damage. Parotitis, bronchial pneumonia, and multiple neuritis are rarer complications and terminal intussusception has been recorded in children.

Course. Fulminating cases die rapidly from toxæmia and dehydration, but in the absence of complications and with appropriate treatment ordinary cases become afebrile in two weeks. Occasionally, however, cases last two or even three months with remittent or intermittent fever, sweating, marked colonic distension and frequent muco-purulent stools ; intense weakness and emaciation develop, death ensuing from toxæmia and intercurrent disease. In other instances the disease becomes chronic, but as a general rule the natural tendency in all types of bacillary dysentery which are properly treated is towards complete recovery without any permanent structural alteration in the colon. Irritable colon is a not infrequent sequela of bacillary dysentery, and this is largely responsible for the misconception that chronic dysentery is a common disease.

Chronic Dysentery. When bacillary dysentery becomes chronic there is almost invariably a history of neglect on the part of the patient or of lack of appropriate treatment. In these circumstances the bowels act more frequently than usual, are foul smelling, generally contain mucus and pus and sometimes blood. Afebrile intermissions may occur in which the stools are normal, but generally mucoid stools persist and the patient does not feel he has made a complete recovery. Febrile exacerbations with frequent dysenteric stools recur, and in the later stages emaciation, anæmia, trophic changes in the skin and œdema of the feet develop. The abdomen becomes scaphoid and the colon palpably thickened and tender; bed sores and intercurrent infections like pneumonia are liable to develop. Dysentery bacilli are isolated with difficulty, Cunningham (**23**) being successful in only 26·7 per cent. of his Indian cases. In many respects the remittent type closely resembles chronic ulcerative colitis of temperate climates, but the ætiological relationship of the latter disease to the Flexner Y. group of organisms is far from proven, and much work needs to be done on both these diseases before they can be regarded as identical.

Diagnosis. Little difficulty is experienced in diagnosing severe Shiga cases, though one type may simulate cholera. Trouble may arise with *Flexner Y* and *Sonne infections*, and these may need to be differentiated by laboratory methods from amœbic, bilharzial and ciliate dysentery, though an acute onset with fever, marked urgency of bowel symptoms and frequent mucoid stools containing bright blood support the diagnosis of bacillary dysentery. Carcinoma of the pelvic colon may cause confusion in chronic cases and sigmoidoscopy or X-ray examination after a barium enema may become necessary for their differentiation.

Sigmoidoscopy is rarely indicated in the acute stages when the bowel shows a uniformly diffuse reddening and hyperæmia associated with white or greenish necrotic membrane and muco-sanguineous exudate. Later, as the membrane separates, superficial serpiginous ulcers more or less transversely situated on the mucosal folds may be observed surrounded by acutely inflamed mucous membrane. In chronic dysentery these ulcers are said to persist and deepen and the mucosa to be largely replaced by granulation tissue showing a red, hyperæmic, granular surface, bleeding readily on instrumentation. The bowel walls then become rigid and spastic, the sigmoidoscopic picture resembling that of idiopathic ulcerative colitis of temperate climates. The history of onset during an epidemic is suggestive, and the isolation of dysentery organisms from the mucoid stools during the acute or later stages will establish the diagnosis.

Prognosis. Shiga dysentery is a very serious disease, and prompt treatment with anti-dysenteric serum and measures to combat dehydration are necessary to save life. Healthy adults with Flexner dysentery generally recover, but children, the ill-nourished and the aged not infrequently succumb.

Prevention. As the disease is spread by contamination of food and water by infected individuals and flies, similar measures to those adopted in enteric fever should be instituted. Prophylactic vaccination has unfortunately not proved successful.

Treatment. Treatment is directed to resting the bowel by a low residue diet and combating toxæmia and dehydration. Good nursing, continuous bed rest and warmth in a cold climate are essential. A preliminary dose of oleum ricini (½ ounce) with tinct. opii (15 minims) should be given, followed by sodium sulphate (1 drachm) given at first two-hourly, then three-hourly and finally four-hourly as the stools improve and until they become fæculent. Only boiled water is permitted for the first twenty-four to forty-eight hours, then lactose, glucose and albumin and barley water followed by meat juice, clear soups, jellies and sprulac. Arrowroot and sago puddings are given later, but milk is never well borne and is contra-indicated. Specific anti-dysenteric serum should be given at once in doses of 80 to 120 c.c.—especially in Shiga infections—

and this decision must be made immediately on the clinical aspects of the case and the naked eye and microscopic features of the stools. When circumstances permit, the patient should be tested for hypersensitivity to horse serum, and, if positive, desensitisation with small initial doses carried out. In toxic cases, gentle colonic lavage with 1 to 2 pints of saline (0·85 per cent.) and bicarbonate (1·5 per cent.) may be used to reinforce the action of sodium sulphate in relieving intestinal toxæmia. Fluid loss must be combated by intravenous injections of glucose (5 per cent.) or hypertonic saline solution as in cholera. Symptomatic treatment includes turpentine stupes and hot fomentations to the abdomen, morphine ($\frac{1}{6}$ gr.) and tinct. opii (15 minims) for griping, and opium and starch enemas for tenesmus. Gaseous distension of the abdomen may be relieved by giving adsorbents like animal charcoal and kaolin by mouth.

Chronic Dysentery. A high calorie, high vitamin, low residue diet is advisable. Rectal lavage with the following solutions are worthy of trial: saline (0·85 per cent.), bicarbonate (1·5 per cent.), yatren (1 in 40), tannic acid (1 per cent.), potassium permanganate (1 in 5,000), etc. Daily injections of 4 to 8 ounces of a 5 per cent. suspension of bismuth subgallate in olive oil, if tolerated, may prove beneficial. Specific treatment in the form of anti-dysenteric serum is not as effective as in acute dysentery. Appendicostomy permits colonic lavage from the cæcum, and cæcostomy or ileostomy affords rest for the large bowel. Operation should, however, only be undertaken in intractable cases where all other measures have failed. Iron in adequate dosage and blood transfusion are of great benefit if anæmia be present, and acid hydrochl. dil. B.P. (1 drachm) should be given thrice daily after food where acid secretion is defective.

CHOLERA

Cholera is an acute specific disease of the small intestine due to Koch's comma vibrio.

Ætiology. Cholera has been endemic in India for many centuries, and epidemics arise in the spring and summer mainly through the movements of pilgrims. Occasional outbreaks have occurred in Asia, Europe and America since 1817. The *Vibrio comma* or *Vibrio choleræ*, which was first discovered in Egypt by Koch in 1883 (**24**), is passed in the stools of carriers, and in this way infects food and water. Flies also disseminate the disease by fouling food, such as sweetmeats and milk, with infected fæces. All races, both sexes, and individuals of all ages are susceptible. Generally cholera vibrios disappear from the stools of convalescents within five days, and only 7 per cent. of patients remain carriers for more than ten days after an attack. Persistent carriers are very rare, but occasionally healthy contacts become carriers without having suffered any bowel disturbance. Though vibrios exist in great numbers in the small intestines, they are not demonstrable in blood cultures. They have been found in limited numbers in consolidated areas in the lungs and other internal organs and have a special predilection for the gall-bladder which may be inflamed. Soluble exotoxins and endotoxins are produced by the vibrios, but only low titre anti-sera have to date been produced by animal inoculations.

Pathology. Rigor mortis sets in early. On opening the abdomen the small intestines are found shrunken and collapsed, the mucous membrane is intensely congested and may show petechial hæmorrhages. Enlargement of the lymphoid follicles in the ileum may also be present. The liver is congested and the gall-bladder distended with viscid, thick bile. The spleen is shrunken and the lungs collapsed and dry. The kidneys are swollen and congested, sometimes showing minute hæmorrhages, while the blood is viscous and tarry. The stools rapidly assume their "rice-water" appearance and several quarts may be passed in a few hours. The fluid is neutral or slightly alkaline in reaction with a specific gravity of 1,006–1,013, and contains sodium chloride, albumin and

mucin. On standing it deposits a finely granular, greyish-white sediment consisting of epithelium, leucocytes, shreds of tissue, crystals of ammonium-magnesium phosphate, blood corpuscles and vibrios. The absence of colour is due to dilution and to the fact that the bile becomes viscous like treacle and cannot be expelled from the gall-bladder. In consequence bile pigment does not reach the duodenum and the normal fæcal pigment, stercobilin, is not produced in the intestine. There is increased viscosity of the blood, the specific gravity increasing from the normal 1,056–1,058 to 1,063 or more; biochemical analysis shows reduced blood chloride, decreased plasma CO_2, and urea and phosphate retention. Hæmatocrit investigations reveal a plasma loss of over 35 per cent. in mild and 64 per cent. in severe cases and a polycythæmia of from 6 to 8 million red cells per c.mm. results. Marked leucocytosis is also common, the counts varying from 15,000 to 50,000 per c.mm. The urine is markedly decreased in quantity, and contains albumin and casts. Anuria may rapidly supervene from inabilty of the heart to maintain the renal circulation owing to decreased blood volume and the increased viscosity of the blood.

Symptoms. *Onset.* The incubation period is generally two to five days. During an epidemic individual cases may show considerable variation in their severity and clinical manifestations, though the majority of them (95 per cent.) conform to the type known as *cholera gravis.* Here the onset is usually sudden, and in a few hours the stools lose their fæculent character and come to resemble "rice-water." Some authorities describe an initial phase lasting twenty-four hours in which there is looseness of the bowels, colic, headache, vomiting and mental depression, but this is not characteristic of the Indian epidemics.

Collapse or Algid Stage. Following the initial purging, which is accompanied by borborygmi but by little colicky pain, vomiting first of food and later of "whey-like" fluid commences. The patient suffers from thirst, the tongue, which was at first coated and white, becomes dry and the epigastrium tender. Painful muscular cramps appear in the legs; the temperature becomes markedly subnormal and the collapse or algid stage, due to fluid and chloride loss and tissue dehydration, sets in. The face is pinched, the skin cold, blue and shrunken, the eyes sunken and the breath loses its warmth. The axillary temperature falls 4° or 5° F. below normal. The pulse, from 90 to 100 per minute, is small, thready and almost imperceptible, the respirations are short and quick—from 35 to 40 per minute. There is profound muscular prostration, but the patient restlessly throws his limbs about in purposeless fashion. The voice is harsh, or may be lowered to a whisper (vox cholerica), or the lips only may move in a mumbled attempt to speak. The systolic blood pressure falls to 50 to 70 mm., while the peripheral veins are collapsed and urinary secretion diminishes or ceases altogether for thirty-six to forty-eight hours. Generally the patient retains complete consciousness though lying apathetic and indifferent except when aroused by painful muscular cramps. This stage, which begins six to seven hours after the first symptoms, generally lasts twelve to twenty-four hours, and is succeeded by the stage of reaction unless the patient dies without rallying.

Stage of Reaction. There is a gradual rise in the skin and mouth temperatures, and a general improvement in the circulation with increase in the blood pressure and urinary output. Restlessness and cramps disappear, the skin gradually regains its natural colour and loses its shrunken appearance, the conjunctivæ are injected and congested patches of dusky redness appear on the face. If the circulation be restored the only danger is that absorption of cholera toxin may lead to hyperpyrexia and death. On the other hand, if the circulation be inadequate to restore renal function, anuria will persist and uræmia result. Should the stage of reaction go on to recovery, convalescence is often slow and may be delayed by complications.

Clinical Varieties. Mild or *ambulatory* cases may occur in which the

disease does not pass beyond a stage of diarrhœa, but vibrios are nevertheless present and such patients act as carriers during an epidemic. A more severe form, *choleraic diarrhœa*, begins suddenly with abundant yellowish-brown fluid stools containing epithelium, associated with borborygmi and cramps in the calves, and may last from a few days to one or two weeks. *Cholerine* is a still nearer approach to *cholera gravis :* the onset is sudden, vomiting accompanies the purging and the fæculent stools may gradually become colourless ; cramps, cooling of the extremities, scanty urine with albumin and casts appear. Recovery is slow. In *cholera sicca* the stage of collapse sets in immediately, and the patient dies before purging commences, though at autopsy there is abundance of watery stools in the alimentary canal.

Complications and Sequelæ. Cardiac failure may occur in convalescence after slight exertion, and parotitis, nephritis, broncho-pneumonia and enteritis may call for special treatment. Before the introduction of intravenous injections for dehydration, sloughing of the cornea and gangrene of the fingers, toes and genitals were commonly enough encountered. Abortion and premature delivery are not infrequent in severe cases.

Diagnosis. Little difficulty arises during an epidemic, but in atypical or sporadic cases isolation of the *Vibrio choleræ* is essential. The differential diagnosis includes the choleraic forms of heat-stroke, malaria and bacillary dysentery, cholera nostras, ptomaine, arsenic and perchloride of mercury poisoning, the early stages of trichiniasis infestation and poisoning by certain mushroom-like fungi. *Cholera sicca* may prove indistinguishable from meningitis until lumbar puncture is performed ; muscular rigidity, retraction of the abdomen and a positive Kernig's sign may be present in both diseases.

Prognosis. Cholera is exceedingly fatal in the very young and the aged, and in pregnant, debilitated or alcoholic subjects. Unfavourable features include prolonged collapse with excessive sweating, prostration, cyanosis, absence of pulse at the wrist and markedly sub-normal temperatures ; cardio-vascular failure, uræmia and hyperpyrexia are of grave significance. Oliguria after the collapsed stage, especially if associated with much albumin, casts and a low urea excretion, is unfavourable and careful urinary measurement should always be made. Where modern treatment cannot be applied, the mortality varies from 40 to 60 per cent., and is greater at the beginning of the epidemic than towards the end. On the other hand, if cases be treated in hospital with modern methods, the mortality is reduced to approximately 11 per cent. (**25**).

Prevention. During epidemics injections of cholera vaccine should be given as they afford temporary immunity for a period of about six months. Unboiled milk, uncooked food, salads, raw fruit and unboiled water must be rigidly avoided. Houses should be fly-proof, all food must be covered, and drinking and eating utensils washed in boiling water and dried by heat. Purgatives should be avoided during epidemics as this may predispose to infection and even the mildest gastro-intestinal disturbance should receive careful attention.

Treatment. The patient is practically starved for the first few days and kept strictly at bed rest ; only boiled water, barley water and glucose are allowed. Kaolin given in a strength of 1 in 3 in water has been given in almost unlimited amounts with the idea of adsorbing cholera toxin. Calcium permanganate pills, 2 grains, every quarter of an hour for eight doses, then half-hourly, may be administered with the object of destroying it. In the absence of high titre cholera anti-sera, the basis of treatment consists of replacing fluid and salts lost from the body by the copious diarrhœa and vomiting. Intravenous injections should be given whenever the specific gravity of the blood rises to 1,063 or over. A systolic blood pressure of 70 mm. or less, especially if associated with cramps, cold extremities, restlessness and cyanosis, is an indication for transfusion. Rogers (**25**) advises two solutions, the first being a hypertonic saline, consisting

of sodium chloride, 120 grains, and calcium chloride, 4 grains, to the pint of sterile distilled water; this replaces fluid and chloride loss. The second is an alkaline solution consisting of sodium chloride, 90 grains, and sodium bicarbonate, 160 grains, to the pint of distilled water; this tends to counteract acidosis and uræmia. In order to avoid conversion of the bicarbonate into the toxic carbonate, the solution is sterilised by filtration through a Seitz asbestos filter, or the specially purified bicarbonate is added just before use to sterile normal saline. During the stage of copious evacuations, each time the patient requires an injection 1 pint of the alkaline solution is given followed by 1 to 3 pints of the hypertonic saline according to requirements. A specific gravity of 1,062 indicates that 2 pints are required; 1,063, 3 pints; 1,064, 4 pints, with the object of keeping the specific gravity below 1,060. Injections may need to be repeated. The rectal temperature must be considered as well as the specific gravity of the blood, for fatal hyperpyrexia may result when hot injections are given to an unconscious patient with a high temperature. This deadly complication occurs when the rectal temperature is 102° F. or higher; if it be 101° F. the solution for intravenous injection must not be warmer than 80° F., *i.e.*, room temperature in the tropics.

In the reaction stage when the temperature rises and circulation is restored, the patient must be closely watched for hyperpyrexia, and cold sponging must be started as soon as the temperature reaches 103·5° F. Threatened uræmia is best treated by hot applications and dry cupping to the loins, and by alkaline solutions given both *per rectum* and intravenously; these are repeated when necessary every few hours until 40 ounces of urine are passed in the twenty-four hours. Intravenous injections of 5 per cent. glucose may also prove helpful. Patients must be kept recumbent in bed for several days to avoid sudden cardiac failure, and, until the kidneys act freely, only junket and farinaceous foods like cornflour and arrowroot should be allowed lest relapse occur. Bacteriophage has been used both in the prevention and treatment of cholera, but at present its value is uncertain.

LEPROSY

(*Lepra : Elephantiasis Græcorum*)

A chronic disease of low infectivity peculiar to man, caused by *Mycobacterium lepræ* or *Bacillus lepræ* and characterised by nodular lesions of the skin and mucous membranes (nodular type) and involvement of the nerves (anæsthetic type).

Ætiology. Leprosy has a widespread geographical distribution occurring, amongst other places, in India, Burma, Siam, China, Japan, parts of Africa, Central America and South America, the West Indies, Mexico and Oceania. In Europe it is common only in Norway. Individuals of either sex and any race and age may acquire the infection. Children are the most susceptible, but the disease is rarely contracted in infancy and is definitely not hereditary. *Mycobacterium lepræ* was discovered in the tissues of lepers in 1874 by Hansen (**26**); it is non-motile and acid-fast, but has never been cultivated on artificial media or successfully inoculated into animals. The bacilli occur in great numbers in skin lepromata, septal ulcers and nasal mucus and less profusely in the implicated nerves. The mode of spread is unknown, but intimate contact with infective cases is essential.

Pathology. Leprosy bacilli spread through the lymphatics of the corium and subcutaneous tissue, producing skin granulomata and involvement of the lymph glands. Three stages are described: (1) a quiescent phase in which the bacilli multiply in the papillary lymph spaces, secreting a glutinous substance and causing loss of skin pigment; (2) a reactionary phase characterised by inflammation with swelling of the skin and disappearance of the glutinous matrix and dissemination of the bacilli and toxins through the blood stream with more general involvement of the corium and also the nerve trunks; microscopically,

large multinuclear lepra cells may be seen; (3) a stage of resolution when the erythema disappears, fibrosis occurs and the skin looks thin and wrinkled. The mucous membranes of the nose, mouth and larynx, the eye, and internal organs like the liver, lungs and the testicles may be involved in advanced cases; the viscera contain numerous bacilli and may undergo lardaceous degeneration. When the nerves are attacked they swell from proliferation of cells in the sheath, become reddish-grey in colour and undergo an axonal degeneration in association with which the anterior horn cells may be affected. Scanty bacilli are demonstrable in the endoneurium and perineurium. Anæsthesia, paresis, paralysis, muscular wasting, deformity and trophic ulcers follow.

Symptoms. The incubation period varies from six months to five years, and often the bacilli remain latent for long periods until some factor such as intercurrent disease precipitates clinical manifestations. There are three main types of the disease: (1) nodular leprosy; (2) anæsthetic or nerve leprosy; (3) mixed leprosy.

(1) *Nodular Leprosy.* Prodromal manifestations include leprotic fever, sweating, shivering, muscular weakness, gastro-intestinal disturbances, especially diarrhœa, alternating dryness and excessive secretion of nasal mucus and epistaxis. The first skin lesions appear as slightly raised erythematous macules (lepra maculosa) which later on show dissociation of sensation and absence of sweating; the face, buttocks, legs and arms are especially involved, and after the primary exanthem has disappeared a brownish discoloration of the skin may result. With a fresh eruption fever reappears and bacilli may be found in the blood. Simultaneously with the eruption, or more frequently after one or two recurrences, reddish-brown elastic nodules appear (lepra tuberculosa) which tend to become more generalised; the dorsal and not the palmar surfaces of the hands and feet are affected, while in size they vary from a small pea to a hazel nut. On the face they produce great thickening of the tissues over the forehead and of the nose, cheeks and lobes of the ears, the countenance acquiring a leonine expression (leontiasis). Hair tends to be lost, especially over the outer third of the eyebrows, the nipples become hypertrophied, while the mucous membrane of the mouth, gums, nose, pharynx and larynx may be affected with nodules, which may disappear, remain stationary or ulcerate. Blindness, dysphagia and vocal changes may result, while tendons and bones may be eroded and joints opened. Secondary anæmia and debility are found in advanced cases.

(2) *Anæsthetic Leprosy.* Prodromata include mental depression, chilliness, malaise, neuralgic pains and paræsthesia, such as burning or tingling which involve especially the facial, ulnar and perineal nerves. Numbness of the hands and feet, anæsthesia of ulnar type and anæsthetic patches somewhat resembling ringworm are early features. Often these anæsthetic patches which have commenced as erythematous, pigmented or depigmented areas become smooth, dry and hairless. After a time the ulnar, perineal and great auricular nerves become palpably thickened and wasting of the hypothenar eminence associated with contraction of the third and fourth fingers appears. Paralyses with atrophy especially involving the interossei of the hands and feet and the muscles of the forearm follow, and claw hand, wrist and foot drop result. Perforating ulcers are common and necrosis or absorption of the small bones with disappearance of fingers and toes ensues, the wounds healing up with remarkable completeness (lepra mutilans). Sometimes the fifth and seventh cranial nerves are implicated and ectropion of the lower lid complicated by corneal ulceration may occur.

(3) *Mixed Leprosy.* Cases in which nerve and skin lesions co-exist are common, but there is a tendency for nerve lesions to show themselves when the skin lesions are disappearing, and *vice versâ*.

Symptoms depend on the stage of the disease. In the quiescent phase the patient may feel quite well and be able to carry on his work satisfactorily; in

the reactionary phase there will be malaise and fever, while in the phase of resolution healing occurs which implies the establishment of a certain degree of immunity.

Course and Complications. The disease generally runs a chronic course with exacerbations and remissions extending over many years, though, where the resistance is low, nodular leprosy may run a rapid, febrile course with widespread skin lesions. The majority of cases die of intercurrent infections like pulmonary tuberculosis, nephritis, dysentery, pneumonia, sepsis with pyæmia and gangrene or local involvement of the larynx with obstruction and pulmonary complications.

Diagnosis. In nodular leprosy the differential diagnosis includes lupus vulgaris, skin tuberculosis, syphilis, yaws, dermal leishmaniasis, molluscum fibrosum and sarcomatosis. In nerve leprosy with ulnar involvement, syringomyelia, Morvan's disease (analgesic whitlow), progressive muscular atrophy, peripheral neuritis and cervical rib call for consideration. In other cases, leucoderma, psoriasis, scleroderma, Raynaud's disease, and even ainhum, may cause confusion. In nodular leprosy clumps of acid-fast bacilli are readily found in nasal mucus, in scrapings of nasal ulcers made under direct vision, using a speculum, and in the serous exudate from nodules and skin granulomata scraped with a scalpel. Smears prepared from the under surface of a piece of skin snipped with curved forceps from the lobe of the ear are valuable in diagnosis, and gland puncture may also reveal bacilli.

In nerve leprosy the earliest skin lesions differ from patches of leucoderma in being anæsthetic to light touch, less extensive and less symmetrically distributed (**27**). Adjacent nerves may be thickened, but lepra bacilli, as a rule, cannot be demonstrated unless a portion of the implicated nerve be excised and examined; the nasal mucus is free from bacilli and diagnosis in such cases has generally to be made on clinical grounds.

Prognosis. This largely depends on the type of the disease and the stage at which the case comes under treatment. Nodular leprosy is generally more serious than anæsthetic, and febrile cases showing widespread, rapidly extending lesions or successive crops of nodules may run a progressively fatal course, despite treatment. Relapses are common and cure is frequently more apparent than real; a guarded prognosis should therefore be given even in early cases. It is very important to keep all patients under observation for at least two years after they have been rendered bacilli-free and after active symptoms have ceased.

Prevention. Compulsory segregation has largely failed owing to the concealment of early cases, and this is particularly unfortunate as modern treatment yields its best results in this stage. Rogers advocates that early cases not yet discharging bacilli should be treated as out-patients in hospitals and dispensaries, and that advanced infective cases should be isolated as far as possible on a voluntary basis by making leper colonies attractive and efficient. When bacilli free, patients should be released and examined periodically to see that they remain so. Children of lepers must be isolated from the parents from birth and brought up separately, and contacts who have lived in the same house as lepers should be bacteriologically examined every few months for five years.

Treatment. It is essential to increase the general resistance by nourishing food, fresh air, regulated exercise and cheerful surroundings. Intercurrent disease must be treated. The sedimentation test is widely used as a guide to treatment; slow sedimentation is favourable, but a high sedimentation rate indicates active infection and contra-indicates drug treatment. Only when the general health is satisfactory and the resistance is high should special drugs be used, otherwise lepra reactions may occur with increase in the local lesions, and even bacillæmia in nodular cases, and agonising pain in anæsthetic leprosy.

Various drugs, including preparations of chaulmoogra and hydnocarpus oil,

their ethyl esters and sodium salts have been used. They should not be given in the active second stage in which the infiltrated and thickened tissues swarm with lepra bacilli. Improvement in early cases may be expected in three or four months, while lesions may have cleared in six to twelve months, but in advanced cases one to two years may be required (**27**).

Chaulmoogra oil by the mouth, commencing with 20 minims t.d.s. and gradually increased until 1 to 2 drachms are administered in the twenty-four hours. Fresh hydnocarpus oil is administered orally in enteric-coated capsules to prevent nausea, and mixed with 4 per cent. creosote to prevent pain if given as an injection. Antileprol, which is a mixture of the ethyl esters of unsaturated acids of chaulmoogra oil, is administered after food in capsules of 1 gramme, the dosage being 1 to 3 grammes daily. Moogrol (ethyl chaulmoograte) is injected weekly into the muscles, beginning with 1 c.c. and increasing the dose every third week until a maximum of 6 c.c. is attained.

Sodium gynocardate can be given by the mouth (12 grains t.d.s.) or as an intramuscular or intravenous injection. Sodium hydnocarpate (alepol) is the more active preparation; 1 to 5 c.c. of a 3 per cent. solution of "alepol" is almost painless, rapidly absorbed and efficient either by subcutaneous or intramuscular injection. For intravenous use a 1 per cent. solution is used.

Recently Muir has been using a special preparation of ethyl esters of hydnocarpus with 4 per cent. creosote injected intradermally. From 0·03 c.c. to 0·06 c.c. is injected at each puncture, as many as 100 punctures being required to inject 5 c.c. The process is painful and time-consuming, and six months may be required to infiltrate all the affected skin.

When lepra reactions occur, hot drinks, an aspirin-phenacetin-caffein nitrate mixture, large doses of alkalies and calcium salts should be administered. Protein shock and small doses of tartar emetic (0·02 to 0·04 gramme daily) may also help. In nerve leprosy the agonising pain may be relieved by ephedrine sulphate ($\frac{1}{2}$ grain) orally, or injections of adrenalin.

Vapour baths, diathermy and surgical stretching of the nerves are useful in nerve cases, and periarterial sympathectomy may assist the healing of trophic ulcers of the feet. Various drugs, including ichthyol, pyrogallic acid, resorcin and chrysarobin, are used in treating the skin lesions, while ultra-violet light is of value in increasing the general resistance.

Melioidosis. This very fatal disease, caused by *Pfeifferella whitmori*, is found in Burma, British Malaya, Ceylon and Cochin China; it resembles glanders, and was first described in man by Whitmore in 1913 (**28**), and was named melioidosis by Stanton and Fletcher in 1921 (**29**). Melioidosis is a disease of rodents, but the exact method by which man acquires it is not understood. *B. whitmore*, which is a bipolar staining organism, is readily cultivated from the blood or nodules, but it is not easy to demonstrate in pus.

Pathology. The internal organs, including the liver, spleen, lungs, intestine and kidneys, may show small caseous nodules which sometimes coalesce to form large honeycombed abscesses. Pustules and bullæ may implicate the skin.

Symptoms. The clinical picture varies within considerable limits. In the most acute cases of septicæmia there is a short burst of fever associated with severe vomiting, diarrhœa and collapse which may resemble cholera in its intensity and kill in a few days. In other cases remittent or intermittent fever may last for weeks or even months before death occurs.

Diagnosis. The clinical types may resemble plague, broncho-pneumonia, typhoid, malaria, liver abscess, infective endocarditis, generalised tuberculosis and pyelitis (**30**). Should melioidosis be suspected clinically, search for the organism in the blood, sputum, urine, cerebro-spinal fluid or pus aspirated from the spleen or liver must be made.

Treatment. The disease in man is almost invariably fatal; but autogenous vaccines are worth a trial.

PLAGUE

(Oriental Plague ; Black Death ; Pestis)

In the Middle Ages *plague* was used to designate any severe or fatal epidemic, but now its meaning is restricted to one particular disease, caused by *Bacillus pestis* and primarily implicating rodents (**31**) and conveyed to man by rat fleas.

Ætiology. The first great epidemic in Europe, the plague of Justinian, occurred in the sixth century, but since 1665, when it devastated London, European epidemics have gradually become less frequent. In 1894 an outbreak occurred in Hong Kong and South-Eastern China ; in 1896 the disease spread to Bombay and other parts of India, when it caused 7 million deaths during the next fifteen years. Since then it has occasionally appeared in different ports of Europe, South Africa and Central and South America. It is now most common in India, Thibet, Uganda and Mesopotamia. Less important centres are Siberia, California, South and tropical Africa. High temperature with a dry atmosphere, *i.e.*, a high saturation deficiency, kills the flea vector, so that fewer cases occur during the hot weather in countries like India. Any person may be affected.

The plague bacillus, *Bacillus pestis* or *Pasteurella pestis*, was isolated from a plague bubo in 1894 at Hong Kong. It is a short, flagellated, Gram-negative rod with bi-polar staining, measuring 1·0 to 1·5 μ in length, and is readily cultivated on artificial media. Guinea-pigs and other laboratory animals are susceptible. In rats, both acute and chronic forms of plague are encountered, and either the large grey or sewer rat (*Rattus norvegicus*) or the smaller and more domesticated black species (*Rattus rattus*) may be affected. Field rats and other rodents, such as ground squirrels, shrews, gerbilles and mice, may be responsible for outbreaks; a species of marmot, the "tarabagan" (*Arctomys bobac*), caused the Manchurian epidemic of pneumonic plague in the winter of 1910–11.

The rat flea, *Xenopsylla cheopsis*, acts as an excellent incubator for plague bacilli, and when it sucks up infected blood the bacilli proliferate rapidly, growing right forward and mechanically blocking the proventriculus, so that blood cannot get through into the stomach. Bacot and Martin (**32**) found that the starving anthropod, on biting another host, regurgitates bacilli back into the wound made by its jaws and so spreads the infection. Pneumonic plague in contradistinction to the bubonic variety is intensely infectious, being directly transmitted by droplet spray infection from person to person ; nurses and doctors frequently acquired the disease during the Manchurian epidemic.

Morbid Anatomy. A primary vesicle is only occasionally found at the site of entry of plague bacilli, while the adjacent chain of lymph glands is acutely inflamed (primary bubo). There is intense congestion and hæmorrhage, with peri-glandular, gelatinous œdema and matting together of adjacent glands ; those more distantly situated are greyish-red and congested. Septicæmia is almost invariable in severe cases, and in the most fulminating type evidence of primary bubo may be lacking. Toxins from the *B. pestis* damage the capillary endothelium and produce congestion and hæmorrhages in the mucous and serous membranes and the skin. The heart muscle, liver and kidneys are congested with cloudy-swelling and fatty change, while the spleen is enlarged, hyperæmic or hæmorrhagic. The brain and meninges show congestion and petechiæ.

Pneumonic plague appears to start as a broncho-pneumonia, but later the whole lobe may be implicated. Congestion of the bronchial mucosa, pleural ecchymoses and adenitis of the bronchial glands are common findings.

Symptoms. The incubation period generally varies from two to five days, but may be prolonged to ten days. Several types are differentiated clinically. (1) *Bubonic Plague.* The disease may be heralded by lassitude, headache, backache, vertigo and shivering, followed by a rapid rise of temperature. Indefinable fear, absent-mindedness, staggering gait and tremulous speech

are not infrequently present as well as nausea, vomiting and diarrhœa. The pulse rate increases to 100 to 130 and the temperature to 103° to 104° F.; occasionally in severe cases it reaches 107° F. The tongue, at first moist and white, soon becomes dry and brown and a typhoid condition may supervene with delirium and coma, sordes on the lips and teeth, failing pulse and cold extremities. The urine is scanty, acid, highly coloured and contains albumin, while oliguria may be replaced by suppression in fatal cases. On the second or third day the local signs of the primary bubo appear in the glands draining the infected bite. The femoral or inguinal glands are implicated in 70 per cent., the axillary group in 20 per cent., and the submaxillary and cervical in 10 per cent. of cases. The glands rapidly swell to the size of a hen's egg or larger, become extremely tender and painful and suppurate if the patient survives the first week. Death generally takes place from the third to the sixth day, and may be preceded by petechial or subcutaneous hæmorrhages, epistaxis, hæmoptysis, hæmatemesis and melæna. During the second week convalescence is generally established, but it may be prolonged by suppurative adenitis or boils and carbuncles involving the buttock, lower extremities or neck. Occasionally fever persists for weeks or even months. (2) *Septicæmic Plague.* The patient is struck down with great rapidity. There is frontal headache, fever, vomiting, delirium and coma associated with splenomegaly and slight general enlargement of the lymph glands. The pyrexia may be only slight, and bleeding into the skin and the mucous membranes occurs with a rapidly fatal termination within twenty-four to forty-eight hours of onset. Diagnosis is made by a positive blood culture. Fulminant cases (*Pestis siderans*) are included in this category. (3) *Pneumonic Plague.* This variety was first recognised in Bombay in 1896. Its onset is with a rigor and the symptoms resemble bubonic plague, but respiratory features become urgent in a day or two and dominate the picture. There is pain and tightness in the chest, dyspnœa, cyanosis, cough, expectoration of a profuse, blood-stained watery sputum teeming with plague bacilli. Râles, crepitations and possibly, near the end, areas of diminished vesicular murmur and resonance are found. Cardiac failure is common, and death occurs almost invariably within four days and generally before definite signs of consolidation are demonstrable. (4) *Intestinal Plague.* This type, which was encountered by Wilm in the Hong Kong epidemic of 1896, is very rare. It is characterised by nausea, vomiting, incessant purging of offensive, bile-stained, liquid stools, often containing blood. Pathological lesions are present in the intestine. (5) *Cerebral Plague.* The mental features so characteristic of ordinary bubonic plague are accentuated, and delirium, fits and coma rapidly supervene; in some respects the condition resembles cerebral malaria. A fatal plague meningitis with cytological exudate and plague bacilli in the cerebro-spinal fluid may also occur. (6) *Cellulo-cutaneous Plague.* In this variety carbuncles appear, having a necrosed ulcerated centre, an indurated edge and surrounding erythema which may be studded with vesicles. Culture reveals the presence of *B. pestis.* (7) *Abortive or Ambulatory Plague* (*Pestis minor*). Here the fever is so slight and the general features so mild that the patient does not take to bed. The lymph glands merely swell and become tender, or if they suppurate they resolve without serious indisposition.

Complications. The ordinary severe bubonic case may develop a fatal septicæmia or pneumonia during the first few days, while in the second week septic complications, including parotitis, boils, carbuncles, cellulitis and bronchopneumonia may complicate convalescence. Sometimes the buboes become indolent and fail to heal for weeks.

Diagnosis. Early in the epidemic difficulty may be experienced; apart from adenitis, those clinical features of special importance are mental dullness, hesitating speech and a staggering gait somewhat suggestive of alcoholism. Plague buboes have to be differentiated from climatic bubo, chancroid or syphilitic

bubo, septic adenitis, the adenitis of rat-bite fever and possibly tularæmia. Puncture of the gland reveals bipolar bacilli in smears and culture; the latter is best done by injecting a little sterile saline into the bubo or painful area, subsequently aspirating and culturing the contents of the syringe on agar slopes. A crucial test is the transmission of plague to the white rat by smearing infected material on its skin. Septicæmic plague is diagnosed by positive blood culture, 0·25 c.c of blood being run on to each agar slope, which in the tropics is subsequently incubated at room temperature.

In pneumonic plague herpes is absent, and the sputum, which is watery and contains bright blood, is not viscid and rusty as in pneumonia; microscopic examinations immediately reveal *B. pestis* in large numbers.

Prognosis. The mortality in bubonic plague is much lower in Europeans (25 to 30 per cent.) than in natives (75 to 80 per cent.). Axillary buboes are less favourable than inguinal, while cervical buboes are specially dangerous owing to the danger of asphyxia. Positive blood cultures are of serious significance and only the mildest septicæmias recover. Liston found that cases showing more than 20 organisms per c.mm. of blood invariably died. Pneumonic plague is always fatal.

Prevention. Wherever possible, rats and fleas should be destroyed and measures taken to prevent contact with man. The building of rat-proof granaries and houses, the evacuation of infected villages and huts during an epidemic, systemic destruction by poisoning and trapping, the fumigation of ships and their protection against rat invasion while in port are measures useful in controlling the spread of plague. Prophylactic inoculation with Haffkine's vaccine is important; 4 c.c. are injected subcutaneously and, though severe reactions follow, immunity lasting from half to one year is established with a single large injection. In Europeans multiple injections with smaller doses can be substituted with benefit.

Treatment. Good nursing, absolute rest in bed and liquid diet are essential. Anti-plague serum, if available, should be given in full dosage intravenously at the earliest possible moment (**33**). Cardiac tonics and intravenous glucose solution (5 per cent.) should be given early. Hyperpyrexia calls for prompt treatment. Hot fomentations, antiphlogistine or belladonna and glycerine may be applied to the buboes, and early incision made when suppuration occurs. Morphia may be necessary for the relief of pain.

UNDULANT FEVER

(Malta Fever; Mediterranean Fever; Abortus Fever, etc.)

This is a prolonged fever with many intermissions and a tendency to relapse; splenomegaly, sweating, anæmia, painful swelling of the joints and neuritis are features of the disease. It may be caused by *Brucella melitensis* conveyed in goats' milk, or by *Brucella abortus*, of which there are bovine and porcine strains.

Ætiology. Malta fever, which is primarily a disease of goats, is endemic in the Mediterranean basin, and human cases have been recorded from the Red Sea littoral, South Africa, India, China, the West Indies, parts of South America, the Mississippi valley and elsewhere. All ages and both sexes are liable. In Malta the disease was most common in the second and third decades, and especially in the dry summer months of July and August. The Maltese appeared less susceptible than garrison troops. Bruce (**34**) in 1887 discovered the organism, *Brucella melitensis*, in the spleen of patients dying of the disease, cultured it successfully and experimentally reproduced the disease in monkeys. It is a small cocco-bacillus which causes a generalised septicæmia, and may be recovered from the blood, bile, fæces, milk and urine. Zammit in 1905 found *Br. melitensis* in the blood of goats and showed that their sera agglutinated the organism.

Specific agglutinins also appear in the milk, which, though containing numerous organisms, may be of good quality.

Other varieties include *Brucella abortus* of Bang, discovered in 1897 (**35**), which causes contagious abortion of cattle and swine and may produce a disease in man indistinguishable from Malta fever. The organism is excreted in the udder of cows, and man may become infected by ingesting infected milk, butter or cheese, in handling the carcases of infected swine or cattle, or by contact with their excreta. Cases are recorded from Southern Rhodesia, where Bevan in 1922 first suggested its relationship to epizootic abortion of cattle, also from South Africa, the United States of America and Europe, etc. The disease is being recognised with increasing frequency in England.

Pathology. There is enlargement and congestion of the liver, marked hypertrophy of the spleen, an increase in pericardial fluid, patchy areas of con-

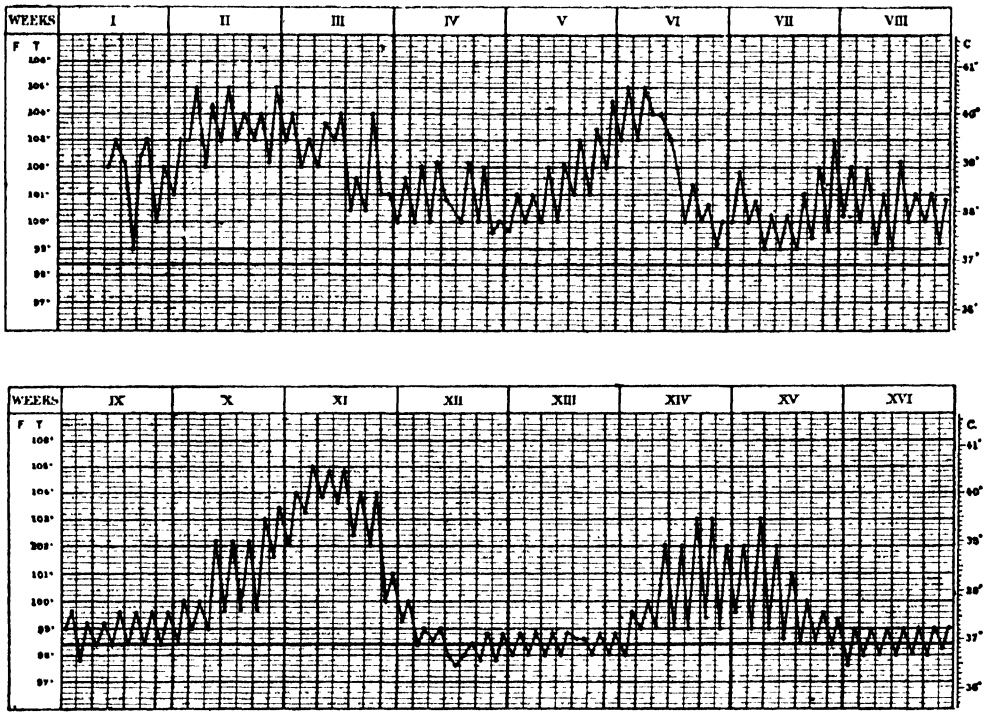


FIG. 97.—Temperature in a Case of Malta Fever of Undulant Type.

gestion in the intestinal mucosa and submucosa and enlargement of the mesenteric glands which may break down and contain semi-purulent matrix.

Symptoms. The incubation period is about fourteen days and the onset generally insidious. Symptoms include pyrexia, headache, pains in the joints, sleeplessness, thirst, furred tongue, loss of appetite and weight, nausea and tenderness in the epigastric region. The bowels are usually constipated, the spleen is generally enlarged and often tender and painful; sometimes there is hepatomegaly, while profuse perspirations occur, perhaps associated with sudamina. Anæmia is often marked and the red corpuscles may fall to below 3,000,000 per c.mm. In about half the cases the joints become red, swollen and painful, and the Brucella organisms may be isolated from the effused fluid. Neuritis is common; it may involve the sciatic or facial nerve, beginning acutely and persisting for a long time in a less intense form. Albuminuria may be present during the acute stages. The headache and severer symptoms may subside in two or three weeks, but the pyrexia often continues for six or nine months and only slowly subsides. The temperature is not necessarily continuously high throughout this period, but may have wavy exacerbations of two or three weeks' duration followed by intervals of lower or normal temperature for a fortnight

or longer (*undulant* type, Fig. 97), but there are several other clinical varieties. (1) *Ambulatory type.* Here symptoms are so slight that the person continues his ordinary occupation; insignificant symptoms with transient fever may develop and rapidly disappear, the serum tests alone revealing infection. Shaw, in Malta, found that 79 out of 525 dock hands at work in Malta gave positive agglutination reactions, when 22 of these positive cases were proved carriers, since Brucella organisms were detected either in the blood or urine or both. (2) *Malignant type.* The patient is suddenly attacked with severe fever, joint pains, vomiting and diarrhœa; cardiac weakness and a typhoidal state frequently develop and broncho-pneumonia may supervene. Death generally takes place from the twentieth to the thirtieth day with hyperpyrexia, temperatures of 106° to 108° F. being recorded. (3) *Intermittent type.* A sudden afternoon rise to 105° F. or higher, associated with chilly feelings or definite rigor develops. Pyrexia terminates with drenching sweats, and the condition can only be differentiated from malaria fever by the absence of parasites. (4) *Continuous type.* There is a uniform fever extending over a period of from four to twelve weeks. Clinically, many cases of abortus fever are typical of the undulant type, but the continuous and intermittent types are perhaps more common.

Complications. The more important include bronchitis, broncho-pneumonia, neuritis, arthritis with effusion, parotitis, orchitis, purpura and suppurative osteitis. In females there may be menorrhagia, abortion, premature labour and mastitis, while children are liable to meningo-encephalitis.

Diagnosis. The diseases liable to be confused with undulant fever include enteric fever, acute rheumatism, tuberculosis, septicæmia, subacute bacterial endocarditis, malaria, kala-azar, amœbic abscess of the liver, occult pyogenic infections and pulmonary lymph-adenoma associated with the Pel-Ebstein syndrome. Early in the disease hæmoculture is the most satisfactory method of diagnosis, and demonstrable septicæmia may last for several months. Liver infusion broth is a good culture medium, but *Br. abortus* must be grown in an atmosphere of 10 per cent. carbon dioxide, or, better still, 1·0 c.c. of suspected blood should be inoculated into the peritoneal cavity of a guinea-pig and cultures subsequently made from the peritoneal cavity in about a week's time, or from the spleen at a later date. With both *Br. melitensis* and *Br. abortus* it is necessary to incubate for at least a fortnight before reporting a negative result. Macroscopic agglutination reactions are of great diagnostic value; dead emulsions of *Br. melitensis* and *Br. abortus* should both be used as antigens. Absorption of agglutinin may be necessary to distinguish the two infections. Agglutinin appears from about the twelfth day onwards, and an ascending series of dilutions of from 1 in 50 to 1 in 10,000 should be employed. Where low titre agglutinations are obtained (1 in 100) the reaction should be repeated in a week's time to ascertain if the titre is rising. The complement fixation test is also valuable, and may be positive in the later stages when the agglutination reaction has become negative. Burnett's intradermal test is performed by injecting 0·05 to 0·1 c.c. of the filtrate of a twenty days' broth culture into the skin of the arm; the reaction, which becomes positive within six hours and lasts one to two days, consists of a round or oval area of infiltration of about 0·5 cm. diameter. It is said to be positive from the seventh to the tenth day of fever and to persist for ten months after recovery.

Prognosis. The mortality rate varies from 2 to 6 per cent. but it is higher in young children and people over forty owing to secondary infection (**36**). Death generally results, with hyperpyrexia during the first three weeks of fever in the malignant types, but at any time a fatal recrudescence may occur associated with cardiac failure, broncho-pneumonia or a toxæmic, typhoid state.

Prevention. The prohibition of the consumption of goats' milk and cream and cheese made from it is advisable, or failing this, boiling the milk renders it safe. Infected animals should be killed off and goats should only be bred from

sound stock. In cases of *Br. abortus* infection, prohibition of the use of infected cow's milk and avoidance of contact with the carcases or excreta of infected bovines or porcines are advisable. In handling Brucella cultures laboratory workers must be exceedingly careful, as infection is rapidly acquired in a fashion which is at present not fully understood; *Br. abortus* infects through the intact skin of guinea-pigs.

Treatment. In so prolonged a fever, careful nursing and a nourishing diet adequate in vitamin-containing foods are desirable and these include sufficient milk, eggs, fish, milk puddings, orange juice, tomato juice and yeast. Vaccines are of doubtful value and the results of specific anti-serum treatment, though promising, are not yet convincing. Specific protein therapy in the form of intravenous injections of T.A.B. vaccine, commencing with 50 millions and working up to 250 millions at three-day intervals, may cure. Various symptoms and complications should be treated as they arise and whenever the temperature exceeds 103° F. cold sponging is indicated.

TULARÆMIA

(Deer-fly Fever; Pahvant Valley Fever; Rabbit Fever)

This is a septicæmic condition resembling bubonic plague, due to *Brucella tularensis* (*Bacterium tularense*), which occurs particularly in rodents. Man appears to be generally infected from handling diseased animals or working with the organisms. Cases have been reported from the United States, Japan, Siberia and Norway.

Ætiology. McCoy, in 1911 (**37**), met with a plague-like disease in ground-squirrels (*Citellus beecheyi*), and in the following year in association with Chapin (**38**) he isolated the causative organism, *Br. tularensis*, which was a small Gram-negative bacillus ($0{\cdot}3 \times 0{\cdot}2\ \mu$). The disease affects rodents in the Western States of America, especially ground-squirrels and jack-rabbits, and is spread by ticks. *Br. tularensis* can pass through the intact skin and in this way butchers and poultrymen may be infected with the glandular type of the disease. Laboratory workers may contract it by droplet-spray infection with anæsthetising infected animals or in handling cultures.

Pathology. In man there is suppurative adenitis of the local lymph glands which break down and ulcerate, or generalised signs of septicæmia with involvement of the spleen, lungs and liver.

Symptoms. There are two types of infection: (1) the *bubonic* type which is usually seen in butchers and poultrymen, with an acute onset with headache, shivering or rigors, pains in the limbs and fever. In these cases a papule is generally present, particularly on the back of the hands, and this breaks down, leaving a ragged ulcer. An acute lymph-adenitis follows with involvement of the epitrochlear and axillary glands; these become swollen and painful and later may adhere to the skin and discharge pus. The average period of fever is twenty-six days and the mean duration of the disease five and a quarter months (Foshay). In chronic cases symptoms may persist for over a year. Sometimes the organism attacks the conjunctiva; ulcers form on the inner surface of the eyelids and swelling and tenderness of the preauricular and cervical glands follow. (2) The *typhoidal* type which particularly affects laboratory workers, characterised by fever, chills, sweats, headache, pains in the joints, malaise and no localising features; the temperature may subside within three weeks, but sometimes irregular fever may continue for many months (**39**), the condition resembling undulant fever and typhoid.

Diagnosis. The occupational history, especially in people handling rabbits in endemic areas, should arouse suspicion, but the final court of appeal is the laboratory. The agglutination reaction is of very definite value, for during the first week the serum fails to agglutinate *Br. tularensis* at 1 in 20 dilutions, while in the second week a rise in titre occurs, reaching a maximum of 1 in 600

to 1 in 1,000 from the fourth to the seventh week. There is a steady decline during subsequent months, a titre of 1 in 100 to 1 in 50 generally being encountered at the end of the year. Guinea-pigs injected with the purulent discharge of the organism develop characteristic lesions. Foshay (**40**) has recently introduced a special diagnostic skin test which enables a diagnosis to be made during the first week of the disease.

Prognosis. In laboratory workers the disease is not generally fatal; in the bubonic type the mortality is about 10 to 20 per cent. if untreated.

Treatment. An anti-serum which has been successfully prepared from goats and horses recently, is given intravenously in a dosage of 15 c.c. on two successive days (**41**) (Foshay) as a rule; by its use the duration of the disease has been shortened by 50 per cent.

OROYA FEVER

(*Carrion's Disease*)

This disease, caused by *Bartonella bacilliformis*, has a peculiar geographical distribution, being confined to valleys between 3,000 to 9,000 feet on the western slopes of the Peruvian Andes. In 1885, Carrion inoculated himself with material from a verruga nodule and died of Oroya fever one month later. An attack of either disease confers immunity to both. Barton in 1909 found small rod-like organisms in the erythrocytes in Oroya fever. In 1926, Noguchi and Battistini cultured the organism on artificial media and successfully [illegible]ed monkeys (**42**); the less resistant developed a disease resembling Ord[illegible], while the more resistant showed only verruga-like nodules. Noguchi [illegible]ted Rhesus monkeys with emulsion of sand-flies from Peru, and subsequently demonstrated *Bartonella bacilliformis* in the blood; two species, *Phlebotomus verrucarum* and *Phlebotomus noguchi*, are regarded as possible vectors.

Pathology. The skin shows petechiæ and a yellowish waxy tinting, the heart is flabby, presenting features of fatty degeneration, while the liver is enlarged, showing areas of zonal necrosis. The lymph glands are swollen and œdematous, the enlarged spleen contains multiple infarcts, and a yellow, granular pigment deposited in the endothelial and splenic cells which fails to give the prussian blue reaction. Red megaloblastic marrow fills the long bones, and ecchymoses often involve the serous sacs. *Bartonella bacilliformis* is found in the reticulo-endothelial cells as well as in the red corpuscles.

Symptoms. About three weeks after visiting an endemic area, malaise, headache and irregular remittent fever appear associated with joint pains and tenderness over the long bones and sternum. The spleen becomes enlarged and palpable, the lymph glands swollen and a hæmolytic megalocytic anæmia with hyperbilirubinæmia rapidly develops. In severe cases the red cell count falls as low as 1,000,000 to 2,000,000 per c.mm. The colour index often exceeds 1·0, while a leucocytosis associated with immature neutrophils and metamyelocytes is commonly encountered. Breathlessness, palpitation, cardiac murmurs, œdema of the legs and retinal hæmorrhages, skin petechiæ and oozing of blood from the gums develop; not infrequently severe cases lapse into coma and die with a subnormal temperature. Verruga nodules may appear during convalescence.

Diagnosis. A febrile hæmolytic anæmia of megalocytic type associated with tender bones and a history of recent residence in the Andes should suggest the diagnosis. The high leucocytosis and the presence of metamyelocytes differentiates the blood picture from pernicious anæmia in which there is leukopænia, lymphocytosis and a neutrophile shift to the right. *Bartonella bacilliformis* is only demonstrated in blood smears in severe cases.

Prognosis. The mortality rate varies from 30 to 40 per cent.

Treatment. Repeated blood transfusions are indicated for severe anæmia, and salvarsan is stated to have been used with success in some cases. Liver extract does not appear to be effective.

Verruga Peruana. This is now regarded as the eruptive stage of Oroya fever in patients with a high resistance to *Bartonella bacilliformis* infection. Noguchi has successfully transmitted verruga nodules by local inoculations from monkey to monkey, and subsequently cultured *Bartonella bacilliformis* from the local lesions. Splenectomised or specially susceptible monkeys may develop systemic manifestations resembling Oroya fever.

Pathology. Verruga nodules consist of vascular granulation tissue showing a marked tendency to ulceration and hæmorrhage. Microscopic examination shows proliferation of the endothelial lining of capillaries and lymphatics, plasma cells and fibroblasts in a delicate vascular reticulum.

Symptoms. From two to three weeks after exposure, fever and severe pains develop in the knees, ankles and wrists, but a few days after the eruption appears the temperature falls to normal. Two types of skin lesions are seen. (1) *The miliary* type involves the face and exterior surfaces of the limbs and sometimes the conjunctivæ and mucous membranes of the nose and pharynx. Pink macules appear which deepen in colour and assume a nodular appearance. These nodules are flat, smooth and either flattened or pedunculated; they bleed readily and heal without scarring. (2) *The nodular type* of eruption develops more slowly but attains larger dimensions and may form ulcerated fungating granulomata, the size of a walnut, which bleed profusely. The eruption comes in crops, involves the flexures of the medium-sized joints and lasts for two to three months.

Diagnosis. This is generally straightforward, especially considering the local geographical distribution of the disease. Secondary yaws, molluscum, contagiosum, Dercum's disease, multiple angiomata and fibro-sacromata may need differentiation.

Prognosis. This is good, the chief danger being hæmorrhage in the nodular type and secondary respiratory infection with the miliary type involving mucous membranes. In children the disease runs a mild course.

Treatment. Skin lesions should be dressed aseptically, and fungating nodules excised under local anæsthesia to prevent hæmorrhage. Blood transfusion and iron therapy are indicated in cases of severe blood loss.

TROPICAL MYOSITIS

(*Tropical pyomyositis ; Myositis purulenta tropica*)

This disease, characterised by acute painful swellings of muscles with or without pus formation, has a widespread tropical distribution. It may affect people of any race or sex. Until recently many held that it was related to *Filaria bancrofti* or *Loa loa* infestation, but that view has now been abandoned. Sayers has shown in the Solomon Islands that patients do not generally give positive intradermal tests for filariasis. Various organisms, including *Staphylococcus aureus*, *Streptococci* and a small bacillus, *B. serofaciens* isolated by Scott in Jamaica, may have a causal relationship. At times the disease may almost assume epidemic proportions as in the outbreak on the island of St. Kitts.

Pathology. The pathological findings are those of an acute coccal inflammation of muscle with serous effusion or actual pus formation. In fatal cases pyæmic abscesses or stigmata of septicæmia are found.

Symptoms. Both the local and systemic manifestations vary within wide limits. Fever, pain and stiffness in the affected muscles, and the appearance of multiple, indurated nodular swellings which may or may not break down and suppurate, are commonly encountered. A neutrophil leucocytosis of 15,000–25,000 cells per c.mm. is the rule. Local complications include synovitis, arthritis and periostitis; while in severe cases pyæmic manifestations including pulmonary abscess or even septicæmia may ensue with fatal consequences. The disease may run a protracted course with numerous relapses.

Diagnosis. The condition has to be differentiated from glanders, melioidosis, filarial abscess and intramuscular gummata (Manson-Bahr).

Treatment. Rest, fresh air, and a nutritious high vitamin diet are important. Abscesses may be incised and drained. In relapsing cases autogenous vaccines are worth a trial or non-specific protein therapy (T.A.B. vaccine) in intractable cases. Intercurrent diseases like syphilis and ankylostomiasis should receive appropriate treatment.

Diseases due to Fungi (Mycoses)

Certain fungoid infections are essentially tropical in distribution, namely, mycetoma, dhobie's itch and Hong-Kong foot due to *Epidermophyton inguinale*, Tokelau ringworm due to *Tinea imbricata*, the peculiar pigmented condition of the skin known as pinta, fungoid infections of the hair (trichosporosis or piedra and trichomycosis) and ringworm of the nails (onychomycosis).

Sporotrichosis, blastomycosis, actinomycosis, and torulosis and aspergillosis are in no way peculiar to warm climates and are described elsewhere.

Moniliasis. Yeast-like fungi are undoubtedly capable of producing infections of the skin, intertrigenous dermatitis, involvement of the nails with paronychia and onychia, mouth thrush and membranous lesions in the vagina, but it is exceedingly doubtful if they ever produce primary moniliasis of the digestive tract. Certainly sprue has no primary ætiological relationship to *Monilia ashfordi*. Monilia infection of the broncho-pulmonary system has been described on a number of occasions.

Rhinosporidiosis. This is a chronic disease caused by *Rhinosporidium seeberi* which produces nasal polypi and papillomata of the cheek, conjunctiva, lachrymal sac, penis and vulva.

Ætiology. The disease has been recorded from India, Ceylon, Cochin China, the Argentine and North America, and it has recently been shown by Ashworth to be due to a yeast-like fungus, *Rhinosporidium seeberi*, belonging to the Phycomycetes. O'Kinealy in 1903 found it in nasal polypi in India. The polypi show round-cell infiltration, epithelial proliferation and fibroblasts in which the large cysts containing daughter cysts in a cellulose coating are found.

Symptoms. As the nose is commonly involved, nasal symptoms predominate and a history of nasal discharge with intermittent hæmorrhages may be obtained, extending over several years. The nasal polypi are soft and vascular, bleed easily and tend to recur.

Treatment. In Madras, Wright has noted disappearance of nasal polypi after a course of tartar emetic intravenously. Generally the polyps have to be removed surgically by a wire snare.

MADURAMYCOSIS

(*Madura foot; pseudo-actinomycosis; fungus foot; mycetoma*)

Maduramycosis or mycetoma is a chronic granulomatous disease usually limited to the lower extremities which is caused by various species of fungi.

Ætiology. The disease is particularly common in India (Madura) and also occurs in Egypt, the Sudan, Algiers, Madagascar, Ceylon, Cochin China, the West Indies, South America and the United States. It is generally confined to country districts and there is frequently a history of traumatic abrasions, cuts or thorn pricks in natives who go barefooted. People of any age or sex are susceptible.

A number of different species and genera have the ability to produce granules in human tissues, the two main groups being the Actinomycotic and the Mycetomatous varieties. These granules present in the discharge from the sinuses are composed of hyphæ with or without chlamydospores and other types of spores and vary in size from 1 to 7 mm. in diameter. They may be hard, soft or cheesy in consistency; their colour may be white, grey, yellow, brown, black or red.

Pathology. The tissues are softened and jelly-like in consistency, containing sinuses with cystic dilatations which communicate with the external nodules and internal granulomatous infiltrations and involve the muscles and bones, forming a honeycombed cheesy mass. For diagnostic purposes the granules are mounted in a 10 per cent. potassium hydroxide on a glass slide, and flattened out with a cover slip. They are best cultured on Sabouraud's maltose medium, being most evident after four to seven days' growth at 37° C.

Symptoms. The onset is generally insidious in character. In the majority of patients a history of trauma of the naked foot is forthcoming ; pain, tenderness, swelling and discoloration of the skin may follow, or there may be a latent and symptomless period until the hard, painless nodules develop. According to Carter the initial lesion may consist of a mottled papule, a deep-seated, fixed nodule, a swollen vesicle or an abscess communicating with a fistula. Though the feet are generally involved, the nose, face and abdominal wall have also been occasionally implicated. Unlike actinomycosis, systemic involvement does not occur. Adenitis, if it be present, is due to secondary bacterial infection. After several months the lesions increase in size and number, the nodules ulcerate and sinuses form, from which is discharged a foul-smelling, semi-purulent fluid containing the characteristic granules. Even in advanced cases pain and hæmorrhage are generally absent, but the foot becomes gradually enlarged, and its concavities obliterated. Secondary infection may occur with serious consequences.

Diagnosis. The presence of swelling, nodules, fistulæ and sinuses from which pus-containing granules are exuded, should arouse suspicion. Curettage and irrigation of the fistulæ should be tried if granules are not demonstrable in the ordinary exudate. The differential diagnosis includes yaws, syphilis, tuberculosis, coccidioidal granuloma and sporotrichosis.

Prognosis. The course of the disease is essentially chronic, extending over many years. There is no tendency to spontaneous cure, and death ultimately results from cachexia or secondary infection, unless proper treatment be instituted.

Prevention. Proper foot-wear should be worn and walking barefoot should be avoided. Where abrasions and wounds occur, they should be treated with iodine and protected by appropriate dressings.

Treatment. Excision and curettage of the nodules, followed by X-ray irradiation are indicated in the earlier cases ; where the tissues are riddled with sinuses amputation alone holds out a reasonable prospect of cure. This operation, if properly planned, is almost invariably successful. Drugs, including potassium iodide, bismuth sodium tartrate and neosalvarsan are of doubtful value.

Coccidioides. (*California disease ; Coccidioidal granuloma.*) An infectious granulomatous disease due to *Coccidioides immitis ;* it may manifest itself in localised skin lesions, or as a systemic infection which proves rapidly fatal.

Ætiology. The disease occurs endemically in North America (**43**), Canada, Brazil and the Argentine. It specially affects males and is most prevalent amongst labouring and agricultural classes. *Coccidioides immitis*, as seen in pus, appears as a spherical fungus with granular protoplasm and a double contoured capsule ; it measures 5 to 6 μ in diameter and reproduces by endosporulation. It is readily cultured on serum agar at body temperature and appears as a mycelial network with long septate hyphæ ; chlamydospores and conidia form in old cultures.

Pathology. The lesions are granulomatous in nature, commencing as tiny nodules, which later may undergo necrosis, caseation, abscess formation, cavitation, fibrosis and even calcification. The histological picture may bear a close resemblance to tubercle.

Symptoms. The disease takes the form of local dermic lesions with or without systemic involvement. The cutaneous and subcutaneous lesions

consist of nodular ulcers involving the dermis or deeper abscesses, gummata or flaccid tumours. The superficial lymph glands of the neck and supra-clavicular region may enlarge, adhere to the skin, break down and ulcerate. Involvement of the lungs is not infrequent. The onset in the acute primary types is accompanied by chilliness, fever, headache and pains in the bones, joints and chest; cough also develops, but true hæmoptysis is rare in early cases. The physical signs are those of pulmonary disease, and tuberculosis is generally diagnosed. The course as a rule is fatal in six weeks to nine months, but in the type secondary to bony or skin lesions the disease is more chronic. Coccidioides cerebro-spinal meningitis may occur as a terminal event in systemic infection, and more rarely primary involvement has been recorded. The cerebro-spinal fluid is under increased pressure and contains globulin, many polymorphonuclear leucocytes and *C. immitis.* Coccidioidal involvement of bones and joints is common in generalised infection, and as a rule is accompanied by skin lesions. Fluctuation in the joint may be elicited and on incision, creamy or sanguineous pus containing *C. immitis* is found. A permanent fistula may result. In addition, metastatic visceral involvement may occur in systemic coccidioides. The blood shows a moderate or marked neutrophil leucocytosis and often a secondary anæmia.

Diagnosis. The disease is protean in its manifestations and apt to be confused with tuberculosis, syphilis, yaws, blastomycosis, sporothricosis, mycetoma and epithelioma. Diagnosis is made by demonstrating *C. immitis* in tissue sections, in smears of pus or in the cerebro-spinal fluid. Inoculated guinea-pigs die with systemic coccidioides.

Prognosis. The disease is essentially progressive, its duration varying from a few weeks to several years. If modern treatment be instituted early, the progress is good in the subacute and chronic cases, but acute cases invariably die in from four to twenty-four weeks.

Treatment. The best treatment appears to be intramuscular injections of colloidal copper every four to seven days combined with injections of coccidioidin (a mixture of the endo and exotoxin of *C. immitis*) cutaneously every eight to fourteen days, according to the local and constitutional reaction of the patient (Jacobson). Carbon dioxide snow applied without pressure may prove useful for the local lesions, and general measures include a nutritive diet, rest, fresh air, cod-liver oil *per os* and glucose combined, if necessary, with insulin injections, 1 unit to each 3 grammes of sugar. Surgery, X-rays, iodides and tartar-emetic have all been employed with doubtful benefit.

Spirochætal Diseases

The spirochætes form an important group of micro-organisms, the vegetable or animal nature of which has not yet been determined. They are elongated, flexible organisms, showing spiral movement and sometimes, in addition, undulations of the whole body and often require special staining or dark ground illumination for their demonstration. The tissue-inhabiting forms such as *Treponema pallidum* require anaerobic conditions for growth, while the blood spirochætes such as *Treponema recurrentis* are aerobic. Noguchi recognised three genera—*Spirochæta, Treponema* and *Leptospira.* Spirochætes are the causative agents of syphilis, yaws, relapsing fever and leptospirosis, while they are constantly present in Vincent's angina, bronchial spirochætosis and tropical ulcer. The *Spirilla,* being non-flexible organisms, are not true spirochætes so that, strictly speaking, rat-bite fever which is caused by *Spirillum minus* should not be included in the present chapter.

YAWS

(*Frambœsia, Frambœsia Tropica, Pian*)

Ætiology. Yaws is chiefly a tropical disease and is found in tropical and subtropical Africa, Ceylon, Burma, Southern Assam, Malaya, Indo-China,

Southern China, the Philippines, Oceania, the northern part of South America including Brazil and the West Indies. A few isolated foci occur in India. It affects almost exclusively dark-skinned races as a disease of childhood: both sexes are susceptible. The causative spirochæte, *Treponema pertenue* (**44**), which invades the tissues through abrasions on the skin, is indistinguishable from *T. pallidum*, the cause of syphilis, except by its distribution in the tissues. Some authorities would identify the two diseases, regarding yaws as syphilis of premature races, but yaws is of non-venereal origin, is never congenital and does not produce abortion or involve the viscera and central nervous system.

Pathology. The primary lesion and the secondary papules are caused by spirochætes lodged in the epidermal layer; histologically there is downgrowth of dermal epithelium into the corium with leucocytes, plasma cells and fibroblasts. Spirochætes are not present in the corium as in syphilis, nor are the blood vessels involved.

Symptoms. The incubation period varies from two to four weeks and may be accompanied by mild fever, generalised toxic pains and gastro-intestinal features. The primary lesion is extra-genital and usually single; the corresponding lymph glands may be hard and tender. In the secondary stages there is intermittent fever, headache, pains in the bones often worse at night, and arthralgia. The rash develops eight to sixteen weeks after infection while the primary lesion may still be present. First the skin becomes scaly, then small papules resembling the primary lesion appear and increase in diameter up to 1 cm., sometimes coalescing to form larger masses. Desquamation of the cuticle over the papule results in a raw, raspberry-like surface which exudes yellowish serum: this dries and forms crusts resembling syphilitic rupia. Finally, the papules dry up and heal leaving evidence of their presence in hypo- or hyper-pigmented areas. The papules have a symmetrical distribution, affect the face, neck, arms, buttocks and genitals and may give rise to troublesome itching. Successive crops may appear over a a period of from three months to three years. The lesions observed in long-standing cases of tertiary yaws include periostitis, osteitis, tenosynovitis, arthritis, ulceration of the palate and bony caries. Bony lesions may involve the long bones, face, hands and feet; exostoses and periosteal nodes resembling gummata may form while rarefying osteitis sometimes leads to spontaneous fracture. Sabre tibia and "boomerang" leg amongst the Australian aborigines frequently result. Chronic ulcers result from the breaking down of subcutaneous granulomata, often on the site of previous lesions, while yaws nodules involving the soles of the feet produce a painful crippling condition known as clavus or crab yaws.

Gangosa, goundou and juxta-articular nodes are generally regarded as sequelæ of yaws and may appropriately receive consideration here.

Goundou. This condition is found on the West Coast and in Central Africa, Sarawak and South America. It affects both children and adult natives and originates as a hypertrophic osteitis of the nasal processes of the superior maxilla. The symptoms at onset include persistent headache, bony pains worse at night, and a purulent nasal discharge often tinged with blood. Later these features subside, and oval, bilateral, nasal swellings develop which may attain the size of a hen's egg; nasal obstruction and interference with vision may follow. The skull, superior and inferior maxilla, clavicle and other bones may be similarly involved. The condition may need differentiation from syphilitic osteitis, leontiasis ossea and acromegaly. Salvarsan injections, and, in the later stages, surgical removal of the exostosed bone are indicated.

Gangosa. This is an ulcerating rhino-pharyngitis resulting in destruction of the palate, nasal septum and nose, the upper lip being left intact. It occurs in the West Indies, Fiji, British Guiana and Central, West and East Africa and Australia; both native children and adults are affected. Severe pain, nasal discharge and fœtid breath result, and in severe cases the voice may be affected.

Finally, the eyes and lacrymal ducts may be implicated and much of the face destroyed. Syphilis, leprosy and American dermal leishmaniasis may sometimes be confused with gangosa, which runs a very chronic course, resulting in death from sepsis or insufflation pneumonia. Salvarsan injections should be given in the early stages and plastic operations undertaken at a later date, though conditions in the tropics rarely permit this being done.

Juxta-Articular Nodes. These are multiple, oval periarticular nodules affecting native children and adults in Equatorial Africa, the West Coast, Java and Siam. Microscopical sections reveal avascular, fibrotic tissue containing areas showing polymorphonuclear infiltration and necrosis. The tumours occur in the vicinity of joints, especially the knee and elbow, and on palpation they feel hard and are painless. They may disappear spontaneously, remain constant in size or gradually attain the dimension of a hen's egg. At first the skin is freely movable over the surface; later it becomes adherent but never breaks down, ulcerates or suppurates. Similar lesions may occur in syphilis and the differential diagnosis lies between rheumatic and syphilitic nodules and onchocerca tumours. The latter are, however, soft and semifluctant, and on needling fluid containing filarial embryos is aspirated; biopsy will also confirm the diagnosis.

Diagnosis. The Wassermann reaction does not help to differentiate yaws from syphilis as it is positive in both diseases, but *T. pertenue* can readily be isolated from yaws nodules. The absence of a primary genital chancre is not conclusive, as chancres are often not found in female syphilitics and are always absent in congenital lues. In differentiating tertiary yaws from syphilis the absence of visceral, vascular and nervous involvement and the rapid therapeutic response to salvarsan may be of assistance. Leprosy, tubercle, dermal blastomycosis and cutaneous leishmaniasis may produce lesions which require differentiation from those of yaws.

Prognosis. Yaws is rarely fatal, runs a prolonged course if untreated, but readily responds to modern specific therapy.

Prevention. Isolation is impracticable, and the most feasible methods of prophylaxis consist of protecting wounds and abrasions and giving specific treatment on a large scale.

Treatment. Certain organic arsenicals and bismuth salts act as specifics; potassium iodide may be useful, but mercury is of no value. Novarsenobillon administered intravenously in doses of 0·6 to 0·9 grammes in adults and in correspondingly decreased amounts to children gives most excellent results: this drug may also be given intramuscularly. While one injection may clear the case clinically, a course of six or more injections is advisable to prevent relapse. Bismuth salts are very effective and are much cheaper for large scale therapy in native races. Sodium-potassium-bismuth tartrate in freshly prepared and boiled solution may be given intramuscularly to an adult each week in a dosage of 0·1 to 0·3 grammes; children tolerate the drug even better than adults, but stomatitis is an unpleasant complication. Other preparations of bismuth, including sodium-bismuth-tartrate, bismuth salicylate, dermatol and halasol, have been used with satisfactory results, though to date less information is available regarding their permanency of cure.

Relapsing Fever. There are two main types—one transmitted by body and head lice and the other by argasine ticks. The varieties transmitted by lice include European relapsing fever due to *Treponema recurrentis*, discovered in Berlin by Obermeier in 1868, North African relapsing fever produced by *T. berberum*, Indian or Asiatic relapsing fever caused by *T. carteri*, and North American relapsing fever attributed to *T. novyi*. The varieties transmitted by the argasine ticks include Central African tick fever due to *T. duttoni* transmitted by *Ornithodorus moubata*, Somaliland tick fever transmitted by *O. savignyi*, Persian and North-West Indian relapsing fever caused by *T. persicum* and transmitted by

O. tholozani or *O. lahorensis*, Spanish relapsing fever attributed to *T. hispanicum* and transmitted by *O. moraccanus*, Central American relapsing fever due to *T. venezuelense* transmitted by *O. venezuelensis*, and Panama relapsing fever due to *T. neotropicalie* transmitted by *O. talaje*.

LOUSE RELAPSING FEVER

(*Spirochætosis, Febris Recurrens, Spirillum Fever, Famine Fever*)

A febrile disease characterised by two or more bouts of fever caused by the spirochæte, *Treponema recurrentis*, and transmitted by lice.

Ætiology. This disease is endemic in certain places, but like typhus it tends to occur in epidemic form over large areas and is particularly common during famine and war. Male adults are most frequently attacked, though women and children may be affected. Mackie (**45**) suggested the body louse as a vector, the details of transmission being subsequently worked out by Nugent, Foley and Nicolle. When a louse has fed on infected blood the ingested spirochætes rapidly disappear, but after a few days reappear in the cælomic fluid; thereafter the louse remains infective for life. Crushing of such lice liberates spirochætes which gain entrance through scratches on the skin or louse punctures.

Pathology. Jaundice is not infrequent and petechial hæmorrhages may be found in the skin. The spleen is enlarged, soft and congested and a frequent site of infarction. The liver is also enlarged and hyperæmic, while the kidneys and heart show cloudy swelling and fatty degeneration. Microscopically spirochætes are demonstrable in the endothelial cells of the liver, spleen and other organs.

Symptoms. The incubation period is five to seven days, the limits being two to twelve. The onset is sudden with rigor, frontal headache, severe pains in the limbs and back and a temperature rapidly rising to 103°–105° F. Anorexia, nausea, vomiting, constipation and photophobia are common. Convulsions may occur in children, while epistaxis is a feature of some epidemics. The face is flushed, the conjunctivæ injected, the pupils contracted, and the tongue dry-coated and occasionally ulcerated. The spleen is enlarged and tender and so generally is the liver. Bronchitis and cardiac dilatation not infrequently develop. A macular rash or even petechiæ occur in some 10 per cent. of cases, specially around the neck and shoulders.

The spironemas, which stain readily with Romanowsky stains, are scanty in the blood smears at the onset of fever, but steadily increase until twenty-four hours before the crisis when they rapidly disappear again. If blood collected between attacks be injected into white mice or guinea pigs spironemas appear in twenty-four hours. A neutrophil leucocytosis accompanies the pyrexia and a leucopænia the afebrile period. The "adhesion" test may be positive: it depends on the fact that in immune but not in normal serum spironemas and platelets clump together. The urine is decreased in quantity and sometimes contains spirochætes: albumin is present, and in severe cases granular and hyaline casts may be found. As a rule the primary fever lasts about a week, but may be as short as three or as prolonged as twelve days: its termination is by crisis with sweating, subnormal temperature, and occasionally collapse with cardio-vascular failure. Relapses by no means invariably occur, but the second bout of fever generally appears about the thirteenth or fourteenth day, and as a rule is not as prolonged as the primary fever (see Fig. 98, p. 1034). A third relapse is not common and a fourth relapse rare.

Complications include parotitis, jaundice, bronchitis, broncho-pneumonia, nephritis, cardiac failure and rupture of the spleen. Hæmatemesis and hæmaturia occur in epidemics where there is a high incidence of jaundice.

Diagnosis. The mode of onset, type of temperature chart and splenomegaly will suggest the diagnosis which is readily confirmed by demonstrating the spironemata in blood smears. Influenza, dengue, malaria, typhus and para-

typhoid need differentiation in cases which do not relapse, and yellow fever and Weil's disease where jaundice has supervened.

Prognosis. The mortality rate varies considerably in different epidemics and averages 10 to 15 per cent. It is particularly fatal in the aged and debilitated, its worst ravages being seen in times of famine.

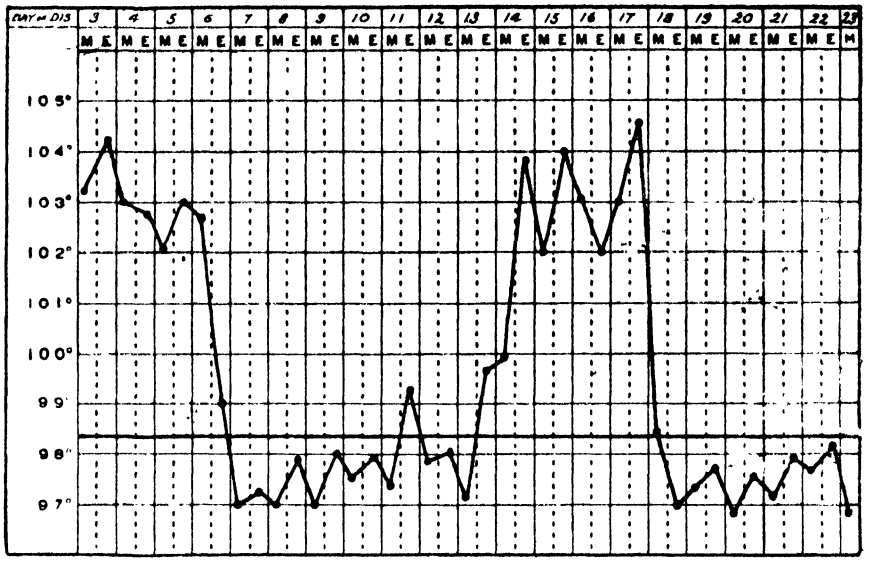


FIG. 98.—Temperature in Relapsing Fever.

Prevention. This follows the lines already suggested in typhus and consists of delousing and isolating cases, etc.

Treatment. Absolute rest in bed, careful nursing, light diet and abundance of fluids are essential. Injections of novarsenobenzol (0·6 grammes) and neo-salvarsan (0·4 grammes) given intravenously in 10 c.c. of distilled water are curative:

TICK RELAPSING FEVER

A disease characterised by repeated bouts of fever caused by *Treponema duttoni*, the spirochætes being transmitted by certain argasine ticks notably *Ornithodorus moubata*.

Ætiology. Christy first described the disease in East Africa. Ross and Milne (**46**) subsequently demonstrated the spirochætes in the blood and Dutton and Todd proved transmission by *Ornithodorus moubata* the following year. In Equatorial Africa the disease is localised to certain houses and camping places infested with ticks, which, once infected, remain so for life and transmit the infection to their offspring. The infected arthropods which live on the ground and in crevices in walls and floors, generally come out and bite at night while the person is sleeping. Spironemas are present in the salivary glands, the coxal fluid and the anal excrement and from these sources man acquires the disease.

Pathology. The morbid anatomy is similar to louse-relapsing fever, but congestive changes in the cord and brain and iritis are more characteristic of *T. duttoni*.

Symptoms. The clinical picture resembles that of louse relapsing fever except that the bouts of fever are more intense and of shorter duration. The average number of relapses is five or six, but there may be as many as twelve. The afebrile intervals also tend to be longer. Diarrhœa, iritis, spastic paralysis, facial neuritis and other nerve palsies are more frequently observed than in louse-borne relapsing fever.

Diagnosis. This presents little difficulty though the spirochætes are fewer and in consequence more difficult to demonstrate in blood smears: laboratory animals are readily infected by blood inoculation.

Prognosis. The mortality rate approximates to 5 per cent.

Prevention. Disinfection of camping grounds and infected houses should be practised and infected sites avoided. Ticks are removed by the local application of kerosene or turpentine and a drop of pure carbolic is subsequently applied to the bite.

Treatment. This is identical with that outlined for louse relapsing fever.

Leptospirosis is the name for several kinds of fever caused by leptospiræ which lodge in the kidneys of rodents and are passed in the urine; thus they contaminate water and fungal slime which are the usual sources of human infection. The best known of these organisms is *Leptospira icterohæmorrhagiæ* which causes classical Weil's disease, but in many countries more than one serological type has been isolated differing from the classical " Weil " strain on agglutination (**47**). Thus three or four strains have been isolated in both Japan and Sumatra, five in Malaya and two amongst outbreaks of Weil's disease in Indian convicts on the Andaman Islands where the predominant strain appears to be identical with " Rachmat " and " Deli " A of the Dutch East Indies.

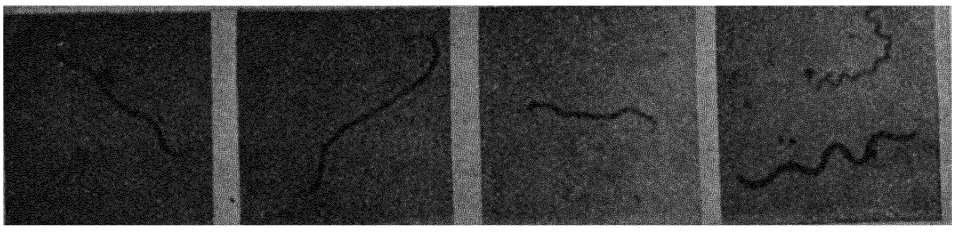
L. hebdomadis, which occurs in field mice, gives rise to a seven-day fever in Japan and a spirochæte serologically identical has been reported from Sumatra, Panama and the Sudan. In Europe there are three varieties—*Leptospira icterohæmorrhagiæ* (classical " Weil " strain) which gives rise to spirochætal jaundice in man and dogs, *L. grippotyphosa*, the cause of swamp fever, characterised by seven to fourteen days' fever with a variable rash but without jaundice, and *L. canicola* which is a specific disease of canines capable of infecting man.

WEIL'S DISEASE

(*Spirochætal Jaundice, Spirochætosis Icterohæmorrhagica, Leptospirosis, Infective Jaundice*)

A febrile disease of sudden onset which may be associated with jaundice occurring about the fourth to the sixth day.

The causative organism, *L. icterohæmorrhagiæ*, which was discovered in 1915 by Inado and Ido in Japan (Fig. 99), is located in the kidney of rats in practically



A B C D

FIG. 99.

A. *L. icterohæmorrhagiæ*, from blood of inoculated guinea-pig
B, C. *L. icterohæmorrhagiæ*, from human blood on second day of the disease before jaundice had appeared.
D. *Treponema pallidum* (upper figure) and *Treponema refringens* (lower figure), from primary syphilitic sore. Magnitude 2,500. (*After A. C. Coles.*)

all countries where surveys have been made; from this source infection arises. The leptospiræ gain access to rat-infested canals and rivers and either transverse the mucous membranes during bathing or " immersion " accidents or gain access *viâ* the abraded skin. Canal workers and bargemen are not infrequently infected. The disease is common in countries like Egypt and Holland where canals abound, and in Japan in river and swampy country, but not where it is high and dry. In addition, the leptospiræ thrive in the fungal slime found on the

walls of coal mines, sewers, gutters and floors of abattoirs and fish shops where rats congregate to feed on offal. This is why Weil's disease is so frequently an occupational one as in coal miners (**48**), sewer builders (**49**), gutter sweepers, fish workers, cane cutters and the like, the leptospiræ gaining access through the abraded skin. Wet, rat-infested trenches were a potent source of infection during the Great War.

Pathology. Jaundice of variable degree is present and petechial hæmorrhages may be observed in the skin, mucous and serous membranes and viscera. The liver is enlarged and bile-stained and on histological section shows fatty degeneration or necrosis of the hepatic cells, while in extreme instances a condition allied to acute yellow atrophy may develop. The kidneys are swollen and jaundiced; there is wide-spread degeneration of the convoluted tubular epithelium, the lumina of which may contain bile and blood casts. The spleen is congested though not necessarily enlarged, the myocardium pale and flabby and the endocardium bile-stained.

Symptoms. The incubation period varies from six to twelve days. The

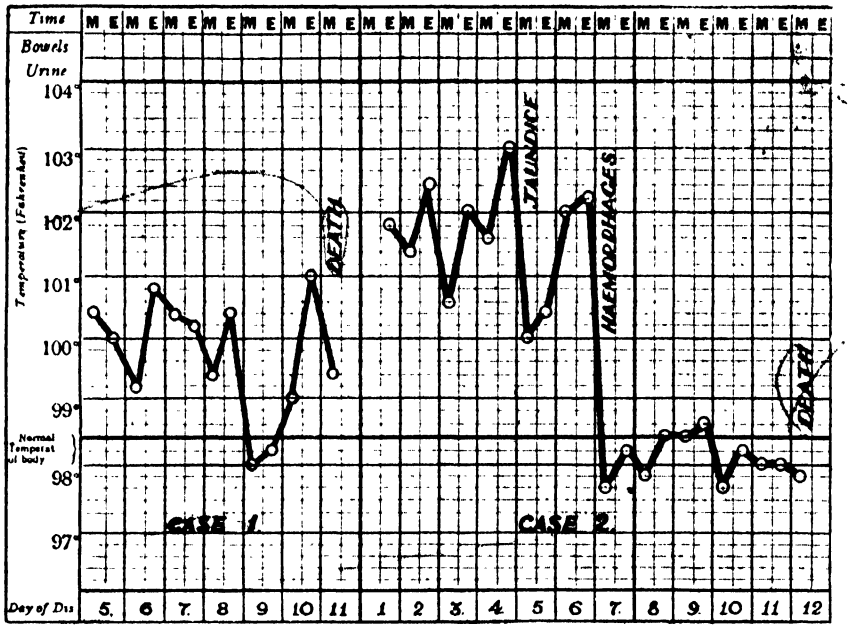


FIG. 100.—Temperature charts in two London sewer workers dying from Weil's disease.

onset is sudden with rigors, headache, vomiting, sore throat, pains in the joints and intense pain and tenderness in the muscles. The patient is completely prostrated, the blood pressure low, the tongue furred, the face flushed and the conjunctivæ and throat injected. The temperature continues to rise, usually oscillating between 102° and 104° F., until the fourth or fifth day when it begins to fall by lysis or more rarely by crisis; the normal is generally reached in seven to fourteen days. Jaundice, which may be very intense, appears about the fifth day, but it may be as early as the second or as late as the seventh in onset. The stools are light brown or occasionally clay-coloured where the obstruction is complete. There is hyperbilirubinæmia and the van den Bergh gives a biphasic or delayed direct reaction. The urine is scanty and contains albumin, bile pigments and sometimes red blood corpuscles. Leucocytosis is marked, amounting to 12,000 to 30,000 per c.mm.; the neutrophil polymorphonuclears are markedly increased and average about 80 per cent. of the total white cells. Skin petechiæ may appear from the third to the fifth day and in addition there may be hæmorrhages from the mucous membranes, the most frequent being epistaxis and malæna. Herpes is common in some epidemics, its incidence being 40 per cent. amongst British troops on the Western Front.

Prior to the onset of conjunctival congestion and jaundice, physical examination may reveal extreme tenderness especially in the calf, neck and abdominal muscles, the patient sometimes calling out with pain when he is being moved in bed. In some instances abdominal rigidity is so marked that an acute abdomen is suspected and the patient may be erroneously operated on, especially if hæmatemesis co-exists. Splenomegaly may or may not be present, but tenderness and enlargement of the liver are the rule. Sleeplessness, nocturnal delirium, a typhoid state or muscular twitchings and convulsions may develop in severe cases and patients may die with anuria associated with marked nitrogenous retention, the blood urea reaching 400 to 500 mg. per 100 c.cm. In other cases cholæmia may develop, associated with drowsiness, hiccup, Cheyne Stokes' respirations, coma and death. In about 50 per cent. of cases jaundice is absent, while renal involvement is minimal. Under these circumstances there is a short febrile attack perhaps terminating by crisis in two to four days, associated with muscle pain, tenderness and transient albuminuria. In cases which recover there is generally no secondary rise of temperature, but occasionally there is a recurrence of fever in the third week associated with an increase in the agglutinin titre of the blood.

Complications include cardiovascular collapse, cholæmia, anuria, iritis, iridocyclitis and alopecia. Convalescence is gradual, but recovery is complete.

During the first week leptospiræ can be cultivated on Fletcher's or Noguchi's serum medium which is inoculated with about 0·5 c.cm. of the patient's blood and incubated at 28° C. A more reliable test consists of the intraperitoneal injection of 2 to 4 c.c. of blood into a guinea-pig which develops fever, hæmorrhages, albuminuria and finally jaundice. Leptospiræ may be found in smears from the liver and kidney and sometimes in the heart blood: subinoculations should be made. In man, after the eighth day leptospiræ disappear from the blood, but subsequently they may be demonstrable for several weeks in the urine either by dark-ground examination or animal inoculation. Schüffner's agglutination test (**47**) and the adhesion test of Brown and Davis (**50**) are also applicable, and are of considerable diagnostic value after the first week.

Diagnosis. The sudden onset of fever characterised by shivering, profound prostration, great muscular pain and tenderness, severe jaundice appearing about the fourth to the sixth day, hæmorrhages, albuminuria and leucocytosis should leave little doubt, especially if the occupation or history suggest contact with rat-infested water or slime. Catarrhal jaundice may present difficulties, but the premonitory gastro-intestinal symptoms, the absence of hæmorrhages and renal involvement and the presence of lymphocytosis associated with a normal white count or leucopænia favour the diagnosis of catarrhal jaundice. Yellow fever also may closely simulate Weil's disease and the demonstration of leptospiræ in blood or urine or specific agglutination tests may alone establish the diagnosis. Relapsing fever complicated by jaundice may also prove confusing.

The atypical and mild types of leptospirosis have to be differentiated from tonsillitis, influenza, dengue and the sand-fly group of fevers, and laboratory data are essential for this purpose.

Prognosis. The mortality varies from 10 to 50 per cent. Cardiovascular collapse, severe hæmorrhages, anuria and cholæmia are ominous features.

Prevention. This consists of rat destruction, avoidance of bathing in infected canals and the protection of skin abrasions in workers whose occupations make them liable to contact with infested slime. Prophylactic vaccine therapy in sewer builders and the like might help.

Treatment. General treatment along the lines laid down for yellow fever should be instituted. Intravenous glucose solution (5 per cent.) is of special value. In addition anti-leptospiral serum prepared from immunised horses should be administered intravenously as early as possible, 60 c.c. being given in twenty-four hours. If this be not available convalescent human serum in a dosage of 30 c.cm. daily may be substituted.

Japanese Seven-day Fever (*Nanukayami*). A febrile disease lasting about a week and resembling mild Weil's disease clinically. The cause is *L. hebdomadis* which infects the kidneys of field mice, the natural reservoir of infection. *L. hebdomadis* differs serologically from *L. icterohæmorrhagiæ*. It is found in the blood during the first week and may be demonstrated by blood culture or guinea-pig inoculation. The leptospiræ subsequently lodge in the kidneys and appear in the urine from about the eighth to the fortieth day. The natural reservoir is the field mouse, *Microtus montebelloi:* in endemic areas of infection about 3 per cent. show leptospiræ in the urine. Agricultural labourers and foresters probably acquire the disease handling infected soil.

Symptoms. The onset is sudden, accompanied by fever which lasts seven days. Prostration and muscular pains are marked, gastro-intestinal disturbances are troublesome, there is furred tongue, injection of the conjunctivæ, enlargement of the lymphatic glands, albuminuria and leucocytosis. Jaundice is infrequent.

Treatment. Specific serum therapy is unnecessary since recovery is invariable.

RAT-BITE FEVER

(*Sodóku. Rat-Bite Disease*)

A chronic relapsing type of fever transmitted by the bites of rats and other rodents harbouring *Spirillum minus;* there is inflammation and ulceration of the healed bite, lymphangitis, adenitis, fever, rigors and a macular or papular purplish rash.

Ætiology. The disease is most common in Japan, China and Bombay, but it also has been reported in England and other European countries, East Africa, West Indies and Australia. The infective agent, *Spirillum minus* (**51**), is a short organism with two to six curves which are very difficult to find in human or animal blood smears owing to their scantiness and small size. About 3 per cent. of house rats in Japan are carriers.

Pathology. Inoculated animals show congestion and swelling of the lymph glands and spleen where spirochætes are found in considerable numbers, and human cases show degenerative changes in the liver and kidneys.

Symptoms. Some two to six weeks after the wound has healed intense pain and swelling occur at the site of the bite which becomes inflamed, breaks down and ulcerates. Lymphangitis and adenitis follow and a series of small vesicles may surround the local lesion. Rigor and temperature now develop, associated with headache, shivering and prostration; nausea, vomiting, joint pains and diarrhœa may follow and in some cases an erythema or a macular purplish rash appears over the limbs, trunk and face: occasionally skin petechiæ or urticaria are seen. After three to eight days the temperature subsides, often by crisis, and the symptoms ameliorate or disappear. The improvement, however, is only temporary, for in a few days fever and other symptoms return. Repeated relapses occur, about six days intervening between the onset of fever in successive bouts. This state of affairs may continue for many months and result in marked debility. Complications include nephritis, paresis and exophthalmos. A leucocytosis with eosinophilia accompanies the fever.

Diagnosis. The history of rat-bite and the breaking down of the local lesion associated with lymphangitis, adenitis and fever recurring every five or six days should arouse suspicion. Spirilla are difficult to demonstrate in smears of blood and white rats or mice should preferably be inoculated for this purpose.

Prognosis. About 10 per cent. of Japanese patients succumb to the disease, but with modern treatment death should not occur.

Treatment. Immediate cauterisation of the bite may prevent infection. Salvarsan or one of the allied arsenical preparations are curative and the injections should be given during the fever at any time except just before or during the crisis.

Protozoal Diseases

Protozoa are unicellular organisms, containing cytoplasm, a nucleus, nuclear membrane, and chromatin, which ingest preformed proteid material in solution or as solid particles (Wenyon) (**52**). They may live a free aquatic life, or be intimately associated with animals as commensals, symbiants, or parasites. Though of little importance in temperate climates, the pathogenic protozoa constitute the most important group of organisms infecting man in the tropics and subtropics.

MALARIA (*Plate 67, 5–16, p. 1053*)

(*Paludism. Ague. Marsh or Jungle Fever*)

Malaria, the greatest menace of the tropics, is an endemic and epidemic disease caused by at least four species of *Plasmodium* which affect the red blood corpuscles and give rise to periodic fever, anæmia and enlargement of the spleen. Transmission is by infected female anepholine mosquitoes.

Historical. Europe suffered severely from ague in the Middle Ages, and cinchona bark, which was brought back from Peru by the Jesuit Fathers in the first half of the seventeenth century, was of incalculable benefit both in controlling this disease and in enabling Sydenham and other physicians to separate malaria from other fevers. Quinine itself was not introduced until 1820. In the first half of the nineteenth century the dark colour of malarial organs and pigment deposits in certain cells were noted. Laveran, when studying the phenomenon of flagellation, first recognised the pigmented malarial parasite in 1880. Manson, after studying the phenomenon of the flagellation of the male gamete in shed blood in 1894, formulated the hypothesis of mosquito transmission, but he thought that the disease was transmitted by swallowing infected mosquitoes in water, and not through their biting man. MacCallum, three years later, recognised that the flagellating body was a fertilising agent. Ross in 1898 demonstrated the transmission and developmental cycle of bird malaria (*Proteosoma*) in grey mosquitoes (culicines), after having noted the immature oöcysts of human malaria in "dapple winged" mosquitoes (anophelines), and predicted the life cycle in human malaria to be similar to that observed in bird malaria. Later in the same year, Grassi, Bignami and Bastianelli described the complete development of malignant tertian malaria in *Anopheles maculipennis*, and actually transmitted malaria to man by the bite of these mosquitoes.

Ætiology. The malaria parasites affecting man belong to the genus *Plasmodium*. At least four species are recognised: (1) *Plasmodium vivax*, which causes benign tertian malaria; (2) *Plasmodium malariæ*, the cause of quartan malaria; (3) *Plasmodium falciparum*, causing malignant tertian or sub-tertian malaria; and (4) *Plasmodium ovale*, which was described by Stephens as recently as 1922. Stephens also described another parasite, *Plasmodium tenue*, in 1914, but its status is doubtful.

Malignant tertian malaria is the commonest variety and has the widest geographical distribution; in the tropics it occurs at all seasons of the year, but in the subtropics it tends to become epidemic in the late summer and early autumn, hence the name of æstivo-autumnal fever. Benign tertian malaria is more common in the more temperate zones; it was responsible for the malaria which flourished in England until the middle of the last century. The three common forms occur in the subtropics, but *Plasmodium ovale* has a very limited geographical distribution in Africa, the few cases reported to date mainly originating in Nigeria. People of all ages may develop the disease, but in endemic areas the infection is commonest in children, who gradually acquire a certain degree of immunity as they grow older. No race is exempt. Immunity probably implies latent infection, and in experimental avian and simian malaria acquired immunity depends on hypertrophy of the reticulo-endothelium system, with augmentation of its phagocytic functions. In India and Africa malaria disappears at a level

above 6,000 feet and in Europe above 3,000 feet. Most of the epidemics studied in the past have been subtropical, and associated with excessive rainfall and malignant tertian malaria. The Ceylon epidemic of 1934 differed. It was strictly tropical; drought conditions due to failure of the South-West Monsoon produced famine, and led to the breeding of the mosquito vector, *Anopheles culicifacies*, in small water holes in the dried river beds in areas of Ceylon where the immunity, as indicated by the spleen rate, was relatively low (Gill). Both species of tertian malaria (*P. falciparum* and *P. vivax*) were equally implicated. Whole villages were depopulated, work ceased in many agricultural areas and 80,000 people died in seven months as a result of the epidemic.

Life History of the Malarial Parasite. While malaria can be transmitted by the injection of blood from an infected patient collected in either the latent or

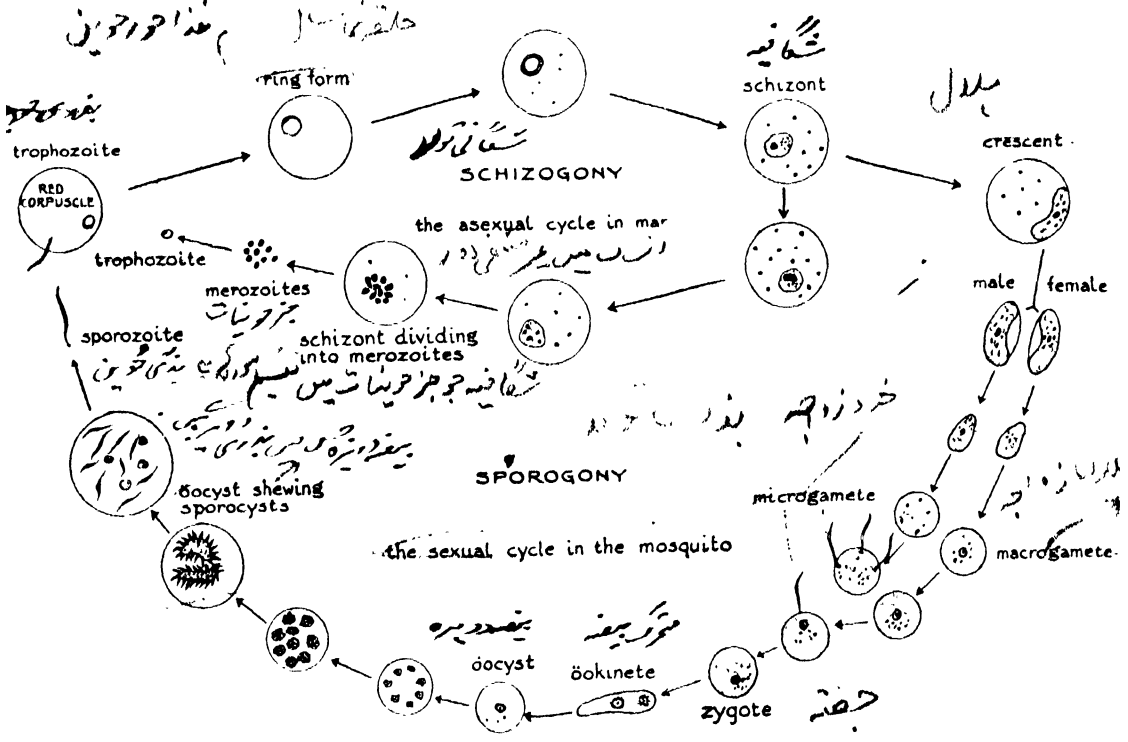


FIG. 101.—Diagrammatic representation of the life cycle of the parasite of malaria.

febrile phase, the disease under natural conditions is only transmitted from man to man through the medium of an infected female anopheline mosquito, which introduces the infecting sporozoites through its hypopharynx at the time of feeding. The parasite undergoes two cycles, one in man and other in the mosquito. In Fig. 101 the life cycle of the malignant tertian parasite is depicted.

Asexual Phase in Man. After the sporozoites are inoculated by the mosquito they pass into the blood stream and enter the red cells where vacuolation of their protoplasm occurs and they change into small rings containing black pigment (hæmozoin). At this stage the parasite exhibits active amœboid movements. The malignant tertian parasite does not affect the size of the corpuscle, whereas the quartan form fills the red cell and the benign tertian parasite actually expands it. As the parasite develops, the pigment collects centrally and the protoplasm and the chromatin divide into spores, forming the sporulating body, rosette or schizont. Later these spores, which are known as merozoites, escape into the plasma, penetrate new corpuscles and restart the cycle. If present in sufficient numbers they give rise to malarial fever, the cold stage of which synchronises with the liberation of the merozoites.

Sexual Phase in the Mosquito. In addition to the forms produced during sporulation in the asexual cycle in man, certain sexual forms or gametocytes appear. These are large, round or oval bodies, filling the corpuscles in benign

tertian infections, and large crescent-like bodies in the case of malignant tertian malaria ; when the latter are taken up by suitable mosquitoes they revert to a circular form. From the male gametes flagella separate off (exflagellation) and these penetrate the female gametocytes and fertilise them, the process being known as zygotism. The resulting body, which is known as the travelling vermicule or oökinet, elongates and penetrates into the stomach wall of the mosquito ; here it becomes circular in outline and develops into oöcysts, which become finally packed with spindle-shaped sporozoites causing hernia-like protrusions on its surface. These finally rupture and the sporozoites escape into the body cavity and ultimately make their way to the salivary glands. During the act of biting, the infected mosquito inoculates these sporozoites which penetrate the corpuscles and restart the infection. The rate of development in the mosquito is dependent, amongst other things, on the external temperature, and under optimum conditions takes about ten days, while the incubation period in man varies from nine to twenty-one days or longer, according to the species of *Plasmodium* involved.

Parasites in the Peripheral Blood. All forms of benign tertian and quartan parasites, as well as of *Plasmodium ovale*, are met with in the peripheral blood, but in malignant tertian malaria the schizonts are not found, owing to the fact that sporulation occurs in the internal organs. Small hair-like rings and large crescents (gametocytes) are alone present. The parasites are best demonstrated by staining with some Romanowsky stain, such as Leishman's or Giemsa's, and certain features, as emphasised by Wenyon (**52**), assist in differentiating the different species.

Ring Forms. In malignant tertian malaria the rings only occupy about one-sixth of the cell, which may show Maürer's dots ; they are generally fine, hair-like in appearance, often containing two chromatin dots, while multiple infection of the same corpuscle is not infrequent. Irregular and flattened marginal forms occur. The rings of *Plasmodium vivax* and *Plasmodium malariæ* are much larger and thicker and contain more cytoplasm, occupying about one-third of the corpuscle ; occasionally *Plasmodium vivax* may show multiple infection of the same corpuscle, though this is rare. The species cannot be determined if only one ring be found.

Partially Grown Forms. In *Plasmodium vivax* the Schüffner's dots are often scattered through the corpuscle, which tends to be enlarged and contain parasites which are irregular in shape and show light-brown pigment. With *Plasmodium malariæ* Ziemann's stippling may be demonstrated in the red cells, which are not enlarged ; the trophozoite resembles a signet ring, the pigment is dark brown or black and the parasite tends to stretch across the corpuscle producing a band-like form.

Adult Forms. The schizonts of *Plasmodium vivax* have sixteen and those of *Plasmodium malariæ* eight merozoites, whereas the gametocytes have a single nucleus and a different distribution of chromatin and pigment. The fourth species of malarial parasite, *Plasmodium ovale*, morphologically resembles *Plasmodium malariæ ;* the infected corpuscles, however, often show distorted shapes and contain Schüffner's dots.

Pathology. Early in the disease the spleen is soft and of a dark red colour, while in chronic infections it is enlarged, hard and of a dark steel-grey hue due to malarial pigment. Often there is peri-splenitis. The liver may be enlarged and plum-coloured, the lungs congested and œdematous and the intestinal mucosa and peritoneum leaden in colour. The brain and its membranes may present a similar discoloration as well as congestion, œdema and punctate hæmorrhages. Sections reveal malarial pigment in the reticulo-endothelial cells of the liver, spleen, bone marrow, etc., while pigmented mononuclears and leucocytes may be observed in the vessels. The liver, spleen and kidney show the Prussian blue reaction due to deposition of a fine brown iron-containing pigment—hæmosiderin

—in the parenchyl cells. The cells of the liver and the tubular epithelium of the kidneys may show cloudy swelling, fatty degeneration or necrosis, while the capillaries of the internal organs, such as the spleen, intestine and liver as well as the brain, may be blocked with emboli of infected adherent erythrocytes. In fatal benign tertian and quartan malaria severe ankylostome infection, intercurrent pneumonia, sepsis or tuberculosis is generally found.

Clinical Pathology. Considerable blood destruction occurs in malaria, the hæmoglobin being converted into an iron-containing pigment, hæmosiderin, and hæmo-bilirubin demonstrable by the indirect van den Bergh reaction. The hyperbilirubinæmia varies from 1·0 to 6·0 units and is responsible for the mild hæmolytic jaundice so often observed clinically. Hæmo-bilirubin is transformed by the polygonal cells of the liver into choli-bilirubin or bile pigment, pleocholia resulting. This, in turn, produces bilious vomitus and dark-coloured stools containing an excess of stercobilin which on re-absorption gives rise to urobilinuria so characteristic a feature of chronic malaria. In severe infections the blood may become watery and a severe hæmolytic anæmia of normocytic type ensues. Demonstrable hæmoglobinæmia and hæmoglobinuria do not occur in uncomplicated malaria as the destroyed corpuscles are broken up within the reticulo-endothelial cells.

Symptoms. The outstanding clinical features of malaria are fever, splenomegaly and anæmia. During the initial attack the pyrexia is often continuous or remittent in type (primary paludism), and only later may it assume its characteristic periodicity.

I. ***Benign Tertian Malaria.*** Attacks of ague generally begin in the forenoon or early afternoon and consist of cold, hot and sweating stages. The cold stage corresponds to the escape of merozoites into the circulation, and the whole phenomenon probably represents a protein shock effect.

(1) *Cold Stage.* The patient feels listless and develops headache, backache, and pain in the limbs, followed by feelings of chilliness. Then the rigor begins. He lies curled up with chattering teeth and shivers so violently that the whole bed shakes. The face is pinched and blue, and the patient covers himself with blankets and rugs in a fruitless effort to keep warm. Though the rectal temperature is considerably above normal, the skin surface at this time is actually cold, due to contraction of the superficial vessels. Vomiting is common and nausea usually present. Toward the end of this stage, which lasts half an hour to two hours, the axillary temperature rises rapidly, attaining a height of 103–106° F.

(2) *Hot Stage.* The body now becomes burning hot and dry and the bedclothes are discarded. The temperature is high, the arterioles relax, the pulse becomes quick, hard and full, the carotids throb, the face is flushed, the head aches, and in severe cases stupor or even delirium may develop. This stage lasts three to four hours.

(3) *Sweating Stage.* The skin now gradually moistens. Sweating becomes profuse for some hours, pain and discomfort disappears, the pulse slows, the tongue becomes moist, and the temperature falls, slowly at first and then more rapidly till a normal level is reached. When the attack is over the patient feels reasonably well, but after an interval determined by the species and number of the parasites another paroxysm occurs. Usually the paroxysm lasts eight to twelve hours, with forty-eight hours interval between the bursts of fever ; cycles developing on consecutive days may result in quotidian fever.

The spleen as a rule is palpable even during the first attack of malaria, and it can often be felt as a soft, tender mass below the left costal margin, moving on respiration. In more chronic cases it is definitely hard and less tender, and in advanced cases may assume large dimensions. Herpes also is common, and a secondary anæmia of moderate degree generally develops. The liver may be increased in size, but this is not as common as in malignant tertian fever. Even if untreated benign tertian malaria rarely lasts more than three years.

II. ***Quartan Malaria.*** The rigor and clinical picture are very similar to that of benign tertian malaria. The temperature may rise to 105° F. or 106° F., but the paroxysm is generally shorter, lasting only four to five hours. Single infections generally cause fever every fourth day with an apyrexial interval of seventy-two hours. Cycles on consecutive days may cause two days of consecutive fever with twenty-four hours clear interval on the third day, while treble cycles may produce quotidian fever.

III. ***Plasmodium Ovale.*** Though in blood films the parasites look more like quartan malaria, the schizogonous cycle takes forty-eight hours and tertian fever results. The general clinical picture resembles that of benign tertian malaria.

IV. ***Malignant Tertian Malaria.*** Three types of fever are met with: (1) the usual tertian type with fever on alternate days; (2) quotidian fever due to a double cycle; (3) continuous irregular or remittent fever attributable to several generations of parasites producing small pyrexial bursts at short intervals. Though chilliness is felt, rigors are not usually present and the temperature rises less abruptly; the hot stage tends to be prolonged and the sweating stage less intense. The whole paroxysm lasts from twelve to eighteen hours. Not infrequently the fever never completely intermits and a remittent type of temperature results. General features, such as backache, headache, nausea, anorexia and vomiting are characteristic, and a severe hæmolytic anæmia may rapidly develop. The spleen though soft is enlarged and tender at this stage and hepatomegaly is common.

Special Forms of Pernicious Malaria. Malignant tertian malaria is very protean in its manifestations, the variable clinical picture being dependent on excessive blood destruction, toxic effects on the renal and hepatic parenchyme cells, and the clumping together of parasitised cells causing plugging of the capillaries in the internal viscera and brain of man. (1) *Hæmolytic Anæmia.* The gravest cases may resemble pernicious anæmia clinically, the counts in extreme instances reaching 1,000,000 to 2,000,000 corpuscles per c.mm. The colour index, however, does not exceed unity, megalocytosis is not marked and the average diameter of the corpuscle is normal. Dyspnœa, palpitation, retinal hæmorrhage, hæmic murmurs, hæmolytic jaundice, bilious stools and dark brown urine are present. (2) *Malarial Jaundice.* There are two distinct types—hæmolytic and toxic. Hæmolytic jaundice is characterised by splenomegaly, bilious vomiting, bilious stools associated with hyperbilirubinæmia, pleocholia and urobilinuria; the indirect van den Bergh is positive and bile pigments and bile salts are absent from the urine which contains a considerable increase in urobilin. Toxic malarial hepatitis presents similar clinical features, but the liver is larger and more tender, epigastric distress is present and hæmorrhage from the gastro-intestine or elsewhere may occur. Jaundice comes on early after the onset of fever, the urine contains bile salts and bile pigments and a direct bi-phasic van den Bergh reaction is often found. Here degeneration of the parenchymatous cells of the liver has supervened. Remittent or intermittent fever may accompany either type, but the old term "bilious remittent fever" has led to considerable confusion in the past and is better abandoned. (3) *Cerebral Malaria.* In cerebral malaria the onset is usually rapid, the patient complains of severe headache, dizziness and drowsiness and may rapidly pass into complete unconsciousness or he may develop hemiplegia, paraplegia, aphasia, convulsions or delirium and mania. The temperature may follow the usual course or hyperpyrexia may develop with cyanosis, stertorous breathing and coma, simulating sunstroke. (4) *Abdominal Malaria.* Gastric, choleraic and dysenteric types of malaria may occur, the clinical features being due to involvement of the stomach, small intestine and large bowel respectively. In algid malaria the temperature falls below normal, and collapse supervenes. The skin is cold and covered with sweat; vomiting and diarrhœa are continuous and intractable, and occasionally blood is vomited or passed *per rectum.* The prognosis in these cases is bad.

Where the peritoneum is implicated peritonism with abdominal pain, vomiting and collapse ensues and acute pancreatitis, cholecystitis or appendicitis may be erroneously diagnosed. The typhoidal form (typho-malaria) is characterised by a continuous fever with little remission, extending over many days ; asthenia and low delirium may develop with a clinical picture resembling that of enteric. Unless the condition be recognised and properly treated, the patient dies. (5) *Cardiac Malaria.* Syncope associated with venous congestion and dilatation of the right heart ensue : the outlook is grave. (6) *Renal Malaria.* Inadequate attention has been paid to this condition, especially in early hyper-infections with malignant tertian malaria ; the urine contains albumin and casts, there is urea retention, and unless specific treatment be given uræmia may develop. (7) *Malarial Cachexia.* In those who have had repeated attacks of malaria, and in the natives, children and adults in hyper-endemic areas, the bodily health becomes seriously undermined. Lassitude, anæmia, a sallow, earthy appearance of the skin, dizziness, anorexia, digestive disorders, hypochlorhydria or achlorhydria, and aching in the joints and muscles, are common features. In severer forms there may be œdema or hæmorrhages unassociated with fever. "Ague cake" spleen is characteristic, being hard and often enlarged to below the umbilicus. The liver may also be markedly enlarged and, owing to dyspepsia, cirrhosis or gastric carcinoma with secondary deposits may be suspected.

Complications and Sequelæ. Neuralgia, especially of the superorbital nerve, neuritis, ulceration of the cornea, iritis, optic neuritis, retinal hæmorrhages and occasionally orchitis may occur. Herpes labialis is common, especially in benign tertian infections, while rupture of the enlarged spleen from slight trauma is liable to occur. Nephritis with œdema is especially frequent in quartan malaria. Soft pigment stones may form in the gall bladder as the result of pleocholia, but true malarial cirrhosis never occurs. Malarial fever not infrequently produces abortion and there is much more danger in withholding quinine or atebrin than in administering them in pregnancy.

Diagnosis. Attacks of malaria are often distinguished by their periodicity and this is especially the case with tertian and quartan fevers, the onset of which is often in the forenoon or early afternoon. Daily rigors are less to be trusted as they occur in various septic conditions, including pyæmia, cholangitis, abscess of the liver, pyelitis and malignant endocarditis. Other points of clinical importance are the presence of splenomegaly, secondary hæmolytic anæmia and the laboratory findings. Blood smears should be made before specific drugs are administered. Where parasites are scanty in the peripheral blood more than one examination may be necessary. The finding of pigmented leucocytes, a mononucleosis during the apyrexial period of 15 per cent. or over, and the presence of urobilinuria are all very suggestive. The therapeutic response to specific drugs may or may not be significant.

Prognosis. In tropical countries malaria is the largest factor in the death rate, and is specially serious in the under-nourished, in young children and in those suffering from intercurrent disease like ankylostomiasis. Benign tertian malaria is not generally fatal, except in the debilitated and anæmic, the very young and the very old, but it definitely predisposes to intercurrent infections which are the chief causes of death. Malignant tertian malaria, if untreated, often kills, but following specific treatment this species of parasite is permanently eradicated more easily than either benign tertian or quartan malaria.

Prevention. Mosquito boots should be worn in the evening and residents should sleep under mosquito nets or where possible live in mosquito-proof houses. The application of volatile oils, such as oil of citronella round the ankles, wrists and neck may be useful. Tropical residents should obliterate the breeding places about their bungalows and gardens and frequently inspect the surrounding areas for mosquito larvæ. The destruction of anopheline larvæ and of their breeding grounds by oiling, spraying with Paris green, or drainage,

are important measures in malarial control. Prophylactic quinine prolongs the incubation period and tends to keep the disease subclinical. It fails, however, to prevent malarial infection. Plasmoquine, on account of its specific lethal action on gametocytes, has superior claims to quinine as a true prophylactic.

Treatment. During the attack the patient should go to bed and remain there until after the temperature has been normal for at least three days. A brisk purge is given at the onset of the fever and hot drinks encouraged. Hot bottles and plenty of blankets are appreciated in the cold stage and during the hot stage an aspirin-caffein-citrate mixture is helpful. Frequent hot drinks containing bicarbonate of soda may be given during the sweating stage. Constipation must be avoided and sodium or magnesium sulphate should be administered regularly.

The specific drugs include quinine, plasmoquine and atebrin. Neosalvarsan can be used with advantage in resistant cases of *P. vivax* infection, but it exerts little effect on *P. falciparum*.

Quinine. Quinine remains the sheet anchor of malarial therapy. During an acute attack it has a less dramatic effect on malignant tertian malaria than on either benign tertian or quartan, but relapse is not so frequent. The drug acts on the schizonts and allays clinical symptoms, but does not kill either the gametocytes or the sporozoites. A number of different preparations are available including the hydrochloride, bihydrochloride, bisulphate and sulphate. There is no agreement regarding the optimum dosage and duration of treatment, but 10 grains thrice daily for the first week, followed by 10 grains twice daily for two weeks, thereafter 5 grains night and morning for three weeks is a reasonable compromise. With the exception of bihydrochloride of quinine, which can be given in non-sugar-coated tablets by the mouth, quinine should be administered in solution. The bisulphate can be readily dissolved by the addition of hydrochloric acid. Deafness and tinnitus may temporarily follow the administration of quinine in larger dosage and is a useful indication to its absorption. Owing to its solubility the bihydrochloride is used for both intramuscular and intravenous injection, the dosage being 10 grains and the concentration 1 grain to each cubic centimetre. Intravenous injections are superior and leave no after-effects, provided the quinine is adequately diluted and injected slowly. It is particularly useful (1) where vomiting is excessive ; (2) in obstinate cases where quinine is ineffective *per os* through malabsorption or other causes ; (3) in such grave types as cerebral or algid malaria where its speedy administration is essential to save life. Idiosyncrasy to quinine may manifest itself in severe erythematous and urticarial rashes and the usual toxic effects such as tinnitus, deafness, amblyopia, visual and gastric disturbances. Children bear quinine well and exhibit relatively greater tolerance than adults. For an infant of one year, 5 grains need not be regarded as excessive. In malarial countries it is sound practice to administer quinine during the puerperium and before operation or anæsthesia. As a general rule, quinine in adequate dosage reduces the fever in thirty-six to fifty-six hours, but occasionally cases are encountered which prove refractory even to intravenous quinine.

Plasmoquine. This drug—a methoxy-quinoline derivative—appears to have little effect on schizonts in malignant tertian malaria, though it destroys the gametocytes. In benign tertian malaria it probably acts on both sexual and asexual forms. The drug is best given in tablet form combined with quinine as quino-plasmoquine. Each tablet contains 0·01 gram ($\frac{1}{6}$ grain) of plasmoquine and 0·3 gram (4 grains) of quinine sulphate, two tablets being given thrice daily after food for six days. A clear interval of four days is allowed and a similar course readministered ; four or five such courses are advocated. Toxic symptoms include nausea, vomiting, headache and a bluish discoloration of the skin due to methæmoglobinæmia.

Atebrin. This compound is a synthetic alkylamino-acridin derivative which

is administered in tablet form in a dosage of 0·1 gram after food, thrice daily, for five to seven days. Like quinine, it acts on the schizonts and compares favourably with that drug in ridding the blood of parasites, relieving symptoms and preventing relapses. Intestinal pain, troublesome dreams and transient yellow tinting of the skin may follow its administration, but serious toxic manifestations are infrequent; patients often prefer it to quinine owing to the short period over which it is administered. It is particularly valuable in quinine idiosyncrasy and blackwater fever, for unlike quinine and plasmoquine it never appears to precipitate hæmoglobinuria. Atebrin mucinate (0·125 gram = 0·1 gram of atebrin) has recently been introduced for intramuscular injection and has been widely used in the Ceylon epidemic, but the general consensus of opinion is that it has not proved satisfactory for dispensary work though efficacious in hospital patients. During convalescence iron may be given in full dosage in the form of Pil. Ferrous Carb. after meals, grains xv being taken three times a day, or as ferri et ammonium citras, grains xxx t.d.s. p.c. Malarial patients should be specially advised against cold baths, bathing, chill, over fatigue and taking alcohol to excess, as these are the factors which precipitate relapse in latent cases.

BLACKWATER FEVER

(*Malarial Hæmoglobinuria. Hæmoglobinuric or Melanuric Fever*)

Blackwater fever results from one or more intravascular hæmolyses in the course of chronic malignant tertian malaria, leading to rigor, fever, backache, vomiting, jaundice, anæmia, hæmoglobinæmia, hæmoglobinuria and perhaps anuria. A lytic substance originating from a metabolic breakdown is probably responsible.

Ætiology. Blackwater fever occurs on the western and eastern coasts of Africa, Nyassaland, Uganda, the Sudan and other parts of tropical Africa; in Madagascar, in the Duars, the Terai and the Jeypore Hill tract in India; in Palestine, Macedonia, Italy and Greece; in the Southern United States, Central America, Panama, Venezuela, Guiana and New Guinea. Invariably it originates in heavily infected or hyper-infected endemic zones of malignant tertian malaria and most frequently occurs after one to five years' residence. Where a patient recovers, recurrent attacks are not uncommon. Adults and children are both susceptible, but native populations may enjoy immunity where European residents and imported natives develop the condition. There is almost invariably a history of chronic malaria, for which quinine has generally been taken at irregular intervals. The exciting causes precipitating an attack are (1) the administration of quinine; (2) chill; (3) over-exertion. Quinine and plasmoquine may both precipitate attacks and possibly they do this through the quinoline ring which is common to both compounds. Cases, however, occur in which no quinine or other drug has been administered and a number of cases have been encountered during pregnancy.

Morbid Anatomy. The post-mortem findings are those of severe hæmoglobinuria engrafted on clinical malaria. The liver is soft and enlarged, the bile thick and tarry, the spleen is much increased in size with diffluent pulp and the kidneys are congested, dark and swollen. Hæmosiderin, giving a Prussian blue reaction for free iron, is found in the liver, kidneys and spleen and malarial pigment is present in the different viscera though not in as large amounts as one would anticipate. The kidneys show cloudy swelling, toxic degeneration and disintegration of the cells of the convoluted tubules, while eosinophilic granular *débris* blocks the lumina of the tubules. There may be cloudy swelling and central necrosis of hepatic cells in the liver lobules, while malarial pigment is generally demonstrable in the Küpffer cells. Jaundice is almost invariably present.

Clinical Pathology. At the beginning of a paroxysm in blackwater fever malarial parasites are frequently demonstrable, but after the second day they

tend to disappear and are generally absent at autopsy. The *urine* varies in colour from port-wine to porter and contains oxyhæmoglobin, generally methæmoglobin and also urobilin in excess. Albuminuria is invariable, but bile is noted only in the most severe cases. The centrifuged deposit is composed of a brown granular *débris* and granular casts; red blood corpuscles are scanty or absent. The *plasma* contains both oxyhæmoglobin and methæmoglobin which is the predominant pigment. Recently a new pigment (**53**) allied to methæmoglobin has been encountered which fails to reduce with Stoke's reagent and does not appear in the urine. Hæmobilirubin is greatly increased, the indirect van den Bergh varying from 5 to 85 units, but direct immediate and biphasic reactions are only found in gravely ill patients with toxic necrosis of the liver. Polyuria may be present or *renal involvement* may lead to oliguria and in some instances to anuria with urea retention, the blood urea rapidly rising to as much as 450 mg. per 100 c.c. before death. The blood urea is markedly increased, the excess being derived partly from destroyed corpuscles and partly through urea retention. Even in non-fatal cases it may reach 450 mg. per 100 c.c. Renal acidosis may develop; under these circumstances the CO_2 combining power of the plasma is markedly lowered, the serum calcium decreased and the blood phosphorus increased. The *anæmia* is normocytic in type and a rapid decrease in the red cell counts follows the onset of hæmolysis, of which there may be several distinct bouts. In severe cases 1,000,000 to 2,000,000 red corpuscles per c.mm. may be lost over-night (see Plate 66).

In blackwater fever the hæmolytic agent appears first to lyse the corpuscles and later to convert the liberated oxyhæmoglobin into methæmoglobin, acting in this respect as an oxidising agent (**53**). Both pigments appear in the plasma and when they reach a sufficient concentration the renal threshold is passed and they are excreted as such in the urine. If the urine be acid in reaction, oxyhæmoglobin which has filtered through the glomerulus is liable to be converted into methæmoglobin and acid hæmatin. Precipitation in the tubules results, causing blockage. Another factor—toxic degeneration of the secretory epithelium of the convoluted tubules—is, however, quite as important in causing the anuria. Both the quantity of blood lysed and the rapidity of its hæmolysis have an important bearing on the capacity of the kidney to recover, and should the amount hæmolysed exceed 540 c.c. within the half-hour, irreparable damage with fatal anuria appears to result. Only 10 per cent. or less of circulating blood pigment appears in the urine; the remainder has to be dealt with by the reticulo-endothelial cell system, with resulting hæmosiderosis, hyperbilirubinæmia and pleocholia.

Symptoms. As a rule, patients think there is an ordinary attack of malaria impending, for which they take quinine. Generally, within a few hours, but sometimes not for days, a rigor and pain in the loins develop, but in cases of less severity the first indication may be the passage of reddish-coloured urine. Following the rigor there is invariably a rise of temperature, which is accompanied or followed by nausea, epigastric discomfort, vomiting and anæmia. The urine soon becomes port-wine or porter coloured, though it may be reddish at first. Jaundice appears within a few hours of onset and is well-established by the second day. The pulse is rapid and at onset the blood pressure is markedly decreased, the systolic reading being 70 to 90 millimetres of mercury. Later, as the shock of the first intravascular hæmolysis passes off and the kidneys become implicated, the blood pressure rises. Headache and photophobia may be severe. As the anæmia increases the patient develops great restlessness and anxiety, the skin becomes pallid, the extremities cold and the pulse rapid and thready. Hiccough, which is almost constant in severe cases, is not incompatible with recovery, but like Cheyne-Stokes respiration it has a sinister significance. Abdominal examination reveals tender enlargement of the spleen and liver and there is often localised tenderness over the gall bladder which is tensely distended

with bile. During the attack, the spleen undergoes a decrease in size, attributable to expulsion of reserve blood to meet the anoxæmia. The temperature at onset resembles a malarial paroxysm and generally attains its maximum height on the first day; subsequently the fever may be either remittent or intermittent, and frequently reaches the normal in three or four days' time, though it may be prolonged for as long as a fortnight. Hyperpyrexia with temperature of 110° F. may precede death. After the hæmoglobinuria has ceased, post-hæmoglobinuric fever may appear and persist for several days. Apart from the average case as above described, several different clinical types are described: (1) *fulminating* types which die in from thirty-six to seventy-two hours as the result of toxæmia or anoxæmia; (2) the *anuric* type, which commences with severe symptoms, catheterisation showing only a small quantity of highly albuminous, perhaps bile-stained, urine, followed later by complete suppression with a normal or subnormal temperature; this condition may last a week or longer before death occurs; (3) *continuous* or *intermittent* type of hæmoglobinuria; the temperature persists and hæmoglobinuria may be either continuous or remittent, several distinct bouts of hæmolysis occurring during the period; post-hæmoglobinuric fever may follow; (4) *hæmorrhagic* type; here cases may develop skin hæmorrhages, hæmatemesis or melæna.

Course and Complications. The complications include hæmolytic anæmia, anuria, post-hæmoglobinuric fever and biliary colic; pigment calculi and cholecystitis are occasional sequelæ. According to Ross (**54**), about 10 per cent. of the cases relapse during the course of an attack. Unfavourable features include intense jaundice, anuria, hyperpyrexia and the appearance of bile in the urine. Dyspnœa, Cheyne-Stokes respiration and a fall of the red cell count to 1,000,000 per c.mm. or less are ominous features, and death is inevitable under these circumstances unless anoxæmia be combated by blood transfusion. The mortality rate is about 30 per cent.

Prevention. The prevention of blackwater is the prophylaxis of malignant tertian malaria. Quinine, if taken prophylactically, should be taken continuously in 5-grain doses daily during the period of residence in an endemic area of blackwater fever. As both quinine and plasmoquine are known to precipitate attacks and atebrin appears free from this danger, patients who have previously had blackwater fever should receive only atebrin for malaria during the febrile stage, followed by quinine later where necessary.

Treatment. Since the hæmolysis itself cannot be controlled the most rational procedure is to treat complications as they arise and combat the known causes of death which are: (1) anæmia, anoxæmia and heart failure; (2) toxæmia; (3) urinary suppression. One is justified in moving a patient only if it places him under better conditions for treatment. The patient must be kept continuously in bed and nursed in the recumbent posture; under no circumstances should he attempt to sit up or do anything for himself. With patients suffering from shock with low blood pressure it is immediately advisable to elevate the foot of the bed, supply hot bottles and bandage the limbs. Fluid in large quantity should be given by the mouth, and if necessary by the rectum and intravenously. Barley water, fruit juices and glucose are allowed, and later milk, junket, arrowroot, custard and Benger's food. Proteins are restricted well into convalescence or until renal function is normal. Vomiting often is troublesome and gastric lavage with bicarbonate of soda may prove valuable. The urine should be alkalised as rapidly as possible by the administration of citrate and bicarbonate; should this fail in its objective 1 pint of doubly distilled water containing 150 grains of bicarbonate of soda solution may be injected intravenously and repeated if necessary. Owing to the liability of converting the bicarbonate into the toxic carbonate during sterilisation by heat, it is better to add bicarbonate powder after the distilled water has cooled, unless it be possible to sterilise the bicarbonate solution by filtration. For anuria, 1 to 2 pints of an

isotonic 5 per cent. solution of glucose are used or smaller quantities of hypertonic glucose (10 per cent. to 20 per cent. solution) may be substituted. Heat and dry cupping should be applied to the loins and mild diuretics like caffein citrate may be given. The bowels should be kept open with a saline purge. Blood transfusion may be necessary in severe cases after hæmolysis has ceased, but it should be given to all gravely anæmic cases during the hæmolytic period where the counts fall below 1,500,000 cells per c.mm., and especially if tachycardia, restlessness, dyspnœa and Cheyne-Stokes respiration be present. Transfusion can be given with absolute safety in polyuric cases, but where oliguria is marked or anuria has set in it should only be given for grave anæmia. Where parasites persist atebrin may be given with safety. Iron should be given in full dosage during convalescence, commencing about the fourteenth day.

Leishmaniasis comprises a group of diseases caused by parasites of the genus Leishmania, and includes kala-azar due to *Leishmania donovani*, Mediterranean or infantile kala-azar caused by *Leishmania infantum*, oriental sore due to *L. tropica*, and espundia or American leishmaniasis due to *L. brasiliensis*. The various Leishmania affecting man are morphologically indistinguishable (**55**), and little assistance is obtained from animal inoculation. Noguchi (**56**) found three distinct serological types—*L. donovani*, *L. tropica* and *L. brasiliensis*; the agglutinating reactions with cultures of *L. donovani* and *L. infantum* were identical. Recently Penna (**57**) has described the presence of visceral leishmaniasis in Brazil, the parasite differing from the Leishmania form of *Trypanosoma cruzi* in sections of the liver, but whether it is identical with *L. donovani* has not yet been determined.

KALA-AZAR (*Plate 67, 4, p. 1053*)

(*Black Fever*)

This is a specific disease associated with splenomegaly, hepatomegaly, emaciation, irregular fever and anæmia caused by *L. donovani*, which can be demonstrated in the peripheral blood or by splenic puncture. The insect vector is almost certainly *Phlebotomus argentipes*.

Ætiology. Kala-azar is found in India, Assam, North China and the Mediterranean littoral, where children are mainly affected; more rarely it occurs in Indo-China, the Sudan, Abyssinia, Mesopotamia and Russian Turkestan. Both Europeans and natives contract the disease. In the human body the parasite occurs as a small, oval structure some 2 to 5 μ long and 1 to 2 μ in breadth, containing a macronucleus or trophonucleus staining bright red and a micronucleus or rhizoplast which is rod-shaped, staining a deep purple red with Romanowsky's stain. Blood obtained by venous puncture or splenic juice generally contains the parasites; these can be cultivated on rabbit blood agar (N.N.N. medium) kept at room temperature (20° to 25° C.) for fourteen days provided bacterial contamination be avoided (see Plate 67). During this period the parasite develops a flagellum and centrosome at one end and a central macronucleus—undoubted evidence that under natural conditions it undergoes development in some insect vector which is almost certainly the sand fly. If sand flies be fed on kala-azar cases, leptomonad forms develop which are capable of producing the disease on injection into hamsters; to date, however, transmission has rarely been attained through the actual bite of experimentally infected sand flies. The Mediterranean form of kala-azar especially affects children. The dog is the natural host and transmission again is by sand flies.

Pathology. *Leishmania donovani* bodies are found in the reticulo-endothelial cells, especially of the liver, spleen, lymphatic glands and the bone marrow, where they multiply and eventually rupture; subsequently they are taken up by the phagocytic cells. They have also been found in the kidneys and intestinal

submucosa. At post-mortem, wasting is marked, and effusions into the serous sacs not infrequent. Early the spleen is soft and pliable, later it becomes hard and fibrous. Perisplenitis, thickening of the capsule and infarction is by no means uncommon. The liver is firm, its capsule thickened, and a nutmeg appearance and fatty degeneration are common. Cirrhosis may eventually result. The parasites are found in large numbers in the Küpffer's cells. The marrow in the long bones is red and soft, due to hyperplasia, and the mesenteric glands are swollen and may show central necrosis. The heart is flabby and dilated, while ulceration may involve the small or large bowel.

Symptoms. Cases may occur a year or more after exposure to infection, but generally the incubation period varies from one to four months. The onset is insidious or sudden with fever which may be mistaken for typhoid or malaria. The temperature may be irregular, remittent or intermittent. Sometimes there is no fever during the day, but a rise occurs later; in others there is a double daily rise in the afternoons and evenings. The skin may show a deepening colour with pigmentation and loss of hair. The liver is palpable in nearly 90 per cent. of cases, presenting a sharp lower border. Splenomegaly is the rule, but during the first month or two it may not be palpable; generally at this stage it is obviously enlarged and feels soft but not tender; later it may attain huge dimensions, conveying a sense of hardness to the palpating hand. The appetite is good but the digestion poor and this in itself may lead to diarrhœa. Night sweats are common. A moderate degree of anæmia with rapid loss of weight and cachexia frequently develops. There may be palpitation, dyspnœa, œdema of the extremities and occasionally puffiness of the face. The blood pressure is low, systolic readings often being below 100 mm. mercury. Congenital cases have been described where an infected mother has transmitted the disease directly to the fœtus. *L. donovani* may be demonstrated in thick blood films, in smears from the liver or spleen or by blood culture. *Splenic puncture:* the patient should be recumbent and the skin sterilised by tincture of iodine; an area is selected an inch or so below the costal margin about midway between the anterior and posterior margin of the spleen. If large enough, an assistant may hold the organ in position to prevent movement and the patient should be instructed to hold the breath when the needle is inserted. After the skin has been anæsthetised, a needle $1\frac{1}{2}$ inches in length is inserted firmly into the spleen in a backward and upward direction, and the attached syringe aspirated. Better results are obtained if the splenic juice contains a minimum of blood. It is essential always to examine the peripheral blood for leukæmia before puncturing the spleen, as fatal hæmorrhage may otherwise result, also to watch the patient for two or three hours after this procedure. Slides are prepared by smearing a drop of the splenic juice on a clean slide, letting this dry and subsequently staining with Giemsa's or Leishman's stain.

The *Aldehyde Test* is of great value and has largely replaced spleen puncture in the large kala-azar clinic at the Calcutta School of Tropical Medicine. Napier's technique is as follows: About 5 c.c. of blood are taken from the median basilic vein and allowed to clot; 1 c.c. of the supernatant serum is subsequently removed with a pipette and 2 drops of commercial formalin are added to it in a small test tube, which is shaken and left at room temperature. If the reaction be positive, a white opacity develops within one to two minutes, and within half an hour sets like blancmange, so that the tube can be inverted without spilling. Mere jellification has no significance, the diagnostic feature being an opaque solidification like the white of a hard-boiled egg. About 80 per cent. of cases give positive reactions as against about 90 per cent. on splenic puncture. The aldehyde test is generally negative during the first three months of the illness.

Blood Picture. The blood changes include anæmia, leucopenia and reduction in the platelet count. The hæmoglobin may be reduced proportionately to the fall in erythocytes so that the colour index approximates to 1; in other cases it varies from 0·7 to 0·8. The anæmia itself is generally of moderate intensity, but

in severer cases the blood picture shows anisocytosis, poikilocytosis, polychromasia and normoblasts. It has been attributed to the crowding out of the erythroblastic marrow by proliferating reticulo-endothelial cells which are heavily parasitised. Leucopenia is extremely characteristic and counts of 2,000–4,000 per c.mm. are common. There is a relative increase in lymphocytes and monocytes with a decrease in neutrophiles and eosinophiles. The coagulation time may be extended while the globulin is raised and the serum albumin, sugar and calcium decreased; euglobulin increases at the expense of the pseudo-globulin fraction.

Complications and Sequelæ. Diseases like influenza, pneumonia and tuberculosis commonly cause death. Otitis media and cancrum oris may be encountered, especially in children. During treatment with antimony compounds, agranulocytosis may develop, and probably the tendency to cancrum oris as well as susceptibility to secondary infection is related to the depressed condition of the leucoblastic marrow as indicated by the leucocyte counts. Epistaxis, bleeding from the gums, melæna and purpura sometimes supervene, and diarrhœa with or without muco-sanguineous stools is frequent; the latter finding, however, should always suggest dysenteric infection (**58**). Chronic splenomegaly, associated with severe anæmia, and hepatic cirrhosis, with or without ascites and demonstrable parasites, are included amongst the sequelæ. Jaundice not infrequently appears within three months of treatment. Post kala-azar dermal leishmaniasis may also occur, beginning within a year of treatment as areas of pigmentation, followed by papulomatous nodules in which *L. donovani* are found. The parasites are confined to the skin and puncture fails to reveal them in either the spleen or liver. Occasionally dermal lesions develop in patients giving no history of previous kala-azar infection.

Diagnosis. Kala-azar has to be differentiated from the fevers associated with splenomegaly, and these include, in order of their importance, chronic malaria, undulant fever, typhoid and the para-typhoid fevers. In children Mediterranean kala-azar needs to be differentiated from certain blood diseases such as Cooley's anæmia commonly encountered in Greece, von Jaksch's anæmia and acholuric jaundice, and it should be remembered that parasites are less common in the peripheral blood than in Indian kala-azar. In both varieties laboratory confirmation should be sought.

Prognosis. The mortality rate in untreated patients is about 90 per cent.; the disease lasts from one to two years in chronic cases. Modern therapy generally results in cure, but a careful watch must be kept for the onset of agranulocytosis which requires immediate injections of nucleotide K.96.

Prevention. As the sand fly is the probable vector, measures directed to its destruction are indicated. The abandonment of infected houses, segregation and treatment of people who have acquired the disease are measures which have proved efficacious in India.

Treatment. General treatment includes rest in bed during the febrile stage, a light nourishing diet adequate in vitamins with iron tonics for the anæmia. Cardiac stimulants such as digitalis are indicated in advanced cases. The old treatment with trivalent antimony compounds like tartar emetic has been replaced by pentavalent antimony derivatives which include neostibosan or von Heyden 693, urea-stibamine, neostam and stibosan von Heyden 471. With neostibosan an initial dose of 0·1 to 0·2 gramme may be given, and subsequently this should be increased to daily injections of 0·3 gramme over a period of eight to twelve days; debilitated patients may require smaller dosage. Toxic features include nausea, vomiting, diarrhœa, giddiness, toxic hepatitis with jaundice, and occasionally an anaphylaxis-like condition with cardio-vascular collapse, urticaria and œdema of the subcutaneous tissues of the face. Insufficiently treated cases relapse, and occasionally patients need larger doses and more prolonged courses of treatment. If agranulocytosis with cancrum oris appears injections of

nucleotide K.96 should be given immediately. Favourable features include a decrease in the size of the spleen, disappearance of the fever, increase in weight, re-establishment of a normal leucocyte count and a negative splenic puncture.

Children affected with Mediterranean kala-azar require more prolonged treatment and relatively a larger dosage of neostibosan or urea-stibamin to cure the condition.

ORIENTAL SORE

(*Tropical Sore. Bagdad Boil. Delhi Boil, etc.*)

An infective granuloma caused by *Leishmania tropica* involving the skin and subcutaneous tissues on exposed parts of the body.

Ætiology. The disease has a widespread distribution in India, the North-West Frontier, Mesopotamia, Arabia, Persia, parts of Africa, Spain, Italy and Greece. Being a disease of towns its endemicity has given rise to many synonyms. Though absolute proof has not yet been obtained, the remarkable development of *L. tropica* into virulent flagellates from the mid-gut to the proboscis of sand flies, like *Phlebotomus papatasii* and *P. sergenti*, suggests them to be the natural vectors of oriental sore. Wenyon, after experimental auto-inoculation, waited six months before the sore made its appearance. Dogs, cats and guinea-pigs are susceptible.

Pathology. The pathology is that of an infective granuloma. There is atrophy of the epidermis, infiltration of the corium and its papillæ with plasma cells, lymphocytes and endothelial cells containing the parasites.

Symptoms. The incubation period varies from a few weeks to six months. An itchy, red papule first appears which develops into a sort of blind boil or becomes covered with yellow crusts and forms a chronic indolent ulcer. The ulcer itself has a granulation tissue base which exudes a thin pus, and possesses well-defined, rounded edges. The sores are particularly common on the face, hands, wrists, feet and legs, and may be single or multiple ; on healing they leave an unsightly scar.

Diagnosis. This is made on the history, the geographical location of the patient, the characteristic local lesions and the isolation of the parasite. To demonstrate *L. tropica*, the edge of the ulcer should be punctured with a dry glass pipette and the material so obtained inoculated on to rabbit blood agar (N.N.N. medium). Smears should also be made and stained with one of the Romanowsky stains, as *L. tropica* can frequently be demonstrated within the endothelial cells.

Prognosis. If untreated the condition may last from six to eighteen months ; and as a rule the patient appears subsequently immune to further infections. The ulcers may be secondarily infected with bacteria, but severe sepsis rarely develops and the condition itself is practically never fatal.

Prevention. Active measures should be directed to the extermination of sand flies and their breeding grounds.

Treatment. Tartar emetic may be given intravenously as for schistosomiasis (p. 1070), a total course of 20 to 30 grains being advisable. Neostibosan has also been employed successfully. Injections of 1 c.c. of berberine sulphate ($\frac{1}{2}$ grain to 1 c.c.) two or three times a week have been utilised with benefit. Vaccines made from cultures of the parasites have been favourably reported on. The application of carbon dioxide snow for five to thirty seconds every ten days and X-ray therapy are especially useful. Ointments containing methylene-blue, iodoform and tartar emetic have been employed ; the latter is used in a strength of 1 to 2 per cent., but unfortunately local sloughing and much pain result.

American Dermal Leishmaniasis. (*Espundia ; Forest Yaws, etc.*) This is an infective granuloma caused by *Leishmania brasiliensis* which involves the skin and not infrequently the buccal and nasal mucous membranes, the lymphatics and lymph glands.

Ætiology. The geographical distribution is limited to Brazil, British and Dutch Guiana, Venezuela, Peru, Paraguay and Bolivia. It is encountered

amongst people living in forests, like woodcutters, but the insect vector is unknown.

Symptoms. The incubation period is from six to ten weeks. Itching papules appear which generally involve the skin and may either develop into blind boils or break down and ulcerate, forming fungoid granulations and large ulcers. Sometimes the marginal membranes of the mouth and nose are implicated, while later the nasal septum and larynx may be involved. General features such as pyrexia, joint pains and pulmonary symptoms develop, and the disease runs a chronic course extending over many years. Untreated patients generally die from intercurrent diease.

Diagnosis. The condition has to be differentiated from leprosy, tuberculosis, syphilis, gangosa and rodent ulcer, and this is best done by demonstrating the parasites in scrapings from the edge of the ulcers or by culture on N.N.N. medium as in *L. tropica* infections.

Treatment. A full course of 40 grains of tartar emetic should be administered intravenously, while other lines of treatment similar to those outlined for oriental sore and kala-azar are applicable.

Trypanosomiasis comprises a widespread group of diseases, caused by flagellate parasites of the genus *Trypanosoma* occurring in the blood and tissues of vertebrates. In Africa man is infected by *T. gambiense* or *T. rhodesiense*, and in South America by *T. cruzi*. *T. brucei*, which causes nagana affecting cattle, wild game, dogs and horses, is generally believed to be identical with *T. rhodesiense*.

AFRICAN TRYPANOSOMIASIS (*Plate 67, 1, 2*)

(*Sleeping Sickness*)

African trypanosomiasis is transmitted by the bite of tsetse-flies infected with *T. rhodesiense* or *T. gambiense*. Clinically it is characterised by irregular fever, circinate erythematous rashes, enlargement of the lymph glands and spleen and rapid pulse. Later the nervous system becomes involved with mental and physical degeneration, lethargy, tremors, shuffling gait, convulsions, coma and death.

Ætiology. Sleeping sickness must not be confused with sleepy sickness, the lay term for encephalitis lethargica. It is confined to tropical equatorial Africa, including West, Central and East Africa, and limited geographically to localities where the tsetse fly abounds. Areas particularly affected are the Congo, Uganda, Rhodesia and Nyasaland. Both sexes and people of any race and age are susceptible; Europeans suffer severely. Though the disease has long been known, it was not until Uganda was invaded in 1900 and its population greatly reduced that serious attention was paid to it. Two species of trypanosomes are recognised, *Trypanosoma gambiense* and *T. rhodesiense*, though they are indistinguishable in human blood and give rise to similar clinical manifestations. The trypanosome (see Plate 67, Figs. 1 and 2) is an elongated flagellate measuring from 18 to 25 microns in length and 2 to 2·8 microns in breadth. Centrally situated, there is a large oval nucleus (*trophonucleus*), while at the blunt posterior extremity one finds a small chromatin mass (*parabasal body*), and adjacent to it a smaller structure (*blepharoplast*) from which proceeds a flagellum. This flagellum runs along the free border of an undulating membrane to the anterior extremity of the organism and projects some distance beyond it. Parasites are found in the blood and lymph glands during the febrile stage and in the cerebro-spinal fluid later, while the disease may be produced in monkeys by inoculation of this fluid. The only means of differentiating the two species is to inoculate infected blood into white rats when post-nuclear forms develop if *T. rhodesiense* be present. Tsetse flies take up trypanosomes when sucking blood from man; the parasites multiply in the gut and pass forward to the salivary ducts and salivary glands where development proceeds. Within three to seven weeks the glossinæ become

infective and remain so for life. *T. gambiense*, the Central African type, is transmitted by *Glossina palpalis*, which may acquire its infection from wild game in in the vicinity of lakes and rivers frequented by this fly. *T. rhodesiense* is spread by another fly, *G. morsitans*, which inhabits arid country and probably acquires its infection from wild game also, Bruce regarding it as identical with *T. brucei*. Both glossinæ bite in the day time, but as they have different habitats prophylactic measures for their eradication vary considerably.

Pathology. The lymph glands draining the bitten area are first implicated, especially those in the neck and groin. They become swollen, inflamed and perhaps hæmorrhagic, undergo degeneration changes and chronic fibrosis. Splenomegaly also results from lymphoid hyperplasia, endothelial proliferation and fibrosis, while the capsule of the organ is often thickened. In the later stages trypanosomes involve the nervous system, producing microscopic changes resembling meningo-encephalitis and meningo-myelitis. Lymphocytic infiltration of the perivascular system is characteristic (Mott), and trypanosomes are found in the intercellular spaces of the brain and cord (York). Neuroglial cell overgrowth, diffuse glial proliferation and chromatolysis of the nuclei of the ganglion cells may be found.

Symptoms. The incubation period is from one to three weeks, but may be sometimes prolonged for some months. In many respects the disease resembles syphilis. Three stages may be recognisable, *i.e.*, the local lesion, a febrile stage and a cerebral stage. (1) *Local Features.* The bite of the infected glossina may cause inflammatory reaction lasting some days, and occasionally a delayed anaphylactoid type of local lesion with marked erythema and widespread indurated swelling of the skin and subcutaneous tissue results some seven to ten days after the bite. (2) *Febrile Stage, or Trypanosome Fever.* The patient develops attacks of fever lasting for a variable period. The temperature is low in the morning, higher at night and of an irregular, remittent or intermittent type. Periods of apyrexia may last for weeks. The pulse is rapid and of low tension, generally about 100 to 120 per minute, and a high rate persists even during the apyrexial periods. There is an increase in the respirations to twenty to thirty a minute. Erythematous rashes also appear, circinate in form, which involve mainly the trunk, and localised puffiness or œdema of the face, legs and feet may occur. The skin is often irritable and dry. Enlargement of the posterior cervical glands (Winterbottom's sign) is a characteristic feature, while the epitrochlear, axillary and supraclavicular may also be involved ; they are enlarged, elastic and soft, but not tender to the touch ; periadenitis is not present. The spleen is frequently palpable and deep hyperæsthesia may develop over long bones like the tibia, a peculiarity being the latent period which intervenes before pain is felt (Kerendel's sign). (3) *Cerebral Stage.* Periods of several months may elapse before the central nervous system becomes involved, and prior to this spontaneous cure may occasionally occur. Once cerebral symptoms develop death invariably follows within a year or so in the absence of treatment. The patient at first lacks concentration and is disinclined for work ; he complains of headache, drowsiness and insomnia, associated with physical weakness, loss of weight and enlargement of the lymph glands. The expression is vacant, the upper eyelids droop, the lower lip falls so that the teeth are exposed, and the lips become dry and cracked. In the intermediary phase, laziness and emotional instability increase. The patient drops off to sleep even in tropical sunlight or when eating. The face is puffy, the countenance apathetic and morose. Speech is mumbled and slow, the gait shuffling and the tongue, lips and hands become tremulous. Reflexes are exaggerated and Romberg's sign is present. The sufferer walks with difficulty, supported by a stick. The temperature is raised a little in the evening and the pulse is often very rapid. In the final stages these symptoms become accentuated. Muscular weakness is extreme, saliva drops from the mouth, the patient lies persistently in one position, either flat on the ground face down, or

curled up on one side, or forward in a kneeling posture. He eats only what is brought to him and stops eating while food is still in the mouth. Bed sores form and flexure-contractions develop. There may be chorea-form spasms and twitchings, rapid wasting and diarrhœa, while papulo-vesicular and pustular eruptions are not uncommon as the patient becomes bedridden. Convulsions, coma or mania may precede death. The terminal picture is not unlike that of general paralysis of the insane.

Complications. Abortion and still-births are not infrequent, while intercurrent diseases, like dysentery and pneumonia, are often fatal. Keratitis and iridocyclitis may develop and both tryparsamide and atoxyl may cause optic atrophy when given in full dosage.

Diagnosis. History of residence in an endemic area is most important, and in these circumstances any irregular fever, especially if associated with enlargement of the cervical glands, should arouse suspicion. Trypanosomes are most easily demonstrated in fluid obtained by gland puncture in the posterior triangle of the neck. The gland chosen must be aspirated into a dry syringe, and according to Broden 87 per cent. of cases show trypanosomes. They may also be found in thick blood films, or in smears from centrifuged fluid. Inoculation of white rats with blood or an emulsion of gland substance is a valuable procedure as it enables the two species to be differentiated. In the later cases lumbar puncture should always be performed. The cerebro-spinal fluid is under increased pressure, contains an excess of globulin and lymphocytes, and not infrequently medium-sized mononuclear cells. The cell count varies from 15 to 1,000 cells per c.mm., but even after centrifuging the cerebro-spinal fluid and animal inoculation trypanosomes are often not demonstrable.

Prognosis. The disease lasts from two to fifteen months, and once the central nervous system is involved it is invariably fatal unless treated. The outlook is very hopeful in *T. gambiense*, provided treatment be instituted before the central nervous system is involved; after this it is more doubtful and should patients relapse with nerve symptoms the prognosis is bad. *T. rhodesiense* causes a far more virulent infection. The death rate amongst Europeans is less than amongst natives—probably because they are treated earlier and under better conditions and are less liable to intercurrent infections.

Prevention. The destruction of big game and the depopulation of endemic areas have proved unsatisfactory, and measures directed to extermination of glossinæ and the avoidance of their bites are to be preferred. Removal of all undergrowth and bush for a distance of 15 feet around lakes and rivers is useful in the case of *G. palpalis*, and ingenious fly traps have recently been evolved which are very efficient. Shorts should never be worn in tsetse-fly areas, the clothes should be white and gloves and veils used where feasible. Whenever possible travelling should be done at night.

Treatment. The general health of the patient must be built up in every way, intercurrent infections eliminated and a nourishing diet, adequate in vitamins, prescribed. A number of drugs exert a beneficial and, in some cases, a curative effect in this disease. (1) Tartar emetic. This is given intravenously three times a week, beginning with ½ grain and working up to 2 grains in 10 c.c. of distilled water. As much as 60 grains may need to be administered. (2) Soamin or Atoxyl (sodium arsanilate). Intramuscular injections are given in a dosage of 3 grains twice weekly or 7 grains once weekly. (3) Germanin, or Bayer 205, is a complex organic urea compound, 1 gramme of which is injected weekly for ten injections. It is especially useful in sterilising the blood in early cases before the central nervous system has become involved, but unfortunately causes nephritis with albuminuria and casts, so that during treatment it is essential to keep the patient in bed on a milk diet. (4) Tryparsamide (N-phenylglycineamido-*p*-arsenate) is especially indicated where the central nervous system is implicated, and is given intravenously in weekly doses for ten to twelve weeks, commencing

with 1 gramme in the first week, 2 grammes in the second and 3 grammes weekly for the remaining period. Children receive relatively larger doses. The drug is toxic and may cause hepatitis with jaundice, arsenical dermatitis or optic atrophy; the latter may be suggested by pain in the eyes, lachrymation, photophobia and failing vision, and unfortunately many cases of total blindness have been recorded. During the treatment the discs should be carefully examined for early indications of optic atrophy.

SOUTH AMERICAN TRYPANOSOMIASIS (*Plate 67, 3, p. 1053*)

(*Chagas' Disease. Brazilian Trypanosomiasis*)

This disease occurs in Brazil and other parts of South America and affects children and adults of both sexes. It is caused by *Trypanosoma cruzi*, which is a short broad trypanosome about 20 μ in length, possessing a central nucleus and a large, ovoid, posteriorly situated kinetoplast (Plate 67, Fig. 3). The disease is transmitted to man by the bite of the reduviid bug, *Triatoma megista*. Trypanosomes are found in the peripheral blood during the first two or three weeks following infection; subsequently they assume a Leishmanial form within the cells of the viscera, where they undergo division and periodically pass back into the peripheral circulation.

Pathology. The Leishmanial forms are found in tissue sections of the voluntary muscles, myocardium and brain of man as well as in the testicles, ovaries, bone-marrow and supra-renals. In these situations they multiply, causing cell destruction and in the nervous system lesions resembling meningo-encephalitis and meningo-myelitis result. There is enlargement of the spleen, liver and lymph glands, and, according to Chagas, the thyroid is swollen, congested and even goitrous.

Symptoms. The incubation period is from seven to ten days. The acute type generally occurs in children under one year and is characterised by fever, splenomegaly, polyadenitis, puffiness and œdema of the face; symptoms of encephalomeningitis may ensue with fatal results. The chronic disease includes cardiac and nervous types, with deranged cardiac rhythm and neurological features, including paralyses caused by intracellular invasion with Leishmanial forms of *T. cruzi*. Recent work has questioned the validity of thyroid involvement associated with this disease, Kraus attributing symptoms such as cretinism and myxœdema to endemic goitre and not to Leishmanial involvement.

Diagnosis. This is generally made in the laboratory. During the first two or three weeks trypanosomes may be found in the peripheral blood and are occasionally demonstrated in tissue juice following muscular puncture. The complement fixation reaction is stated to give a positive reaction in 87 per cent. of cardiac cases.

Treatment. Measures should be directed towards the eradication of the insect vector, *T. megista*. None of the drugs effective in African trypanosomiasis are efficacious here, so treatment is largely symptomatic and directed towards the system particularly involved.

AMŒBIC DYSENTERY

Amœbic dysentery is caused by an invasion of the large bowel by *Entamœba histolytica*, producing local ulceration and the passage of several stools daily containing brownish mucus or dark red blood. The colon is often thickened and tender, while complications including amœbic hepatitis and liver abscess are not uncommon.

Ætiology. Amœbic dysentery, caused by *Entamœba histolytica*, is mainly found in the tropics and subtropics, though sporadic cases may be encountered in temperate climates. Walker and Sellards (1913), when studying experimental infections amongst condemned prisoners in the Philippines, proved that *E. histolytica* was pathogenic to man, and *E. coli* a harmless commensal. People of

both sexes and any age may acquire the disease, though it is relatively uncommon in young children. Man becomes infected by swallowing the cysts of *E. histolytica* in water or in food which has been contaminated by carriers or infected fæcal material conveyed by flies. In the duodenum and small intestine the cyst walls are dissolved by the pancreatic juice and the amœbulæ escape and subsequently invade the mucous membrane of the large intestine. The tissue-invading amœbæ which are present in fæcal mucus are of large size, being 20–30 μ in diameter; they are actively motile and contain ingested erythrocytes. As the lesions begin to heal these large forms are replaced by pre-cystic amœbæ, while the tissue-invading forms are confined to the bowel wall. These pre-cystic amœbæ measure only 7–18 μ in diameter, are less actively motile and resemble *E. coli* in containing no red cells. The cysts of *E. histolytica* are met with in the fæces of carriers and chronic sufferers from the disease; they contain one, two or four nuclei and have characteristic chromidial bodies. Under the influence of the intestinal juices the four-nucleated amœba bursts through a small pore in the cyst wall and subsequently divides, giving rise to eight small amœbulæ, each of which ultimately develops into an adult *E. histolytica*.

Pathology. The tissue-invading amœbæ present in fæcal mucus invade the surface epithelium between the gland crypts, causing superficial erosions, and subsequently burrow deeper into the connective tissues, producing gelatinous necrosis and sometimes thrombosis of adjacent venules; as the process extends small abscesses form which burst, producing superficial ulcers with undermined edges. Ultimately, large bottle-necked ulcers, an inch or more in diameter, filled with cell *débris*, mucoid material and amœbæ, may develop in the submucosa. Common sites for ulceration are the cæcum, ascending colon, sigmoid colon and the rectum; the process rarely, if ever, extends above the ileo-cæcal valve. Between the ulcers the intervening mucosa appears healthy, a state of affairs which is not encountered in bacillary dysentery. In some instances ulcers extend to the muscular coats or peritoneum; adhesions may form, and occasionally extensive sloughing and perforation lead to peritonitis. When the ulcers heal pigmented scarring of the mucosa results, and, if sufficiently deep, thickening and scarring on the peritoneal surfaces of the bowel may be observed.

Symptoms. The incubation period varies from three weeks to three months. The onset is insidious in at least 90 per cent. of cases. At first the stools are liquid and indistinguishable from an ordinary diarrhœa; as the condition progresses fæcal material becomes mixed with brown mucus and degenerated blood, three to six such stools being passed daily. In 10 per cent. of cases the condition resembles bacillary dysentery, having a sudden onset with fever, abdominal colic and purging, associated with the passage of sanguineous, mucoid, brown stools. In the average case, however, constitutional disturbances are slight; there is little or no pyrexia, while headache, nausea and vomiting are absent. Colicky abdominal pain is characteristic, and tenesmus is present where the rectum is involved; dysuria and frequency of micturition may also be noted under these conditions. As the disease develops there is considerable loss of weight, the skin becomes dry and of an earthy-brown hue, and loss of appetite, dyspepsia and a mild or moderate anæmia of secondary type follow. On palpation the pelvic colon and sometimes the cæcum are thickened and tender. Sigmoidoscopy is invaluable. The first lesions appear as small superficial yellowish nodules, with scattered petechial hæmorrhages in the mucosa; later, painless, yellow ulcers, surrounded by a zone of erythema, appear, and if scrapings from the bases of these be examined the vegetative forms of *E. histolytica* are readily demonstrable. The mucosa between the ulcers appears normal. Occasionally a more generalised proctitis and colitis, similar to that observed in kittens, may be encountered; there is œdema and swelling of redundant mucosal folds which bleed readily on trauma, and large numbers of motile *E. histolytica* are found in the scrapings. Rarely an amœbic granuloma may occur in the rectum and pelvic colon which

simulates carcinoma ; from this it may be differentiated by miscroscopic section of tissue removed during sigmoidoscopy and by its rapid disappearance under emetine treatment. The blood may show some secondary anæmia ; only a slight leucocytosis of from 10,000 to 15,000 cells per c.mm. develops, and generally the neutrophiles are not increased above 75 per cent. unless some complication like hepatitis or abscess has supervened.

Course and Complications. Local complications include intestinal hæmorrhage, perforation with local abscess or peritonitis, post-dysenteric adhesions and amœbic appendicitis. Amœbic hepatitis and liver abscess are the commonest complications, while amœbiasis of the spleen, abdominal wall, seminal vesicles, testicles and brain have all been recorded. Clinically the latter simulates cerebral tumour.

The course of amœbic dysentery is essentially chronic and there is a marked tendency to both spontaneous recovery and relapse. A peculiar feature is the extraordinary latency of infection in certain patients. Contact carriers may give no history of dysentery, while patients with well-marked hepatitis or amœbic abscess may never remember having had any serious bowel disturbance.

Diagnosis. The differential diagnosis includes chronic bacillary dysentery, ulcerative colitis, bilharzia dysentery, ciliate dysentery caused by *Balantidium coli*, carcinoma and diverticulitis. Sigmoidoscopy, laboratory investigation of the excreta and X-ray examination may prove essential. Diagnosis is made by demonstrating large motile amœbæ containing red blood corpuscles in the fæcal mucus in the early stages and the pre-cystic amœbæ and cysts in the stools of chronic cases and carriers. Several non-pathogenic amœbæ may occur in human fæces, and include *E. coli*, *Endolimax nana*, *Iodamœba butschlii* and *Dientamœba fragilis* ; considerable experience is required for their identification. Examination of scrapings of ulcers obtained during sigmoidoscopy often enables *E. histolytica* to be demonstrated in doubtful cases. The nature of the pathological exudate and the presence of Charcot-Leyden crystals may suggest, but by no means prove, the presence of an *E. histolytica* infection. X-ray examination after a barium enema is mainly of value in eliminating other diseases of the large bowel with mucoid stools.

Prognosis. In the absence of complications cases invariably recover with modern treatment, and most of them can be permanently cured. Occasionally intractable cases are encountered in which drugs fail to eradicate infection ; even so treatment does much to relieve symptoms and prevent the development of complications. Colonic perforations are generally fatal.

Prevention. Flies and human carriers are the main sources contaminating food and water, and it is particularly important to ascertain that people employed in the kitchen, such as cooks and waiters, are free from infection. Latrines should be well separated from kitchens and all food carefully covered with wire gauze coverings ; if possible bungalows should be kept fly-proof. Uncooked vegetables and fruit should be washed in permanganate solution before being eaten and drinking water boiled or chlorinated. In camps, latrines should be so constructed that the fæces are passed into vessels containing disinfectant and subsequently destroyed in an incinerator or by burial.

Treatment. Patients passing blood and mucus should be put to bed on a simple low residue diet and specific drugs administered. The curative properties of ipecacuanha were recognised before the various types of dysentery were differentiated. Rogers in 1912 demonstrated the specific action of one of its main alkaloids, emetine (**59**), in the treatment of amœbiasis. *Emetine* is a toxic drug which may poison the myocardium ; for this reason patients must be confined to bed when receiving emetine treatment. The alkaloid is injected subcutaneously or intramuscularly in a dosage of 1 grain daily for ten to twelve days in an average sized adult, but in the debilitated and those of low body weight smaller doses are advisable. Children receive a dose proportionate to age, those under three not exceeding $\frac{1}{6}$th grain and those under six $\frac{1}{3}$rd grain per day. The

drug has a cumulative action, and for this reason injections should not be repeated until an interval of three weeks has elapsed. Toxic symptoms include diarrhœa, asthenia, extreme muscular weakness and paresis of the limbs. At first emetine tends to slow the pulse, but where poisoning ensues tachycardia and cardiac irregularities may follow which sometimes prove fatal. The main indication for injecting emetine is hepatitis or amœbic abscess, the tissue-invading amœbæ in this situation being eradicated more effectively by the alkaloid than by any other known treatment. *Emetine-Bismuth-Iodide* (E.B.I.) is preferable in chronic cases and in carriers showing cysts. Owing to its tendency to cause nausea and vomiting, it should be given on an empty stomach late at night in gelatine capsules at least four hours after the last meal. A sedative like tincture of opium (15 to 20 minims) or luminal (1 grain) may be given with advantage quarter of an hour before the capsules are taken. The course consists of 3 grains administered at night over a period of ten to twelve days, during which a light, low residue diet is advisable. Patients under this treatment lose weight, develop bradycardia and show a fall in blood pressure of from 10 to 20 mm. mercury. Some authorities advocate *Emetine-Periodide* (E.P.I.) for the reason that it causes less vomiting; it is given in a dosage of 6 grains per day in gelatine capsules for a period of ten days.

Arsenicals. Certain of the synthetic arsenicals have been used with considerable benefit in amœbiasis and, besides being amœbicidal, have a tonic action on the body. *Stovarsol* is given in tablet form, 4 grains twice daily for seven to ten days, but toxic erythema and even exfoliative dermatitis may follow its use. *Carbarsone*, which is a pentavalent arsenical, is definitely superior to this drug and is a very effective amœbicide both for the vegetative forms in the intestine and their cysts. Its results, however, have proved disappointing in hepatitis or amœbic abscess. Carbarsone is administered in a dosage of 0·25 gramme after breakfast and after dinner at night for a period of ten days, and can be given with safety to ambulatory cases on a full diet. In these respects it possesses great advantages over the more toxic emetine preparations, and where patients cannot go to bed is superior to all other treatments. *Yatren* No. 105 is an iodine-oxy-quinolin-sulphonic acid preparation and can be given either *per os* or *per rectum*. The adult dose consists of ½ to 1 gramme of the powder in gelatine capsules twice daily for ten days. When given as a retention enema the bowel is washed out in the morning with 1 pint of sodium bicarbonate solution, and an hour later 200 c.c. of a 2·5 per cent. solution of Yatren is run into the rectum from a tube and funnel. Most patients have little difficulty in retaining this solution for eight hours. *Anayodin* consists of Yatren and 22 per cent. sodium carbonate to increase its solubility. It is given in keratin-coated pills, 4 grains, the adult dose being four pills thrice daily after food for eight days. A very efficacious treatment in chronic cases consists of *Emetine-Bismuth-Iodide* at night, with retention enemas of *Yatren* in the morning, and this leads to cure in at least 90 per cent. of cases.

Amœbic Hepatitis and Liver Abscess. The geographical distribution of amœbic hepatitis and liver abscess coincides with that of amœbic dysentery, but owing to the long latent period which may intervene between acquiring the bowel infection and the development of hepatitis or liver abscess this is not always evident. Again, only about 80 per cent. of cases of liver abscess give a history of diarrhœa associated with the passage of blood and slime *per rectum*, while multiple examinations of the stools and of scrapings obtained during sigmoidoscopy may fail to demonstrate *E. histolytica* or its cysts.

Pathology. The first stage in infection of the liver consists of the so-called amœbic hepatitis, and here the *Entamœbæ* have been carried up *viâ* the portal vein and distributed through the liver as emboli derived from thrombosed vessels draining submucous ulcers in the large bowel. Local necrosis of tissue follows and fusion of adjacent foci gradually produces an abscess, the commonest site for

which is the superior surface of the liver, especially on the right side. About 80 per cent. of abscesses are found in the right half of the liver, 10 per cent. in the left half and the remaining 10 per cent. in both. This peculiar distribution appears to depend on streamline effects in the portal vein. Where a large destructive abscess involves one half of the liver a left-sided compensatory hypertrophy of the other follows. Amœbic abscess of the lung may result from direct spread of a liver abscess through the diaphragm, but much more frequently the pathological condition at the right base is found to consist of collapsed lung or areas of broncho-pneumonia produced as follows: Immobility of the diaphragm secondary to an adjacent hepatic abscess leads to defective ventilation, air absorption and pulmonary collapse; finally, secondary bacterial infection supervenes. Amœbic abscesses may reach a great size and contain as much as 2 to 6 pints of chocolate or anchovy sauce pus; of those that rupture over 50 per cent. do so into the lung or pleura and about 25 per cent. into the peritoneal cavity. Other adjacent structures such as the pericardium, stomach, intestine, vena cava or kidney may be involved, and occasionally the bile duct. The pus is bacteriologically sterile in 80 to 90 per cent. of cases. The organisms which have been isolated include streptococci, *B. coli*, *Staphylococcus aureus*, *B. pyocaneus* and anaerobes. Generally the walls of liver abscesses are composed of shaggy necrotic tissue, the fibrous tissue barrier not being nearly as well developed as in hydatid cysts; for this reason secondary infection is a more dramatic complication in amœbiasis. Microscopic section of the wall of the abscess reveals vegetative amœbæ only in the deeper zones and in the areas of hyperæmia surrounding the abscess; they are absent from the necrotic lining and this explains why amœbæ are not demonstrable in pus until two to five days after the abscess cavity has been drained or aspirated.

Symptoms. A history of amœbic dysentery or diarrhœa while resident in the tropics or subtropics is frequently obtained, but the incubation period is very uncertain, liver symptoms appearing in some cases within a few weeks of an acute attack of dysentery and in others being delayed as long as twenty years after the patient has left the tropics. Rogers (**60**) recognised two types of liver lesions: (1) so-called amœbic hepatitis which consists of miliary amœbic abscesses originating from emboli containing *E. histolytica* lodging in the terminal portal venules; (2) frank amœbic abscess—generally single, but sometimes multiple.

Amœbic Hepatitis. This condition commences insidiously, with irregular remittent fever and sweating, and these features may be the only obvious clinical manifestations for weeks. The liver is generally enlarged, but pain and tenderness are by no means invariable. There is a moderate leucocytosis with some increase in the neutrophile polymorphonuclear cells, and investigation of the fæces may reveal cysts of *E. histolytica*. Functional tests for liver efficiency are of little value, since the condition is not a true hepatitis, and healthy hepatic parenchyma intervenes between the miliary amœbic foci.

Amœbic Abscess. The preliminary symptoms are similar to those described for amœbic hepatitis, and as the abscess develops the liver enlarges and pain and tenderness increase. Should the abscess be located in the upper right half of the liver and impinge on the diaphragm it causes referred pain to the right shoulder and deficient air entry at the right base, with physical signs such as diminished vesicular murmur and crepitations associated with a dry cough (tussis hepatica). Later it may rupture through the diaphragm and produce a secondary pulmonary abscess. Left lobe abscesses may simulate gastric conditions and most frequently are present in the epigastrium. Tenderness and rigidity of the left rectus are present, œdema of the abdominal wall may indicate pointing, and in some cases actual fluctuation is demonstrable. Rupture may occur into the base of the left lung, the stomach or the pericardium. Abscesses on the inferior aspect of the right half of the liver are associated with marked downward enlargement of that organ and tenderness and rigidity of the right

rectus and adjacent muscles. Pain may be referred to the appendical area or the abscess may bulge into the right loin space. A feeling of weight is often complained of when walking; the patient may hold his right arm and fore-arm to the side to splint his liver, and for the same reason he commonly sleeps on the right side. In large abscesses, especially of the right side, bulging enlargement may be obvious, and in doubtful cases the chest should be measured. The fever is generally irregular, at first being normal in the morning, followed by an evening rise with considerable sweating, while later intermittent fever with rigors may ensue. Other features include loss of weight, a sallow earthy colour of the skin, moderate anæmia, nervous irritability and not infrequently sleeplessness. X-ray examination is of value. In abscesses involving the superior surface it reveals immobility, elevation and sometimes bulging or pointing of the diaphragm and lesions at the right base. In central liver abscess there is sometimes, but by no means invariably, an area of increased density.

Laboratory investigations reveal a moderate leucocytosis of 15,000 to 25,000

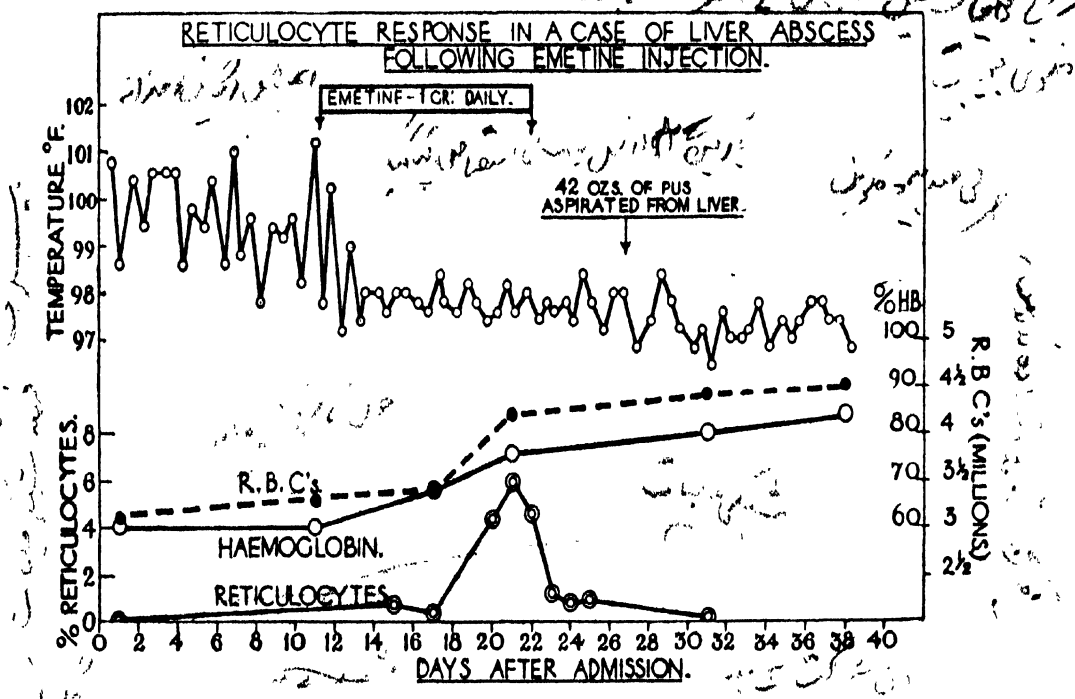


FIG. 102.—Temperature chart in liver abscess. Note disappearance of pyrexia three days after injections of emetine commenced.

per c.mm. with polymorphonuclears from 75 to 90 per cent. Urobilinuria is common. Thick, chocolate or anchovy sauce pus containing degenerate polymorphonuclear leucocytes, cholesterin and hæmatoidin crystals is almost pathognomonic of amœbic abscess, while the stools may contain the cysts of *E. histolytica*; not infrequently, however, even multiple fæcal examinations are negative.

Complications. The most fatal complications are secondary streptococcal infection or rupture into the lung, pleura, peritoneum or adjacent viscera. Pulmonary lesions, including collapse, broncho-pneumonia and pleural effusion, are not uncommon, especially where the abscess impinges on the diaphragm. Jaundice and hæmatemesis are rarely recorded, but they may both occur.

Diagnosis. Liver abscess may simulate a variety of conditions, including subphrenic abscess, perinephric abscess and suppurating hydatid, all of which may implicate the base of the right lung. Suppurating pylephlebitis, cholecystitis, septic cholangitis especially complicating clonorchis infestation, bilharzial cirrhosis, gumma, primary carcinoma of the liver and malaria hepatitis may also cause difficulty. The history of diarrhœa and dysentery, the presence of cysts of *E. histolytica* in the stools, fever of hectic type associated with upward

enlargement of the liver and pulmonary features, the leucocytosis and the X-ray findings are important features. The aspiration of anchovy sauce pus from the abscess clinches the diagnosis, and short of this the dramatic drop of temperature within forty-eight to seventy-two hours of commencing emetine treatment favours its amœbic origin (see Fig. 102).

Prognosis. The prognosis depends on the type of treatment adopted, the presence of complications such as secondary bacterial infection or rupture into adjacent viscera, and on whether the abscess is multiple or single. Hepatitis responds specifically to emetine injections. Aspiration under sterile conditions combined with emetine injections (1 grain daily for ten days) has led to a great reduction in mortality, the figures varying from 1·6 per cent. to 14·4 per cent. Open operation with incision and drainage has a high mortality owing to secondary bacterial infection, especially if the transpleural approach be necessary.

Treatment. *Emetine:* Amœbic hepatitis and small abscesses of the liver are curable by emetine injections alone, 1 grain being given daily for ten to twelve days. A total course of 12 grains should not be exceeded even in patients of high body weight, while those under 8 stones should not receive more than 8 grains in one course; where necessary the injections may be repeated in two or three weeks' time. Even in the presence of large abscesses which need aspiration later the temperature falls to normal in about three days, and there is a more gradual fall in the leucocyte count. If there is any anæmia a reticulocytosis is observed from the seventh or eighth day. Pain and discomfort are generally decreased by emetine in hepatitis or small abscesses, but where the abscess is about to burst these symptoms may increase and then immediate aspiration is required.

Aspiration. Unless the site of the abscess is indicated by local features such as tenderness, œdema of the tissues, bulging, or by X-ray findings, the liver should be thoroughly explored by a needle of fair-sized calibre not exceeding 3½ inches in length so as to avoid perforation of the vena cava. If an abscess on the upper aspect of the right lobe be suspected the needle or cannula should be inserted into the eighth or ninth interspaces on the right anterior axillary line and pushed inward, backward and slightly upward, aspiration being maintained by means of a large syringe attached to the needle or a Potain's aspirator. Failure to locate the abscess at the first attempt is frequent, and as many as eight punctures in different areas of the liver may be made before pus is obtained. Generally aspiration can be performed under local anæsthesia, but in certain cases a general anæsthetic may be preferred. As a rule one complete aspiration suffices, but sometimes the fever and leucocytosis persist or recur owing to the cavity having refilled, and then repeated aspirations may prove necessary.

In abscesses involving the inferior surface of the right lobe or in small left lobe abscesses exploratory puncture may be deemed inadvisable owing to the danger of causing peritonitis. Under these circumstances an exploratory incision should be made through the anterior abdominal wall and the abscess aspirated either with a Potain's aspirator or rubber tubing attached to a water pump. Subsequently the liver should be sutured and the wound closed without drainage, provided the pus be sterile.

Incision and Drainage. Practically the only indication for this operation is where secondary bacterial infection has occurred. Under these circumstances the cavity must be drained and continuous irrigation of the abscess cavity with Dakin's solution or eusol as advocated by Kilner (**61**) should be employed. Where an hepatic abscess ruptures into the lung the contents are generally coughed up through an hepatico-bronchial fistula and the condition generally clears up with emetine injections. After the liver abscess has healed the patient must undergo a course of treatment for his colonic infection, and for this purpose either emetine-bismuth-iodide or carbarsone are indicated. Emetine injections, though lethal to amœbæ in the liver or lung, frequently fail to eradicate bowel infection.

Ciliate dysentery is an ulcerative condition of the large intestine caused by *Balantidium coli*.

Ætiology. This ciliate has a widespread geographical distribution in different parts of Europe, Asia, Africa and America. Infections occur in people having occupational associations with pigs, which are the main source of infection. *Balantidium coli* is pear-shaped, measuring 50 to 80 microns in length and 30 to 55 microns in breadth. The peristome is situated at its anterior end, while internally there is a sausage-shaped macronucleus, a micronucleus and vacuoles. The exterior is covered by longitudinal rows of cilia over the whole surface. Encysted forms are found in the fæces and reproduction is by transverse fission.

Pathology. The ulcers, which are very similar to those in amœbic dysentery, have undermined edges. The ciliates are found in the ulcer base and surrounding tissues as well as in the lymph spaces, blood vessels and lymphatic glands in the infected area. The ciliates are found occasionally in the lower part of the small intestine, but rarely produce ulceration there.

Symptoms. Many cases are latent, patients having no bowel disturbances at all and the ciliates being found accidentally. Diarrhœa and definite dysentery with the passage of muco-sanguineous stools are found in other cases, and anæmia, inanition and digestive disturbances follow. Intestinal perforation or hæmorrhage may occur, but never abscess of the liver.

Diagnosis. Sigmoidoscopy reveals the presence of ulcers in the large bowel resembling those of *Entamœba histolytica*, and diagnosis will depend on the demonstration of the ciliates in scrapings from the ulcer bases or in the excreta. The *Balantidium coli* not infrequently disappears from the stools of infected individuals for considerable periods of time, but reappears later. During the latent intervals diagnosis is impossible.

Prognosis. If latent cases be taken into consideration the mortality is about 7 per cent., while in those showing colonic manifestations it is 29 per cent.

Treatment. A diet low in carbohydrate and high in protein and fresh vegetables has been advocated, and arsenical preparations like stovarsol in doses of 0·2 gramme twice daily after meals for one week, or carbarsone 0·25 gramme twice daily after food for ten days are worth a trial. High colonic irrigation with various solutions including quinine, silver nitrate and iodine have been recommended, while methylene-blue *per os* or given as an enema (1 in 3,000) can be tried. Owing to the spontaneous disappearance of the ciliates from time to time it is difficult to assess the value of different remedies.

Flagellate Diarrhœa. The human intestinal flagellates are *Giardia intestinalis* described by Lambl in 1859, *Trichomonas hominis* described by Davaine in 1860, and *Chilomastix mesnili* discovered by Wenyon in 1910. Their pathogenicity is not universally accepted and no pathological evidence is forthcoming that they ever invade the intestinal mucosa. They appear to be more common in people suffering from diarrhœa than in normal individuals, but the encysted flagellates are often found in normal stools. Dobell has shown that the free flagellate forms are especially adapted to a fluid environment and for this reason they may only appear when the stools become liquid or loose. Of the three flagellates, *Giardia intestinalis* has the greatest claim to pathogenicity.

Giardiasis or Lambliasis. The normal habitat of *Giardia intestinalis* (*Lamblia intestinalis, Giardia Lamblia*) is the jejunum and duodenum, while occasionally it passes up the bile ducts or back into the stomach. A decrease or absence of hydrochloric acid predisposes to infection and after short-circuit operations such as gastro-jejunostomy, *Giardia* may appear in the gastric juice. They are pear-shaped flagellates varying from 10 to 18 microns in length and 5 to 10 microns in breadth and possess a concave sucker on the ventral surface of the body. The cysts are ovoid bodies from 8 to 14 microns in length and contain four small spherical nuclei, central axonemes and flagelli. No cytostome is present, fluid nourishment being absorbed through the surface of the body.

Pathology. As Wenyon points out, hyper-infection may lead to mechanical irritation of the surfaces of the small intestine, but there is no tendency to penetration of the epithelial surfaces or to ulceration.

Symptoms. The flagellate forms are only found in loose stools which may contain an excess of mucus, but never of blood. Whether the flagellates are responsible for the diarrhœa or the loose stools permit flagellates appearing in carriers containing encysted forms is controversial. Where no other pathogenic agent is present it appears rational to attempt to eradicate the infection. Cases, however, never die or become really seriously ill in the absence of an associated cause.

Treatment. Where achlorhydria exists hydrochloric acid therapy is indicated. No certain specific drug is available, but carbarsone, stovarsol and yatren appear sometimes to lead to the disappearance of both the flagellate and encysted forms. A diet high in protein and green vegetables and poor in carbohydrate is advised by Hegner. Lavage of the duodenum with concentrated magnesium sulphate solution (25 per cent.) may also prove useful.

Helminthic Diseases

There are three groups of helminths which may produce disease in man: (1) Trematodes or flukes infesting the intestine, liver, lungs or vascular system; (2) Cestodes or tape-worms which occur as adults in the intestine or as cysts in the tissues; (3) Nematodes or round-worms which may have either an intestinal or a somatic location. Pathogenic effects result from reflex disturbances, depressed gastro-intestinal function, anæmia of different types, direct mechanical action, the deposition of eggs and embryos in the tissues, secondary bacterial infection, toxic substances secreted by the parasites and helminthic anaphylaxis which is by no means an uncommon phenomenon.

Diseases due to Trematodes or Flukes

The trematodes or flukes are parasitic non-ciliated worms with an unsegmented body which is generally flattened though sometimes more or less cylindrical. One or more suckers are present, the anterior one, known as the oral sucker, surrounding the mouth. In man their habitat may be the intestines, the bile ducts, the lung or the portal system and adjacent plexuses of veins.

Fascioliasis. Several flukes of the family *Fasciolidæ* are known to infest man and other animals. The most frequent human species is *Fasciolopsis buski* (*Distoma crassum*), while that most commonly infesting animals is *Fasciola hepatica* (*Distoma hepaticum*). *Fasciola gigantica* has only once been recorded in a human being. Fascioliasis is a rare infection in man.

(1) *Fasciola hepatica* is commonly encountered in sheep, where it inhabits the bile ducts, causing liver rot; occasionally man is infected.

Ætiology. The eggs which are found in the fæces are operculated and oval in shape (130–145 × 70–90 μ) containing a miracidium. On escaping in water the miracidia infect snails of the species *Limnæa truncatula* and develop into sporocysts, rediæ and cercariæ in the liver. On escaping the cercariæ encyst on grass, etc.; the cyst wall is digested in the duodenum and the emerging meta cercariæ find their way to the bile ducts, after penetrating the gut wall and piercing the liver from the peritoneal surface.

Pathology. In animal infections the flukes mechanically obstruct the bile ducts, producing cystic dilatation and jaundice. Their toxins induce hypertrophy of the lining epithelium and a biliary type of cirrhosis with or without ascites. Generalised toxæmia associated with eosinophilia may result. Secondary infection may lead to infective cholangitis and liver abscess. Occasionally *F. hepatica* involves the blood vessels, lungs, ocular and subcutaneous tissues and even the brain.

Symptoms. If the infection be a light one there are no symptoms. In severe cases an enlarged tender liver, dyspepsia and other symptoms develop and death may finally result from infective cholangitis or liver abscess.

Diagnosis is established by demonstrating the operculated eggs in the fæces. In Syria in the Lebanon it is customary in connection with certain religious ceremonies to eat the raw livers of sheep and goats and if these be infected with *F. hepatica* the flukes not infrequently attach themselves to the human pharynx where they may produce œdema and congestion involving adjacent structures such as the soft palate, larynx, and eustachian tubes. Difficulty in swallowing, deafness and dyspnœa may be induced and if œdema of the glottis develops death from asphyxia may ensue. The disease locally is called halzoun.

Prognosis. This is grave in severe hepatic infections unless appropriate treatment be adopted.

Prevention. Halzoun is readily prevented by refraining from eating raw infected livers, while care regarding boiling of water and not eating watercress or raw vegetables in infected areas will prevent hepatic fascioliasis.

Treatment. There is little information regarding the specific drug treatment in human beings, but both carbon tetrachloride and filix-mas administered in a dosage appropriate to body weight and repeated in twenty-four hours are very effective in sheep. Treatment with calcium salts has been found advisable wherever calcium deficiency exists, as this procedure exerts a protective influence on the liver, preventing the development of the toxic necrosis which sometimes follows the administration of carbon tetrachloride.

(2) *Fasciolopsis buski* (*Distoma crassum*). This is a giant intestinal fluke which is found in China, Assam, Bengal, Malaya and Borneo.

Life Cycle. The immature ova escape in the fæces and after three to seven weeks the miracidium attains maturity; it escapes through the operculum and invades the liver of certain molluscs (*Planorbis cornosus* and *Segmentina nitidula*, etc.) where it produces sporocysts, rediæ and cercariæ, which on escaping encyst on such water plants as water chestnut and water caltrop. It is by eating infected corms that man becomes infected, the cercariæ encysting and maturing in the duodenum.

Pathology. At autopsy the flukes are found attached to the mucosa of the small intestine—particularly the duodenum and occasionally the stomach and large bowel. Localised inflammation, hæmorrhages and even abscesses may result.

Symptoms. In light infections the patient complains of epigastric pain and dyspepsia relieved by taking food. In severer cases these symptoms may be accentuated and later a dry harsh skin, œdema of the face and extremities, asthenia, emaciation, diarrhœa and ascites may develop.

Diagnosis. The disease may simulate enteric infection or gastric or duodenal ulcer, but the eosinophilia will suggest helminthic infestation, and examination of the fæces shows the operculated ova of *F. buski* (120–130 × 75–80 μ).

Prevention consists in sterilising night-soil and boiling water caltrops and water chestnuts before use as food.

Treatment. Carbon tetrachloride in a dosage of 3 c.c. followed by an aperient or two doses of beta-naphthol (2 c.c. each) are curative.

Paramphistomiasis. There are two species of the family *Paramphistomidæ* which produce disease in man, namely *Gastrodiscoides hominis* and *Watsonius watsoni* (*Pseudodiscus watsoni*). *W. watsoni* is reddish-yellow in colour, inhabits the duodenum and jejunum and measures 8–10 mm. × 4–5 mm.; its ova are 120–130 μ long and 75–80 μ broad. *Gastrodiscoides hominis* has a large posterior sucker by which it adheres to the mucosa of the colon: it is 5–8 mm. long and 3–4 mm. broad, its ova measuring 150 × 72 μ. Symptoms consist of intestinal disturbances, including the passage of bilious stools and diarrhœa. Diagnosis is made by finding ova in the fæces. Carbon tetrachloride (3 c.c.) appears to be specific.

Clonorchiasis. This disease is produced by the Chinese liver fluke, *Clonorchis sinensis*, which invades the bile ducts of man and other mammals, producing biliary cirrhosis (see Plate 68, 20).

Ætiology. *Clonorchis sinensis* is a spatulate fluke (10–20 mm. × 2–5 mm.) having operculated, yellowish-brown ova (27–35 × 11–20 μ). The eggs are passed in the fæces and the contained miracidium escapes into water, penetrating the œsophagus of the snail vector and burrowing into the periesophageal space where sporocysts, rediæ and cercariæ are formed. On escaping the cercariæ penetrate the scales and flesh of certain fresh-water fish of the family *Percidæ*, *Gobiidæ* and *Anabantidæ*; man is infected by eating the raw or undercooked fish. The gastric juice digests the outer capsule; in the duodenum the adolescaria escape and ascend the common bile duct to the liver, the left lobe of which is especially involved owing to the straighter course of the left bile duct (Faust).

Pathology. There is first desquamation of the biliary epithelium and ingestion of blood by the flukes which mechanically block the biliary passages, causing biliary stasis. Proliferation of biliary epithelium, periportal hyperplasia around masses of dead eggs, thickening of the ducts and general toxæmia follow. In hyper-infections the pancreatic ducts may be involved while secondary bacterial infection may lead to cholangitis and local abscesses.

Symptoms. In mild infections the disease is sub-clinical, but in severer infections anorexia, epigastric pain, discomfort and fullness after meals, diarrhœa and wasting follow. Enlargement of the liver, jaundice, œdema and ascites may occur.

Diagnosis is made by demonstrating the operculated ova in the stools.

Prognosis. Severely infected cases occasionally die from sepsis or other intercurrent disease, but the moderate and milder infections recover.

Prevention. This consists in adequately cooking fresh-water fish before its consumption, or in the destruction of the snail vector, which is much more difficult of achievement.

Treatment. Tartar emetic, if given intravenously, definitely reduces the intensity of infection, and Faust advocates gentian violet in the early cases as it invariably reduces the egg-cell counts. Gentian violet may be given as intravenous injections of an 0·5 to 1·0 per cent. solution on alternate days in quantities of 40 c.c.; a total course not exceeding 6 grammes or 100 grains is advisable. Alternatively, it may be administered orally in keratin-coated pills in a dosage of 2½ grains thrice daily after meals for ten days (Faust).

Paragonimiasis. This is a disease caused by the Japanese lung fluke, *Paragonimus westermanii*, which invades the pulmonary tissues and gives rise to cough and blood-stained sputum containing the operculated eggs of this parasite.

Ætiology. *Paragonimus westermanii* (*Distoma westermanii; D. ringeri*) is found in Japan, China, Formosa and Korea. The adults measure 7·5–12 mm. × 4–6 mm. and form cysts in the lung where the broad, oval, operculated eggs are deposited; they reach the exterior in the sputum, and occasionally in the fæces. Once the miracidium has become mature it emerges from its operculated shell and invades some species of *Melania* snail, notably *M. libertina*, where sporocysts, rediæ and later cercariæ are formed. The latter encyst in the gills, muscles and liver of certain fresh-water crabs or cray-fish such as *Potamon obtusipes*, etc. When raw or undercooked infected crab is eaten, the cyst wall is digested by the gastric juice and the adolescaria emerges in the duodenum, penetrates the small intestine, invades the abdominal cavity, perforates the diaphragm and pleura and so gains access to the bronchus where it encysts in inflammatory tissue and matures.

Pathology. Localised and generalised pulmonary fibrosis, cystic dilatation of the bronchi and tubercular-like abscesses are found. The cyst-like formation round the fluke generally communicates with the bronchus and by this means the eggs escape into the air passages. Similar cyst-like lesions may

occur in the intestinal mucosa, the pancreatic and bile ducts, the peritoneum, mesenteric glands, spleen, liver, pleura, muscles, testicles, orbit and brain.

Symptoms. Naturally the clinical picture varies with the distribution of the parasites, and a number of different types are described. (1) *Pulmonary type.* This is characterised by cough and hæmoptosis; there is rusty-brown or anchovy-sauce coloured sputum containing operculated eggs, while the physical signs are those of bronchial pneumonia, bronchiectasis or pleural effusion. (2) *Abdominal type.* Where the liver, spleen, pancreas or intestine are involved the clinical picture suggests disease of these organs. (3) *Cerebral type.* This may manifest itself by headache, insomnia, loss of memory, aphasia, ocular disfunction, Jacksonian epilepsy and paresis or paralysis of different types including hæmiplegia and monoplegia.

Diagnosis. History of residence in an endemic area is important and hæmoptosis occurring in patients from the Far East should always lead to laboratory investigation for the operculated eggs of *P. westermanii* in the sputum or fæces. Eosinophilia is common. The blood may yield a positive complement fixation reaction if tested against an antigen made from the adult flukes.

Prognosis. In severe infestations the prognosis is bad and cerebral cases are almost invariably fatal.

Treatment. Fresh-water crab and cray-fish coming from infected waters in endemic areas should not be eaten. Emetine and tartar emetic may temporarily relieve the pulmonary symptoms, but it is doubtful whether they really cure.

Schistosomiasis. Man is the definitive host of several species of blood flukes of the family *Schistosomidæ* which inhabit the portal system and its tributaries and deposit their ova in certain of the hollow viscera such as the bladder (*Schistosoma hæmatobium*) and entero-colon (*Schistosoma mansoni* and *Schistosoma japonicum*). Occasionally man is infected with certain bovine species such as *S. bovis* and *S. matthei*, while in the Belgian Congo Fisher (**62**) has recently described a new species—*S. intercalatum*—which, like *S. hæmatobium*, possesses terminal-spined eggs, but whose habitat is the human intestine and not the bladder.

Life Cycle. When bilharzial eggs come in contact with water ciliated miracidæ escape, invade some suitable fresh-water mollusc, make their way to the liver and develop into sporocysts. These sporocysts in four to five weeks' time produce mature cercariæ, which on escaping into water have twenty-four to forty-eight hours in which to find a suitable host or to die. Though occasionally man may acquire the disease by drinking infected water, a much more common route is *viâ* the skin during bathing. The cercariæ invade the tissues through the sweat glands and proceed *viâ* the blood vessels to the portal system where they attain maturity in from six to seven weeks.

VESICAL SCHISTOSOMIASIS (*Plate 68, 22-25, Plate 69.*)

(*Urinary Schistosomiasis Bilharziasis*)

This is a chronic disease caused by *Schistosoma hæmatobium* characterised by vesical symptoms including terminal hæmaturia and terminal-spined eggs in the urine.

Ætiology. *S. hæmatobium* appears to have originated in the Nile Valley where it has existed for thousands of years, and actually Ruffer demonstrated the calcified eggs in the renal pelvis of a mummy of the 19th Dynasty. The adult worms were described by Bilharz in Cairo in 1851. The female is located in the gynæcophoric canal of the male worm which is simply a flat fluke with its edges enfolded like a curled leaf. The ova possess a sharp, terminal spine and measure 120–160 × 40–60 microns. The intermediary host is *Bulinus contortus* in Egypt, *Physopsis africana* in Natal and *Planorbis metidjensis var. dufouri* in Portugal. From the Nile Valley the disease has spread along caravan routes by invading armies and by the slave traffic to different parts of the world, including Africa, Madagascar, Cyprus, Portugal, Palestine, Persia and Arabia.

Pathology. Though the adult worms may be found in the mesenteric veins, their chief habitat is the vesical, prostate and uterine plexuses of veins which communicate *viâ* the inferior hæmorrhoidal plexus with the portal system. Ova are found in largest numbers in the bladder, prostate, seminal vesicles and urethra in the male and the cervix and vagina in the female. Since these plexuses drain into the inferior vena cava stray ova naturally filter out in the lung rather than in the liver, as is the case with the intestinal schistosomes. The various lesions which may be produced include bilharzial pseudo-tubercles, papillomata, ulcers, chronic fibrosis and thickening and contractures of the bladder wall. The lower third of the ureters is not infrequently involved, while ova may be deposited in the prostate, seminal vesicles and peri-urethral tissues. Bilharzia granulomata of the penis and vulva are sometimes encountered. Egg deposits in the lung may lead to mild degrees of pulmonary fibrosis. Lesions in the liver and intestine are less frequently associated with this species owing to the more scanty egg deposits in these situations ; ova are not infrequent in the appendix.

Symptoms. In the early invasive stages fever, urticaria, eosinophilia, generalised body pains, headache, rigors and cough associated with splenomegaly and hepatomegaly may occur during the second and third months. Some three to twelve months may elapse before vesical symptoms appear and occasionally they may not be noted for several years. The early symptoms include burning urethral pain on micturition, frequency, urgency, perineal pain, aching of the loins and hæmaturia which is aggravated by exercise—especially horse-riding. The terminal hæmaturia occurs at the end of micturition and may be present more or less constantly or intermittently, lasting for a day or two. Sometimes intervals of many months intervene in which macroscopic blood is altogether absent from the urine. The blood is generally bright red, though occasionally dark worm-like clots may be passed ; in the later stages it may be equally distributed throughout the whole specimen and here the source of bleeding is papilloma or carcinoma. Backache and loin pain are not uncommon and pain may also be referred to the perineum, along the urethra or to the supra-pubic region. Where the prostate is involved hemospermia may result and ova be demonstrated in the prostatic secretions at a time when they are absent from the urine. Occasionally dysenteric-like symptoms appear associated with the passage of terminal-spined eggs in the stools, and it is not uncommon to find them in fæcal mucus if searched for, even in the absence of intestinal symptoms.

Physical examination may reveal tenderness in the supra-pubic region, while on rectal examination there may be tenderness of the prostate and seminal vesicles.

Cystoscopy. The earliest indications of bilharzial infection are diffusely scattered, submucous tubercles which often involve the trigone and base of the bladder. Later papillomata, ulcers and "sandy patches" may appear, the latter being manifest by a bright yellow reflex caused by calcified ova. Involvement of the ureters, calculi and carcinoma may be revealed during cystoscopy. *X-ray Examination.* Uroselectan injections may demonstrate polypi, calculi, dilated ureters or hydro-nephrosis, while radiograms of the lung may also show pulmonary fibrosis. *Urinary Examination.* At first the urine is acid in reaction, showing a deposit of blood and mucus. Microscopic investigation reveals pus cells, erythrocytes and terminal-spined ova which are specially concentrated in the last few cubic centimetres. Several examinations may be necessary before ova are demonstrable. With the onset of bacterial infection the urine becomes alkaline and copious deposits of pus occur. Renal insufficiency is indicated by lowering of specific gravity and a diminished capacity to excrete urea as indicated by the various tests of renal function (*q.v.*); nitrogenous retention develops. *Blood count.* A high grade eosinophile leucocytosis is encountered in the early invasive stages associated with urticaria and fever, the total leucocytes equalling 15,000 to 25,000 per c.mm., while the eosinophiles vary from 15 to 70 per cent. Later the total count and eosinophiles decrease and in chronic cases may become

normal. *Complement fixation reaction.* During the early invasive stages, before eggs appear in the urine, the serum gives a strongly positive reaction against an antigen prepared as an alcoholic extract of cercarial infested livers. This reaction persists in many cases throughout the whole course of the disease, but its intensity often decreases and the percentage of positive reactions is lower in the more chronic phases of schistosomiasis. The reaction is essentially of group nature and fails to differentiate the different species of schistosome infecting man. *Intradermal test.* This test reveals hyper-sensitiveness to bilharzia protein and is performed by injecting intradermally 0·25 c.c. of a 1 per cent. filtered saline extract of cercarially infested liver. Positive reactions are obtained in a large proportion of patients who have suffered from schistosomiasis, but no indication is afforded as to whether the infection is of immediate or remote origin.

Complications. Secondary bacterial infection may result in septic cystitis, ascending pyelonephritis and pyonephrosis, while bilharzial stricture or blockage

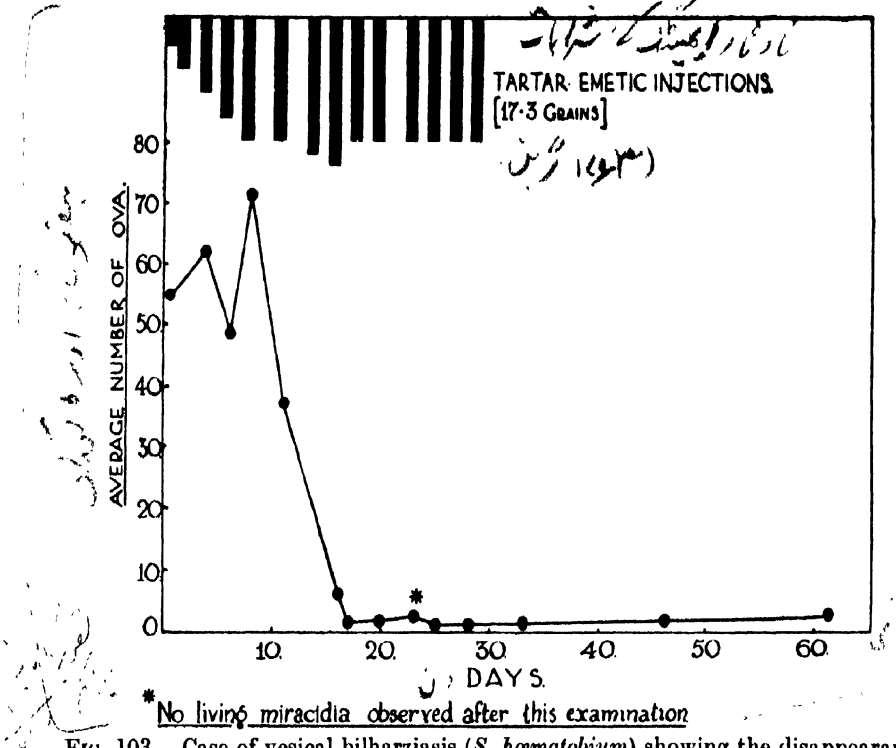


FIG. 103.—Case of vesical bilharziasis (*S. hæmatobium*) showing the disappearance of viable ova from the urine following tartar emetic treatment.

of the ureter by papillomata may result in back pressure leading to hydronephrosis or chronic interstitial nephritis. Penile carcinoma, urethral fistulæ and peri-urethral abscess are not uncommon, while calculi and vesical carcinoma are late complications. Fergusson stressed the association of *S. hæmatobium* and vesical carcinoma, pointing out that it was the common cancer of Egypt. Bilharzial granulomata may involve the labia, vagina, cervix, uterus and Fallopian tubes in addition to the vesical lesions described above.

Diagnosis. Various investigations such as microscopic examination of urine for terminal-spined ova, cystoscopy and serological tests described will enable a diagnosis to be made.

Prognosis. In the early stages the prognosis is entirely satisfactory provided appropriate treatment be instituted. Renal insufficiency, secondary bacterial infection and the incidence of such complications as carcinoma naturally increase the gravity of the disease.

Prevention. The avoidance of contact with infected water, the elimination or destruction of the snail vector, the prevention of contamination of water supplies with excreta and the eradication of the disease by specific remedies constitute the measures destined to prevent this disease.

Treatment. Specific drugs are available, the most important being the trivalent antimony compounds—tartar emetic and fouadin. Emetine hydrochloride exerts a lethal action on the adult schistosomes, but owing to its toxic properties it is less satisfactory. (1) *Tartar emetic.* The treatment of schistosomiasis by tartar emetic was successfully introduced by Christopherson who gave the drug intravenously in 10 c.c. of saline every second day, commencing with ½ grain doses and increasing each injection by ½ grain until a maximum of 2 grains was given. A fresh solution must be prepared on the day on which the injection is administered, and sterilised by boiling. For an adult of average weight the total course should equal 30 grains. The action of the drug is to kill the schistosomes in the vascular system and following its use viable ova rapidly disappear from the excreta (Fig. 103). Owing to its tendency to cause vomiting the drug should be given on an empty stomach some four hours after a meal. Spasmodic cough often follows in half to one minute, and during the later stages muscular pains not infrequently follow its administration. In uncomplicated cases the drug is well tolerated, but patients with renal involvement, sepsis or hepatic cirrhosis are unsuitable. During intravenous injections the greatest possible care has to be taken not to inject the drug into subcutaneous tissues as otherwise severe inflammation and extensive necrosis and ulceration result. (2) *Fouadin or neo-antimosan.* It possesses the great advantage that it can be injected intramuscularly instead of intravenously, while toxic manifestations are rare. The injection should be given in an all-glass syringe, 6 per cent. solution being utilised. The total course consists of 40 c.c. given in a series of nine intramuscular injections covering a period of fifteen days. (3) *Emetine hydrochloride.* Tsykalas advocates emetine in a dosage of 1½ grains daily for a period of ten days. Though effective it is a dangerous drug and now that fouadin is available for intramuscular use in both children and adults there is little reason for its administration. Various complications referred to in the text must be treated along medical and surgical lines as they arise.

INTESTINAL SCHISTOSOMIASIS

This is a chronic colitis caused by *Schistosoma mansoni* occurring in various parts of Africa and South America. The adult worms inhabit the branches of the portal veins in the liver and the mesenteric veins. Their eggs, which possess sharp lateral spines, measure 140–150 × 60–70 microns and are an elongated, oval shape. *Planorbis boissyi* is a common vector in Egypt, *Physopsis africana* in Natal and *Planorbis olivaceus* in South America and *P. quadeloupensis* in the West Indies, which were infected through negro slaves coming from West Africa.

Pathology. Egg cell deposits may in the early stages lead to congestion and excessive mucus production and later to tiny tubercles, small sessile masses or pedunculated growths which may attain an enormous size and on sloughing leave a circular ulcer in the colonic mucosa. The appendix is commonly implicated and bilharzia tubercles may involve the subserous coats and be mistaken for tuberculosis. In the later stages periportal hepatic cirrhosis is common and this may be associated with splenomegaly. Bilharzial myelitis of the spinal cord has been recorded.

Symptoms. Primary fever with urticaria, eosinophilia, bronchial features, abdominal pain, hepatomegaly, splenomegaly and diarrhœa may occur, while later lateral-spined eggs appear in the fæces. The pyrexia lasts from one to seven weeks and was not uncommonly seen in British troops in Egypt during the Great War. Bowel symptoms appear from about the third month after exposure to infection and may be so mild that little attention is paid to the condition. Generally there is a history of acute attacks of diarrhœa and the passage of blood and mucus in the stools associated with tenesmus. These attacks occur at intervals and are precipitated by chill and dietetic indiscretion.

In between attacks the stools are solid and often coated with mucus in which lateral-spined eggs are found, while in chronic cases bilharzial papillomata may form, producing soft masses palpable through the abdominal wall; they may cause considerable distress if present in the rectum and may protrude through the anus, causing prolapse. Bilharzial granulomata and fistulæ may implicate the buttocks and anus and occasionally epithelioma supervenes. Periportal cirrhosis and splenomegaly not infrequently complicate chronic cases and this parasite is one of the accepted causes of Egyptian splenomegaly.

Diagnosis. In addition to demonstrating ova in the fæces, sigmoidoscopy and the complement fixation reaction afford important information in diagnosing these bilharzial lesions from those of amœbic and ciliate dysentery and ulcerative colitis. Repeated stool examinations may be necessary to demonstrate ova in light infections. Sigmoidoscopy may reveal small hæmorrhages or whitish bilharzial pseudo-tubercles in the early stages and later papillomata and ulcers. Scrapings from these lesions obtained with a blunt curette generally contain demonstrable ova.

Prognosis. Except in advanced cases with cirrhosis or other severe complications modern therapy is effective.

Treatment. Prophylactic and curative treatments are similar to those already described for vesical schistosomiasis. Splenectomy may be necessary in cases of Egyptian splenomegaly due to *S. mansoni*.

ASIATIC SCHISTOSOMIASIS

(*Katayama Disease, Yangtze Valley Fever.*)

This disease is a chronic colitis encountered in the Far East, caused by *Schistosoma japonicum*. The worms inhabit the portal system, while their eggs are oval, measuring 70–100 × 60–75 microns and show a lateral knob. The intermediary hosts are operculated snails; in the Yangtze Valley *Oncomelania hupensis* is the vector and in the south-east coast of China and Japan *Oncomelania nosophora*. Cases have been recorded in the Philippines and Formosa.

Pathology. At autopsy colonic thickening with scarring and possibly papillomata involving the mucosa are found. The mesentery is thickened and shortened, and large, firm retroperitoneal glands may be found matted together resembling tumours. Other lesions consist of thrombosis of the portal and mesenteric veins, periportal cirrhosis of the liver and splenomegaly. Fibrosis of the lungs and granuloma of the brain are recorded.

Symptoms. Cercarial dermatitis may result from the invasion of the skin by cercariæ with any of these schistosomes, but it appears particularly common in the Asiatic type, reaching a maximum in one to one and a half days. The initial toxic stage is characterised by an irregular remittent fever which may last several weeks and is often associated with urticarial rashes, transient œdemas of the subcutaneous tissues, pain in the epigastrium and hypogastrium, vomiting, diarrhœa, dyspnœa and cough. Examination may show splenomegaly, hepatomegaly, moist sounds and dullness at the bases of the lungs and intense eosinophilia. In this stage the complement fixation reaction is strongly positive and dermal hyper-sensitivity may be demonstrated. The next stage sets in from the end of the third month onwards with tenesmus, and the passage of mucosanguineous stools containing lateral knobbed ova. The colon now becomes tender and palpable and digestive disturbances and signs of malnutrition appear. The third stage presents evidence of portal obstruction with ascites and hepatic insufficiency. Bilharzial granulomata of the brain present a picture suggestive of cerebral tumour including headache, vomiting, optic neuritis, various forms of nerve paralysis and epilepsy of Jacksonian type.

Diagnosis. During the toxic stage enteric fever, food poisoning and pulmonary tuberculosis may be suspected, but the eosinophilia and complement

fixation reaction should enable the bilharzial origin of the condition to be recognised even before ova appear. Dysenteric features associated with enlargement of the liver are common to both amœbiasis and intestinal schistosomiasis and diagnosis is only possible by sigmoidoscopy and laboratory procedures.

Prognosis. In patients subject to repeated reinfection death is not infrequent, but provided the liver is reasonably healthy and intercurrent disease is not present the response to modern therapy is satisfactory as a rule. It is, however, the most difficult of all human species to cure.

Treatment. Treatment is similar to that outlined for other species of schistosoma infestations. Cases with cerebral granulomata should receive an intensive course of tartar emetic treatment before decompression is attempted.

Heterophyidiasis. This disease is due to infection with flukes of the family *Heterophyidæ*. Three species may infest man—*Heterophyes heterophyes*, *Heterophyes katsuradai* and *Metagonimus yokagawai*.

Heterophyes heterophyes (*Distoma heterophyes*, etc.): this minute fluke infests the intestine of man and other mammals like the dog and cat. It is exceedingly small, measuring only 1–1·7 × 0·3–0·4 mm. and deposits oval-shaped, light-brown operculated ova measuring 28-30 × 15–17 microns. Man becomes infected by eating mullet in which cercariæ have encysted. Infections with the other species are so rare that no detailed description is necessary.

At autopsy the flukes are found attached by their suckers to the intestinal mucosa where they induce mild inflammatory reactions and local eosinophilia. In milder infections the condition is sub-clinical, but where larger numbers of parasites are present intestinal disturbances result with indigestion, diarrhœa and malæna. Diagnosis is made by finding the operculated eggs of *H. heterophyes* in the stools. Regarding treatment, carbon tetrachloride, beta naphthol and thymol are all effective. Owing to the small size of the flukes the stools must be strained through fine mesh muslin as they are liable to be lost on ordinary sieving.

Diseases due to Cestodes or Tape-worms

Adult cestodes are elongated, ribbon-like structures divided transversely into segments known as proglottides, while at the narrow anterior end is the scolex which is joined to the segmented portion by a narrow neck. Adult tape-worms produce intestinal tæniasis in man and other animals acting as definitive hosts. Somatic tæniasis results where the developmental stage is passed in the muscles or tissues of the intermediary host.

Intestinal Cestodiasis. (1) *Tænia solium*: the pork tape-worm is encountered in the upper third of the small intestine of man. It measures from 6 to 10 feet in length, possesses a globular head, four suckers, a rostellum and two circular rows of hooks which alternate with each other. The uterus lies in the long median plane of the proglottis, is tubular in shape and possesses not more than twelve branched lateral diverticula. Its ova are spherical in shape, measure 30 to 40 microns in diameter, have a thick walled shell and contain an oncosphere with three pairs of hooklets. The gravid proglottides become detached and are evacuated in the fæces where they disintegrate and liberate the eggs. These are taken into the alimentary tract of the intermediary host, the pig, either in contaminated water or when the animal is grubbing for food. Man himself sometimes becomes the intermediary host. On ingestion the shell is dissolved and the oncosphere is liberated in the stomach; subsequently it passes through the gut wall, enters the circulation and is deposited in the connective tissues of the muscles, where a capsule is formed around it as a result of tissue irritation. Here it develops into a bladder-like structure known as *cysticercus cellulosæ* which varies in size from 5–20 × 5–10 mm. When these cysticerci are eaten by the definitive host the bladder is digested and the scolex liberated. In the upper

part of the small intestine the scolex fixes itself to the gut wall and the neck proceeds to bud proglottides. The cysticercus stage is normally found in the muscles of the pig and human infections are acquired by eating "measly" pork which has been insufficiently cooked. The processes of pickling and smoking fail to kill cysticerci (see Plate 68, 28–30, p. 1066).

(2) *Tænia saginata:* the beef tape-worm is only found in the intestinal tract of man. It measures 9 to 12 feet, but occasionally is double this length. The scolex is pear-shaped or cubical, possessing four lateral suckers, no rostellum and no hooks. The uterus is tubular, median in position and possesses fifteen or more branched lateral diverticula, a feature which differentiates it from the proglottis of *Tænia solium*. Its eggs are indistinguishable from those of *Tænia solium*. The cysticercus stage is found in the ox (*Cysticercus bovis*) and man becomes infected by eating underdone beef. The cysterci die when cooked in water at a temperature of 48° C. (see Plate 68, 26 and 27).

(3) *Dipylidium caninum:* this tape-worm is normally a parasite of the intestine of dogs and cats, but is sometimes found in young children. Its length varies from 10 to 40 cm. and its breadth from 1·5 to 3 mm. It does not appear to be pathogenic.

Other rare human infections include *Bertiella satyri*.

(4) *Diphyllobothrium latum* (*Dibothriocephalus latus*): the broad, fish tape-worm varies in length from 6 to 30 feet, is greyish in colour and inhabits the small intestine of the dog, cat, fox and man. Its head is almond-shaped and possesses no armature. The eggs are operculated, elliptical in shape and measure 70 × 45 microns. Within three to five weeks the fertilised egg is transformed into a hexacanth embryo which escapes into water and after being ingested by cyclops it develops in the cœlomic cavity into a procercoid larva. If the infected crustacean is now swallowed by plankton-feeding fresh-water fish, such as pike, perch, salmon and trout, the larva develops in the muscles of the fish into the plerocercoid stage and man becomes infected by eating its flesh, provided it be insufficiently cooked.

Symptoms. Often no symptoms are produced, but in other patients dyspepsia, loss of appetite, colicky abdominal pain and diarrhœa ensue, while headache, convulsions and strabismus may be encountered in children. Infestations with *D. latum* are occasionally associated with severe megalocytic anæmia which responds specifically to liver extract treatment, but is only permanently cured if the tape-worms be eliminated by proper treatment.

Diagnosis. Diagnosis is based on the identification of the parasite by the demonstration of its segments or ova in the fæces. Eosinophilia may suggest helminthic disease. Skin hyper-sensitiveness to tape-worm protein may be demonstrated by the intradermal test.

Treatment. Filix-mas cures most patients provided there is preliminary dietetic treatment and adequate purgation with salines follow. For the two previous days the bowels should be opened with aperients and a liquid diet taken. Extractum filicis liquidum should be given in gelatine capsules containing 30 minims of the drug at 8.0, 8.20 and 8.40 a.m., while in cases which have previously been unsuccessfully treated an additional 30 minims may be given at 9 a.m. combined with 30 minims of oil of turpentine. Two hours later sodium sulphate (½ ounce) is administered. All motions for forty-eight hours after treatment should be collected, sieved and examined against a black background to identify the head of the worm. It takes about three months for segments to reappear where the worm has survived. An alternative treatment is carbon tetrachloride, which is given in capsules in a dosage of 3 c.c. for adults. This is followed by a saline purge three hours later. If there is any suggestion of calcium deficiency, calcium lactate, 30 grains thrice daily should be given for several days prior to the administration of this drug. Anæmia, if associated with intestinal tæniasis, should be treated with full doses of iron in the case of *Tænia saginata*

and *Tænia solium*, and with liver extract in megalocytic anæmia associated with *Diphyllobothrium latum* infestation. Where gastric secretion is depressed, acid hydrochlor. dil. B.P. in a dosage of 1 drachm thrice daily after meals in diluted orange juice, is advisable.

Somatic Cestodiasis. After cestode eggs or proglottides are swallowed by the intermediary host, the embryonal shell is digested and the embryo set free: it attaches itself by means of its hooks to the intestinal wall, burrowing its way into the blood vessels and so to the internal organs or tissues for which it has a predilection. As a result of tissue irritation a limiting capsule forms around it and within this the larva develops. A number of different types are found, known as (*a*) a plerocercoid when it becomes tape-like with an invaginated scolex, (*b*) a cysticercoid when only slight bladder formation ensues and (*c*) cysts in which the bladder is well developed. Three varieties of these cysts are found: (1) a cysticercus proper in which there is one bladder and one scolex; (2) a coenurus in which there is one bladder cavity and numerous scolices; (3) an echinococcus in which these scolices develop in brood-capsules; daughter cysts may also be formed.

(1) *Sparganum mansoni.* This is the plerocercoid stage of *Diphyllobothrium mansoni* and has a life history resembling *D. latum*—the broad fish tape-worm. The habitat of the adult worms is the intestine of the dog and cat, and the ciliated embryo after escaping by the fæces must be ingested by a cyclops, *C. leucarti*, in which it develops into a procercoid larva. If this be now swallowed by a suitable ophidian, avian or mammalian host, including man, the cyclops is digested and the freed larva pentrates the stomach wall, travels subperitoneally to the somatic muscles, including those of the iliac and lumbar region, pleura, urethra and eye, where it undergoes an asexual multiplication by transverse fission. Many spargana are thus produced from a single plerocercoid. Should this infested tissue be eaten by the dog or cat the mature tape-worm, *Diphyllobothrium mansoni*, develops. The adult stage has never been observed in man.

Symptoms. Ocular sparganosis is common in the Tonkin Delta, and inflammation with pain, redness, injection of vessels, œdema, lacrymation and ptosis may result. Chinamen often acquire ocular infection through the practice of applying spargana-infected frogs for the treatment of ulcers. Myositis with pain, swelling and œdema of the adjacent subcutaneous tissues may ensue when the somatic muscles are involved.

Diagnosis. This is dependent on demonstrating the unbranched sparganum larvæ embedded in a slimy matrix in the tissues.

Treatment. Surgical removal of the larvæ is performed whenever feasible.

(2) *Sparganum proliferum.* This species of Sparganum affects man in Japan, but the adult stage and the life cycle are both unknown (Faust). Clinically, large numbers of spargana invade the tissues, producing extensive nodules and honeycombing, and where the lymphatics are implicated elephantiasis is said to result.

Cysticercosis. This is the cystic stage of *Tænia solium* which may involve the somatic muscles, the heart and its valves, the brain and its ventricles, the liver, lungs, orbital tissues and eye. Cysticercosis occurs in Europe, especially Germany, and is encountered in Africa, Madagascar and in soldiers returning from India and Egypt. Man probably acquires the disease by auto-infection or eating uncooked food contaminated with segments or ova of *T. solium*.

Pathology. The cyst, which may or may not be surrounded by a fibrous tissue capsule, consists of an opalescent bladder containing a single invaginated head with hooklets. In the eye, ventricles and pia mater cysts show little tendency to be encapsulated. Their size depends on their situation and age. In the brain they tend to be round and in the muscles to be oval in shape, attaining a length of 20 mm. when mature. Brumpt (**63**) points out that if the cyst dies or undergoes calcareous degeneration there is an intense local leucocytosis and

even suppuration may result. MacArthur (**64**) holds that death of the larvæ is associated with an increase in the quantity of fluid and that they then act as foreign irritants and often produce symptoms for the first time partly by mechanical means as a result of their swelling and partly from toxic effects. Calcification may occur in the scolex before it involves either the capsule or the cyst. Hypertrophy of the heart muscle and valvular trouble due to calcified cysticerci are described by French workers.

Symptoms.—The incubation period is difficult to establish since the majority of cases are not cognisant of having harboured the adult *T. solium*. Probably it varies from a few months to several years in different cases. Prodromal symptoms are not common, but in certain cases during the invasive stage a history of fever, headache, myalgia and swelling of muscles subsequently found to be affected may be forthcoming.

(1) *Muscular Type.* The clinical manifestations are determined by the distribution and death of parasites. Palpable cysts may be detected in the subcutaneous tissues and muscles of any part of the body including the head, face, eyelids, tongue, lips, trunk and limbs. On palpation the size is generally that of a small pea, but occasionally they may appear as large as a pigeon's egg (MacArthur). Latency is a characteristic feature and cysts may suddenly appear or disappear in the most evanescent fashion. Muscular pains, tenderness and cramps may be complained of.

(2) *Nervous Type.* Epilepsy is by far the commonest manifestation. One out of every five soldiers returning from India with so-called idiopathic epilepsy does so on account of cysticercosis. The attacks may be Jacksonian in type, with or without loss of consciousness, or like those of petit mal. Aura, biting the tongue, sphincter incompetence and post-epileptic stupor may be present. Sometimes fits occur when subcutaneous cysts are first detected, at other times several years may elapse before epilepsy supervenes. Other cases present focal lesions of different types and cerebral tumour, disseminated sclerosis, encephalitis, and various psychoses associated with mental dullness, defective memory, disorientation, melancholia, acute mania and even delusional insanity may be simulated. Periods of exacerbation are often followed by intervals of quietude, so that at different periods the one patient may be regarded as suffering from delusional insanity, disseminated sclerosis and cerebral tumour.

(3) *Ocular Type.* Distension of the eye itself, exophthalmos, conjunctivitis, iritis, opacities in the vitreous, choroiditis or detachment of the retina may be produced. Cysts may be lodged either in the anterior or posterior chamber.

Naturally these types are not clear cut, but depend on predominant regional distribution of cysticerci. Other organs like the heart and liver are occasionally involved.

Diagnosis. Muscle and subcutaneous cysts may be mistaken for lipomata, von Recklinghausen's disease, secondary malignant deposits and nodular leprosy. The history of fits in a person who has resided abroad and has a clean family history and no head injury, syphilis or neoplasm is suggestive, while the cysts if palpable should arouse suspicion. Biopsy under local anæsthesia is always advisable ; after incision of the cyst capsule a translucent membrane possessing a " milk spot " caused by the invaginated scolex is found. X-ray examination of the root of the neck, upper arms, fore-arms, thighs and legs may reveal calcified scolices or fully developed elliptical cysts (about 2·3 cm. long), but seldom of the skull. Eosinophilia is rarely present and immunological tests such as the complement fixation reaction and the intradermal skin test, though sometimes useful, are frequently disappointing as negative results may occur in quite heavy infestations. Both tests are group reactions to *Tænia* protein and fail to differentiate the various species of *Tænia* infecting man. (Plate 70.)

Prognosis. According to MacArthur the most dangerous time is the sixth to the eighth year, as this is when grave intensification of existing cerebral

disturbances most frequently takes place and patients who have previously been free from cerebral features develop them. The general tendency once the cerebrum is involved is one of mental deterioration, but sometimes even those who have developed fits may recover completely. In consequence the prognosis is always difficult.

Prevention. Individuals infested with *T. solium* should be treated effectively without delay, and under-done pork should be avoided. Rigid inspection of pork at abattoirs by competent inspectors should be instituted.

Treatment. Surgical intervention is not of value and all that can be done is to control fits by means of luminal and bromide.

ECHINOCOCCOSIS (*Plate 68, 35–37, p. 1066*)

(*Hydatid Disease*)

Hydatid disease in both man and domestic animals is the cystic or larval stage of the dog tape-worm, *Echinococcus granulosus*.

Ætiology. Infection is acquired by handling and fondling infected dogs or eating uncooked food or water contaminated with their fæces. Though hydatid disease has been recorded in all countries it is specially common where the sheep-raising industry flourishes as in Australia, New Zealand, Argentine, South Africa, Iceland, Bulgaria, Roumania and Algiers. In certain parts of Europe, like Greece, it is not uncommon. Indigenous cases occur in the British Isles.

Echinococcus granulosus (*Tænia echinococcus*) is a minute tape-worm measuring 3 to 6 mm. in length which inhabits the small intestine of dogs, jackals, wolves and occasionally domestic cats. The head is small, measuring 0·3 to 0·5 mm. in diameter and possesses a rostellum, a double row of rose-thorn hooklets and four suckers. The fourth or terminal segment is larger than the others and contains the sexual organs and eggs. The eggs, which measure 30 × 36 microns, resemble those of the other cestodes and contain a six-hooked embryo. As the terminal proglottides mature, they become detached and are passed in the fæces, so that a dog may excrete hundreds or even thousands of eggs daily. These eggs, either singly or in masses, may be swallowed in contaminated food or water by the intermediate host and on reaching the stomach and duodenum the shell is digested and the hexacanth embryo escapes, boring its way through the intestinal wall into one of the mesenteric vessels. Generally it is filtered out in the capillaries of the liver which it may reach in eight hours; less frequently it localises in the lung capillaries and elsewhere. The young embryo now loses its hooklets, becomes vacuolated and transformed into an hydatid follicle; many months later an elastic cyst is produced containing clear, limpid fluid surrounded by a lining membrane and adventitia. The cyst membrane consists of (1) an endogenous or germinal cellular layer which secretes hydatid fluid and buds little cysts containing scolices known as brood-capsules; (2) an outer laminated or exogenous layer composed largely of hyalin, the function of which is essentially protective; it is laid down by the endogenous layer. In addition, local host reaction produces a fibrous tissue barrier known as the adventitia which walls off the cyst from the surrounding tissues. On incision the cyst membrane is readily separated from the adventitia. As well as the fluid and brood capsules the original mother cyst may give rise to daughter and grand-daughter cysts containing scolices; the latter are really the embryonic heads of future tape-worms and are capable of retraction or evagination (Plate 68, 35, p. 1066) under a suitable stimulus. Sometimes the endogenous layer of the mother cyst fails to breed brood-capsules and daughter cysts and it is then known as a sterile cyst. At other times exogenous budding occurs; this is particularly common in bone and occasionally it is encountered in the liver where it forms a hard, globular, multilocular mass containing numerous alveoli containing cyst membrane and a jelly-like matrix. Alveolar hydatid of this nature in man has been

attributed to a separate parasite, *Echinococcus alveolaris*, but the existence of second species is improbable.

Distribution of Cysts. Hydatid cysts have been recorded in practically every organ and tissue of the body, but about 70 per cent. of primary cysts occur in the liver. Next in frequency in adults are the lung, muscles and subcutaneous tissues, kidney, spleen, bones, orbit and brain (Dévé) (**65**). In children brain hydatid is about seven times more frequent than in the adult, whereas bony hydatid is rare. Cysts are almost as frequently multiple as single ; in the former event the liver is almost invariably implicated and two to six cysts are the rule, but as many as forty to sixty primary cysts have been recorded.

Changes in the Cyst. The local pressure effects depend on the site of the cyst, its rate of growth and the compensatory changes which take place in the implicated viscera. Sooner or later, however, some complication such as rupture, entry of bile, suppuration or death and degeneration of the cyst occurs. As age advances the adventitia becomes denser and less vascular and defective nutrition may result in non-secretion of fluid, collapse of the cyst and caseous degeneration of parasitic tissue with the production of putty-like *débris* in which convoluted layers of laminated membrane may still be recognised after many years. Infiltration with calcium salts, first of the adventitia and later of the whole cyst, may follow.

Symptoms. The incubation period varies with the rate of growth of the cyst which is slow in bone and rapid in the brain and lungs. From five to thirty years may elapse before symptoms are produced, and autopsy records show that the condition is subclinical throughout life in at least 30 per cent. of cases. Not infrequently it is the presence of some accident such as rupture or suppuration which draws attention to the presence of the cyst for the first time.

Diagnosis. (1) *Hydatid material.* Hydatid fluid may be aspirated during exploratory cyst puncture or pieces of membrane resembling grape skins may be coughed up or passed in the fæces or urine. Hydatid elements like scolices and hooklets may also be identified. Laminated membrane has a characteristic appearance, its curled edges resembling the leaves of a book. The fluid itself is clear like water or faintly opalescent, having a specific gravity of 1,008 to 1,015, and containing from 0·12 to 0·15 per cent. of coagulable protein as well as considerable amounts of sodium chloride (0·55 to 0·65 per cent.). Centrifugalisation generally reveals hooklets or scolices (Plate 68, 36 and 37). When the head is evaginated the scolex measures nearly 3 mm. in length and, in addition to its four suckers and double row of hooklets, the cytoplasm contains characteristic calcarious bodies. (2) *Leucocyte count.* A local accumulation of eosinophiles and a general eosinophilia accompany the early invasive stages, but the blood count may have returned to normal long before clinical symptoms are produced. Prior to operation only about one-third of patients with echinococcus are found to have an eosinophilia. Rupture of a cyst is followed by a definite eosinophilia and a post-operative rise occurs whenever fluid has been absorbed. Suppuration secondary to coccal infection leads to a neutrophil leucocytosis with decrease in the eosinophile elements. (3) *Precipitin test.* This is best performed by mixing 0·4 c.c. of carbolised sheep hydatid fluid (0·5 per cent.) with 0·4 c.c. of fresh clear serum (**66**). Final readings are made after thirty-six hours at room temperature, a positive reaction being indicated by the formation of a fine flocculent precipitate which slowly sinks to the bottom of the tube. The test is positive in some 65 to 80 per cent. of cases. (4) *The Complement fixation reaction.* Either hydatid fluid or an alcoholic extract of scolices may be utilised as antigen, sheep cysts being most suited for the purpose (**67**). Positive reactions are obtained in about 80 per cent. of patients before operation, but if those who have been formerly operated on be excluded the number does not exceed 60 per cent. Rupture or suppuration lead to absorption of antigen and 95 to 100 per cent. of sera are positive after these complications. Negative results are obtained in

degenerated or old cysts with a greatly fibrosed adventitia, also in sterile cysts, the fluid of which is poorly antigenic. A post-operative rise in complement fixation antibody is generally demonstrable, and this circulating body only slowly disappears. At least two years must elapse before any prognostic significance can be attached to a persisting positive reaction. (5) *Intradermal test* (Casoni reaction). This consists in the injection into the dermis of 0·25 c.c. of hydatid fluid filtered to ensure its sterilisation. Two types of reaction are encountered : (1) an immediate white wheal rapidly increasing to a diameter of 2·4 cm. or more with irregular peripheral out-runners and surrounded by a zone of erythema ; (2) a delayed reaction characterised by a large area of erythema with a defined margin and swelling of the deeper subcutaneous tissues due to œdema coming on some six to twenty-four hours after the injection. The skin is tightly stretched, but not actually painful, though in hypersensitive individuals considerable discomfort and itching associated with great swelling, redness and even local vesiculation may ensue. Some 98 per cent. of active hydatid cases react positively so that a negative reaction in a suspected case is strong presumptive evidence against echinococcosis provided the injected fluid be antigenic. A positive reaction, on the other hand, by no means proves the presence of an hydatid cyst since the reaction is of group nature and cases of both intestinal tæniasis and cysticercosis in man may react positively as well as individuals sensitive to the protein of the host from which the fluid was obtained. Furthermore, as dermal sensitivity persists for many years after the complete surgical removal of all cysts, it follows that a positive skin test has no essential relationship to existing infestation.

Hydatid Anaphylaxis. Anaphylaxis, embolic phenomena and secondary echinococcosis may follow puncture or rupture of a cyst and the escape of hydatid elements into blood vessels or the serous sacs. Anaphylactic manifestations include sudden onset of urticaria, œdema, erythema and pruritis with or without chemosis, injection of the conjunctivæ, pallor, cold extremities, tachycardia, low blood pressure, syncope, tightness of the chest, asthmatic cough, cyanosis, dyspnœa, nausea, vomiting, diarrhœa, passage of blood *per rectum*, extreme nervousness, delirium, convulsion and coma. There is a concomitant eosinophilia, and death may occur rapidly from cardiovascular shock associated with intense bronchial spasm with or without pulmonary œdema or œdema of the glottis.

Sensitisation probably develops during the invasive stage before the formation of the laminated layer, and it is the escape of fluid following puncture or rupture many years later which precipitates the anaphylactoid reaction. Dermal sensitiveness to hydatid protein is always demonstrable in such cases and passive hypersensitiveness can be transferred by serum injections into either animals or man. Rarely the syndrome may be accidentally reproduced in its entirety when injecting hydatid fluid during skin testing in hypersensitive subjects. For this reason it is advisable to keep such patients under observation for at least an hour and to inject adrenalin (10 minims of 1/1,000 solution) immediately symptoms appears.

Hydatid of the Liver. About 75 per cent. of all hydatid cysts affecting man are situated in the liver and of these four out of every five occur in the right half of that organ. In contradistinction to amœbic abscess they tend to present at the inferior surface. *Simple or univesicular cysts.* These cysts which contain brood capsules and scolices, but no daughter cysts, occur specially in children and young adults. As a rule a tumour in the right hypochondrium or epigastrium is the first thing noted. If the anterior and inferior surface be implicated it presents as a rounded, cystic, non-tender swelling continuous with liver dullness which may attain enormous dimensions. Considerable deformity of the chest wall may result in children, due to widening of the intercostal spaces and bulging of the costal margin. As a rule pain is absent and the general health satisfactory.

According to Dew (**68**) rupture is rare under the age of fifteen years. *Multivesicular cysts.* Cysts containing daughters are much more characteristic of adult life and frequently the condition is only recognised when a large tumour has developed or complications have supervened. There may be discomfort, a feeling of weight or actual pain in the hypogastrium. If colicky in nature pain suggests the passage of cyst contents down the biliary passages and is often mistaken for gall-stone colic. Gastric disturbances are common and include a sense of distension after meals, nausea, heart-burn and even vomiting. Dyspnœa and cough only develop where the diaphragm is encroached upon. Jaundice may be transient or persistent and in the latter case rupture into a bile duct or suppuration has supervened. Ascites is rare.

Physical examination in about three out of four cases reveals a rounded, cystic tumour continuous with liver dullness due to a cyst located on the inferior aspect of the liver; it is not tender and is freely movable with respiration. Hydatid fremitus or hydatid thrill, if present, is pathognomonic. Where the cysts develop downward below the stomach and colon a renal tumour may be simulated. Pulmonary signs at the right base are infrequent unless the cyst implicates the upper aspect of the liver (25 per cent. of cases) and impinges on the diaphragm. X-ray examination is necessary here to differentiate subphrenic from pulmonary cysts; immobilisation, distortion and elevation of the diaphragm may result. Cysts involving the upper aspect of the left half of the liver cause cardiac displacement and tend to present in the epigastrium in front of the colon and stomach; palpable enlargement in this vicinity, however, is much more often due to left compensatory hypertrophy associated with a large destructive cyst of the right half of that organ.

Complications. These include suppuration and rupture into a bile duct, the peritoneal cavity, the thorax, the alimentary tract or elsewhere.

(1) *Suppuration.* About 90 per cent. of suppurating cysts are multivesicular. The pus is always bile-stained, generally fœtid in odour and may be associated with a variety of organisms including *Bact. coli*, staphylococci, streptococci, *Bact. proteus*, *Vibrion septique* and *Bact. aerogenes capsulatus* (**68**). Generally there is a history of previous dyspepsia, abdominal discomfort, pain or jaundice, but in some cases the onset is quite sudden, the earliest symptom being hepatic pain, often colicky in nature. Constitutional symptoms are, as a rule, less marked than would be expected and depend on the thickness of the adventitia and the virulence of the invading organism. The temperature is by no means constant, but intermittent fever with evening rises is common. In addition, rigors, sweats, anorexia, vomiting and diarrhœa develop, weakness increases, the skin becomes pale or jaundiced and later dyspnœa, wasting and cachexia result. Anaerobic infections are rapidly progressive with grave constitutional features.

Physical examination may reveal a tender tumour continuous with liver dullness, but with limited mobility owing to adhesions; the rectus is often rigid and respiratory movement limited. An effusion at the right base is frequently associated with subdiaphragmatic suppurating cysts, or signs of dry pleurisy, pulmonary congestion or broncho-pneumonia may be present in this situation. A neutrophil leucocytosis results with decrease in eosinophile cells. Suppurating hydatid may be confused with subphrenic abscess, amœbic liver abscess, cholecystitis, cholangitis, pylephlebitis, basal pneumonia, perinephric abscess or an acute abdominal crisis such as a perforated duodenal ulcer. The history, the presence of a rounded tumour, immunological tests and X-ray examination will assist in their differentiation.

(2) *Intra-Peritoneal Rupture.* This is accompanied by peritoneal shock. There is sudden upper abdominal pain, vomiting, collapse and tachycardia. Anaphylactic symptoms, including urticaria and pruritis, may be superadded. Later still, where bile has leaked into the peritoneal cavity, the abdomen suddenly

enlarges and free fluid is demonstrable (choleperitoneum). Peritonitis follows if the original cyst was infected, while secondary peritoneal echinococcosis results years later with multiple cysts scattered throughout the peritoneum due to the implantation of daughter cysts, brood capsules and scolices.

(3) *Intra-Thoracic Rupture.* The tendency of cysts situated on the superior surface of the liver is to work upwards, elevating the diaphragm, compressing the lung or producing a passive pleural effusion ; in some cases rupture through the weakened diaphragm into the adjacent lung tissue may follow, while in others it occurs into the pleural cavity or a bronchus. Generally suppuration precedes rupture. Hepato-bronchial cysts with or without empyema may result, in which case the sudden expectoration of bile-stained pus containing hydatid membrane or other elements will enable a diagnosis to be made. Natural cure may follow, but the presence of daughter cysts and the difficulty of draining a hepatico-bronchial cyst through a small bronchus militate against this, and prolonged suppuration, hæmoptysis, abscess formation or gangrene usually necessitate surgical interference.

Treatment. This is essentially surgical unless the cyst be degenerated and calcified, when operation is contraindicated. Aspiration, apart from open operation, should never be attempted owing to the risk of anaphylaxis, secondary echinococcosis and secondary bacterial infection.

Hydatid of the Lung. Next to the liver the most frequent site of echinococcosis is the lung, 10 to 15 per cent. of cysts occurring in this situation. The right lung is at least twice as frequently involved as the left. Cysts are generally subpleural, but occasionally may be deep or para-bronchial and generally contain scolices or brood capsules, but no daughters. This is important, for following rupture into a bronchus spontaneous cure more readily follows. The adventitia is thin, but owing to their high content in sodium chloride these cysts show up well with X-rays, giving a characteristic spherical shadow.

Simple Cysts (univesicular). These generally attract little attention and only one case in four is diagnosed prior to rupture or suppuration. A previous respiratory infection may be the starting point of symptoms. Pain in the chest is uncommon, but discomfort or a feeling of weight may be complained of. Cough is a common symptom and is dry at first ; generally it causes little anxiety until profuse expectoration due to bronchitis, pneumonia, secondary infection or hæmoptysis supervenes. The latter complication occurs in 60 per cent. of cases and may be slight or extremely severe. Frequently a diagnosis of phthisis, new growth or aneurysm is made. In deeply seated cysts pressure on a bronchus may lead to dyspnœa and orthopnœa, while large cysts may cause an obvious bulging in the chest demonstrable by mensuration and occasionally displacement of the heart. As a rule, however, the apex beat is normal. In pulmonary cysts the outline is demonstrably circular, vocal fremitus is diminished, percussion yields a flat dull note and breath sound are absent or diminished. In cysts at the right base dullness merges into liver dullness and X-ray examination may be necessary to differentiate the condition from pleural effusion or subdiaphragmatic cysts. Congestion, collapse and infection or pericystic pulmonary tissue with corresponding physical signs may lead, especially in children, to the diagnosis of broncho-pneumonia.

Complications. Pulmonary cysts may rupture into a bronchus or into the pleura with the production of pleurisy, empyema or pneumothorax and occasionally they even implicate the pulmonary vessels and heart. *Rupture into a Bronchus.* Following this accident there is a fit of paroxysmal coughing and a saltish-tasting fluid wells up into the mouth and nose ; the expectoration is frothy, usually blood-stained and may contain hydatid membrane or other elements. Often the patient gives a history of coughing up "grape skins." Death may occur from anaphylaxis or actual drowning in hydatid fluid. Other features include pain and recurrent hæmoptysis. Physical examination reveals

signs of a cavity of variable dimensions with a tympanitic or cracked-pot note on percussion, increased vocal resonance, cavernous breathing and whispered pectoriloquy. Spontaneous cure sometimes results or the cyst may suppurate, producing recurrent hæmoptysis, fever and a profuse, fœtid, frothy expectoration associated with severe coughing; night sweats and rigors may also occur. Other patients present little or no fever. If long standing, wasting, anæmia and clubbing of the fingers may ensue.

Treatment. Deep para-bronchial cysts, especially if causing no inconvenience, should not be operated on as 80 per cent. undergo spontaneous cure (Dew) (**68**). All suppurating cysts should be opened and drained and large subpleural cysts operated on without delay; owing to the risk of bronchial flooding the patient should be so placed that the incision is made into a dependent part of the cyst cavity. Ether administered by the intratracheal route is the best anæsthetic.

Hydatid of the Brain. Primary hydatid cysts of the brain are rare in adults, but by no means infrequent in children. Usually they are single and univesicular and not infrequently associated with hepatic echinococcosis. Secondary cerebral cysts follow rupture of a cardiac cyst, are usually multiple and associated with secondary cysts in the spleen or kidney. Headache, vomiting, optic neuritis are common and localising neurological features may occur or Jacksonian epilepsy develop. In advanced cases X-ray may show osteoporosis and thinning of the cranium. With secondary cysts there may be a history suggestive of intracardiac rupture followed by a latent period before signs of increased intracranial pressure become manifest.

Treatment. Secondary cysts being multiple are inoperable, but primary cysts should be trephined without delay. The prognosis is very grave and 50 per cent. of cases die with hyperpyrexia and cardiovascular shock, the sudden release of fluid pressure resulting in cerebral œdema.

Renal Hydatid. Hydatid cysts of the kidney are generally secondary and may be located in the cortex or medulla: latency is characteristic and no symptoms may arise until quite large round cystic tumours have been produced. The general health remains good, though in large cysts an aching pain in the loin may be complained of. Rupture into the renal pelvis with passage of membrane or daughter cysts produce recurrent attacks of renal colic and intermittent hydronephrosis may develop. Transient hæmaturia may be present and the diagnosis is generally made by finding hydatid membrane, scolices or hooklets in the urine. Suppuration results in a tender renal swelling; there is persistent renal pain, frequent painful micturition and fever. The urine contains pus cells and hydatid elements.

Hymenolepis nana. This dwarf tape-worm of man, common in the Southern United States, South Europe and India, lives in the small intestine: it is probably identical with the species found in mice and rats. It measures 2·5 to 4·0 cm. in length, has 4 hemispherical suckers and a short rostellum with a single row of hooklets. The eggs contain an onchosphere and measure 30 to 45 microns in diameter. No intermediate host is required as the eggs hatch in the small intestine. The embryos penetrate the villi, develop into cercocysts, return into the lumen and become attached by their heads to other villi where they develop into mature worms (see Plate 68, 31–34, p. 1066).

Symptoms. In hyperinfection severe reflex and toxic symptoms may arise in children. These include abdominal pain, diarrhœa, insomnia, giddiness and convulsions. Eosinophilia is common. Diagnosis is made by finding ova or segments in the stools.

Treatment. Both felix-mas and oil of chenopodium are effective in eradicating infection.

Man has occasionally been infected with *Hymenolepis diminuta*, the common cestode parasite of the rat and mouse. Various insects, such as earwigs, rat

fleas and cockroaches serve as intermediary hosts and man becomes infected by accidentally ingesting infected insects in flour or meal.

Diseases due to Nematodes

Strongyloidiasis. Only the female, *Strongyloides stercoralis*, is found in man and it reproduces parthenogetically. The worms reside deep in the mucosa of the duodenum and jejunum where they lay their eggs from which the embryos escape. In a normal stool only motile embryos are found, but during diarrhœa the eggs themselves may appear; these measure 50 to 60 microns long and 30 to 34 microns broad and closely resemble ankylostome ova. On escaping from the fæces, the rhabditiform larvæ moult and may produce filariform larvæ with or without the intervention of a sexual cycle. In either case the filariform larvæ penetrate the skin or oral mucous membrane of the host and pass *viâ* the venous circulation to the right heart and lungs; here they break through the

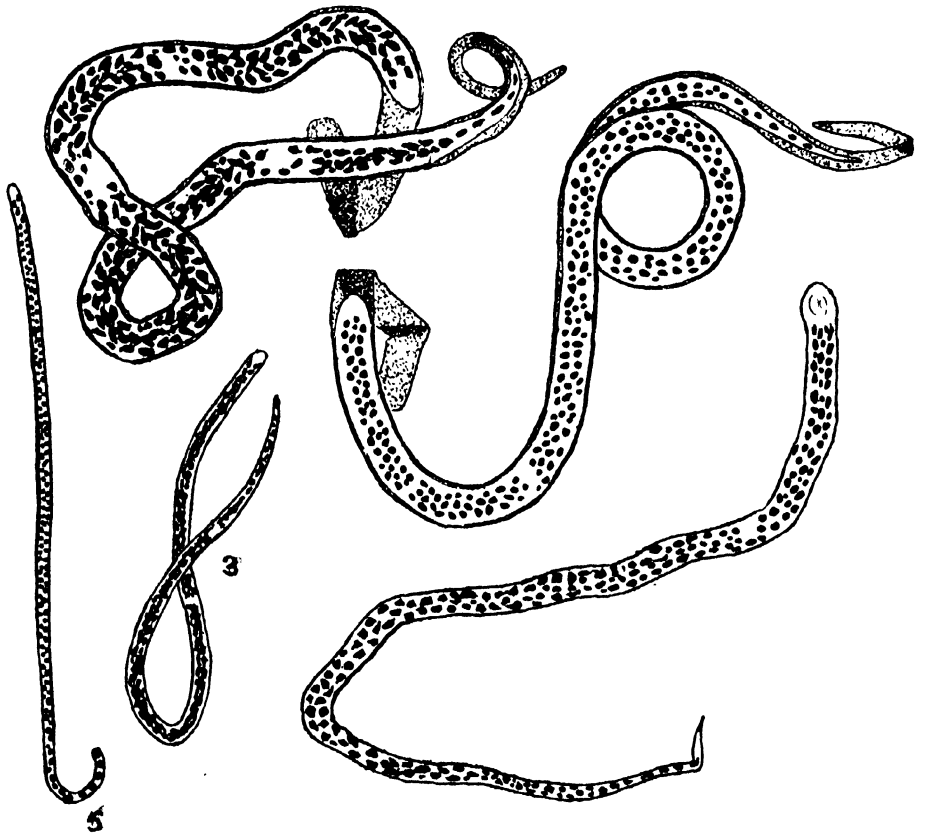


Fig. 104.—Microfilariæ of the blood and skin. 1. *F. loa.* 2. *F. bancrofti.* 3. *F. perstans.* 4. *O. volvulus.* 5. *Ag. streptocerca.* 6. *Mf. Malayi*, not shown, is almost identical with 1.

Species.	Insect host or vector.	Habitat of adult in man.	Habitat of embryo in man.
F. bancrofti	*Culex fatigans*	Lymphatic glands, ducts	Peripheral blood, night.
F. ozzardi	*Culicoides furens*	Mesentery	Peripheral blood, all hours.
F. perstans	*Culicoides austeni*	Root of mesentery	Peripheral blood, all hours.
Loa loa	*Chrysops silacea*	Skin and conjunctiva	Peripheral blood, day.
Onchocerca volvulus	*Simulium damnosum*	Subcutaneous nodules	Epidermis, especially loins.
Agamofilaria streptocerca	Unknown	Unknown	Epidermis, especially loins.
Mf. Malayi	*Mansonioides spp.*	Unknown	Peripheral blood, night.

pulmonary capillaries into the alveoli and migrate up the respiratory tract to the epiglottis and thence to the intestine where the adult female burrows into the tissues. About seventeen days elapse before the worms are mature and rhabditiform larvæ appear in the stools. *S. stercoralis* infection has a very similar geographical distribution to ankylostomiasis and not uncommonly affects man in the tropics. Enteritis may result from the activity of the gravid female worms in the small intestine where extensive erosions of the mucosa may result.

Symptoms. A primary dermatitis may result from the rhabditiform infection of the skin and pulmonary symptoms may follow a few days later associated with eosinophilia. Generally no intestinal symptoms are present, but in severe infections epigastric discomfort and diarrhœa may occur. Occult blood may appear in the stools and urticarial and œdematous rashes may be noted especially in the perianal region associated with intense pruritis due to local invasion by rhabditiform larvæ escaping in the fæces in sensitised individuals. Dermal sensitivity may be demonstrated by injecting saline extracts of strongyloid as described by Fülleborn.

Diagnosis. This is dependent on the demonstration of rhabditiform larvæ in the stools. They are easily found if the fæces be mixed with water and strained through muslin, and differ from hook-worm embryos in having a shorter pre-œsophageal buccal cavity. Where eggs occur in the stool they can be differentiated from hook-worm ova by the presence of larvæ.

Treatment. This consists in the administration of gentian violet as advocated by De Langen (**69**). The course consists of administering three keratin-coated pills containing 2½ grains of this drug thrice daily after meals for a period of ten days.

Filariasis. Several species of the family *Filariidæ* are known to infest man. These include *Filaria bancrofti* (*Wuchereria bancrofti*), *Filaria loa* (*Loa loa*), *Filaria perstans* (*Acanthocheilonema perstans*) and *Filaria ozzardi* (*Mansonella ozzardi*). In addition there are two larval *Filariidæ*, the adults of which have not been found—*Microfilaria streptocerca* described by Macfie and Corson (**70**) in 1922, which is commonly present in the skin of natives of the Gold Coast, and *Microfilaria malayi* recorded by Brug (**71**) in 1927, occurring in the peripheral blood in the Far East (see Fig. 104 and Table).

FILARIA BANCROFTI (*Plate 68, 12–15, p. 1066*)

Ætiology. *F. bancrofti* is found in most tropical and subtropical countries, being specially prevalent in the West Indies, Central and Southern America, India, Southern China, the Pacific Islands, the West Coast of Africa and Queensland. The adult worms inhabit the lymphatics and periglandular lymphatic spaces where they discharge their embryos into the lymph by which means they reach the blood stream. The embryos disappear from the peripheral blood during the daytime and reappear at night, definite nocturnal periodicity being the rule. According to Lane this phenomenon is due to daily cyclic parturition on the part of the female worms, whereas Manson's view of *Microfilaria* periodicity was based on the fact that during the daytime the embryos live in the lungs and thoracic vessels, only appearing in the peripheral blood at night. The embryos measure 230 to 320 microns long and are 7·5 to 10 microns broad and are enclosed in a loose sheath which is simply the egg membrane which has become stretched during development. In the case of filariasis in the Pacific Islands no periodicity exists, and though this parasite is generally regarded as being identical with *F. bancrofti* on morphological grounds, this appears doubtful. The mosquito transmitter there is *Aëdes variegatus* which bites in the daytime. The usual intermediary host for *F. bancrofti* is the *Culex fatigans* mosquito, as originally shown by Manson. The embryos are sucked up in the blood at night and undergo a series of metamorphoses in the thoracic muscles of the mosquito,

from which they finally migrate into the proboscis and are reinoculated into man during biting. After penetrating the peripheral blood-vessels they ultimately reach the lymphatics, attain sexual maturity, mate and subsequently produce *Microfilariæ*. The time taken for this development within the insect vector varies from ten to forty days. Man is the only known definitive host.

Pathology. Generally filarial worms produce an eosiniphilia, but little or no damage to the tissues. The embryos themselves appear to produce no pathogenic effects when circulating in the blood stream. In some patients, however, definite injury to the lymphatic system and lymphatic glands ensues which may result in filarial lymphangitis, filarial abscess, varicose groin glands, chyluria, chylocele, cystitis, lymph scrotum, chylous ascites and elephantiasis. Elephantiasis mainly affects the lower extremities, the scrotum and the vulva, while the mammary glands are occasionally affected. These pathological changes are partially the result of mechanical obstruction and partially due to the verminous adenitis and lymphangitis set up by helminthic toxin resulting in fibrosis, obstruction and lymph stasis. The *rôle* of the streptococcus is debatable, but probably secondary streptococcal infection engrafted on lymph stasis is the basis of the acute lymphangitis with fever. Small nodules sometimes occur in the course of the lymphatics composed of inflammatory tissue surrounding dead worms.

Symptoms. The disease is sub-clinical in the majority of patients who act merely as carriers. If there is mechanical obstruction to the lymph flow, however, filarial lymphangitis is prone to occur. Known also as elephantoid fever, this condition starts suddenly with chilliness or actual rigor, followed by a high temperature, leucocytosis, tender enlargement of the lymph glands and lymphangitis, red streaks extending up from inflammatory foci in the affected parts. Palpable nodules may be found in the course of the inflamed lymphatics. When lymphuria and chyluria are present the patient passes milky urine often mixed with blood. Cystoscopy may reveal the dilated ruptured lymphatic varix discharging milky fluid into the bladder.

Diagnosis. In sub-clinical cases the infection may be recognised by finding embryos in blood collected from 10 p.m. to 2 a.m., or eosinophilia may suggest the necessity for this examination, but once elephantiasis has developed microfilariæ are rarely demonstrable. The new intradermal test, using *Dirofilaria immitis* extract as antigen, is of value in distinguishing filarial types of elephantiasis from elephantiasis nostras. Excision of nodules in the course of the subcutaneous lymphatics and subsequent section will reveal adult worms, while X-ray examination may indicate their presence provided they have calcified.

Prevention. Prevention depends on protection from mosquito bites and the extermination of the intermediary vector.

Treatment. No specific drug treatment is known. During an attack of lymphangitis the patient must be put to bed and treated along general lines. O'Connor states that spraying filarial nodules with ethyl chloride may abort the fever if applied early in the attack. Elephantiasis is treated by the application of pressure in the form of elastic stockings or bandages, and by resting the limb in the elevated position so as to decrease lymph stasis. Surgical intervention may be necessary for certain of these elephantoid conditions and special plastic operations have recently been devised with the object of restoring the lymph flow through pedicle grafts of healthy tissue and so relieving lymphœdema (McIndoe and Gillies) (72).

Filaria perstans (*Acanthocheilonema perstans*) was first discovered by Daniels in British Guiana, while Manson identified the microfilaria in the peripheral blood of negroes from the Congo. The disease exists in a considerable part of tropical Africa, including the West Coast as well as in Venezuela, Trinidad, parts of the Amazon Valley and elsewhere.

Ætiology. The adult worms are elongated, filiform nematodes, the male

measuring 45 mm. and the female 70 to 80 mm. The microfilariæ vary in number in the peripheral blood, being present both day and night, and tend to concentrate in the cavities of the heart, the great arteries and the pulmonary vessels. They are smaller than *F. bancrofti* and *L. loa* embryos and measure 200 × 4·5 microns ; they are sheathless and may be observed to undergo remarkable contractile movements during microscopic examination of the blood. The disease is transmitted by a midge, *Culicoides austeni*, and Sharp has shown its complete metamorphosis and the presence of pure larvæ in the proboscis some seven to ten days after experimental infection. *Culicoides grahami* is also probably a vector.

Symptoms. Europeans are not commonly infected, but in Uganda and the Cameroons 90 per cent. of natives may be carriers. Pathological lesions and symptoms have not been determined with certainty, but some authorities believe lymph varix may result.

Diagnosis. This depends on demonstrating the microfilariæ in the peripheral blood.

Treatment. Extermination of the intermediary host which breeds in forests, jungles and swamps would diminish the incidence of the disease. No specific treatment is known.

Filaria ozzardi (*Mansonella ozzardi*) is found in the West Indies and adjacent parts of South America. The microfilariæ, which move actively in blood films, are sheathless and non-periodic. Only the female worm is known with certainty and measures 65 to 81 mm. in length. The insect vector has been shown by Buckley to be *Culicoides furens*, though Fulleborn obtained partial development in *Anopheles maculi-pennis*. Adult worms have been recovered from the mesentery and sub-peritoneal tissue, but there is no evidence that they are pathogenic or produce clinical symptoms. **Diagnosis.** This is made by discovering the microfilariæ in blood films. No pathological reactions have yet been associated with this parasite.

LOA LOA

(*Calabar Swelling*).

The disease, characterised by the appearance of worms, *Loa loa*, beneath the skin and conjunctiva and the presence of fugitive swellings, is widely distributed in West Africa and is specially prevalent in the Cameroons. It is transmitted by certain species of mangrove flies, *Chrysops dimidiata* and *C. silacea*, which feed during the daytime. The microfilariæ have a diurnal periodicity and are taken up into the stomach of the *Chrysops* when the fly sucks up blood from an infected patient ; after breaking out of their sheaths, the microfilariæ enter the muscular and connective tissues of the abdomen, undergo a series of transformations, migrate to the head and make their way through the labium during feeding about the tenth day. The fly remains infective for a period of four to five days.

Pathology. The adult worms inhabit the subcutaneous and retro-peritoneal tissues, being found under the peritoneum, pleura and pericardium as well as in the voluntary muscles and the myocardium. Klotz has described nodular fibrosis of the spleen associated with the presence of microfilariæ (*Loa loa*). The calabar swellings themselves never suppurate, and result from local anaphylactoid reaction with exudation of serum and eosinophile infiltration induced by the discharge of helminthic protein into the tissues by adult worms. The swellings are unrelated either to the death of the parent worm or to the discharge of embryos into the tissues as was previously suggested.

Symptoms. The worms may be found beneath the skin in a variety of situations including the extremities, face, back, chest, breasts, penis, tongue, eyelids, conjunctivæ and the anterior chamber of the eye. There is a definite predilection for the tissues around the eye. When crossing the conjunctiva

considerable irritation and congestion may be produced accompanied by pain, swelling and dimness of vision. Considerable pain may also follow the migrations of the worms in the region of the neck of the bladder. Clinically, the worms give rise to puffy, white swellings (calabar swellings) which are generally painless and involve the subcutaneous tissue of the skin ; they attain the size of a hen's egg or larger and last two or three days. The swellings may be single or multiple and recur in different parts of the body for months or even years. When occurring in the hand or fore-arm they may be associated with a sense of weakness, and where the skin is tightly bound down, as in the scalp, may cause acute discomfort or actual pain. Urticarial rashes or even asthma occasionally develop. Calabar-like swellings may be reproduced experimentally by the subcutaneous injection of filarial protein solution, and even urticaria and asthma may follow in a sensitised subject. The disease has been known to last as long as fifteen years.

Diagnosis. A history of residence in an endemic area associated with transient swellings or the appearance of worms in the vicinity of the eye is highly suggestive of this infection. Almost invariably there is a marked increase in total leucocytes and a high eosinophilia of from 10 to 60 per cent. Embryos may be demonstrable in blood collected from 10 a.m. to 2 p.m. ; not infrequently, however, they are absent, especially in the early cases, and under these circumstances the complement fixation reaction, using *Dirofilaria immitis* as antigen, is invaluable as it is almost invariably positive. Intradermal sensitiveness to filarial protein is also found in the vast majority of patients harbouring *Loa loa* (**73**).

Prognosis. The prognosis is good, but the worms may prove troublesome for many years and swellings occur intermittently leading to temporary disability.

Treatment. No known specific treatment is available, but where it is feasible superficial worms should be extracted under local anæsthesia. In cases with urticarial and asthmatic syndrome desensitisation by injection of progressively increasing doses of a sterile saline extract of filarial protein may prove successful. Care must be taken, however, to avoid anaphylaxis, and the initial injection can with benefit be combined with adrenalin given subcutaneously.

ONCHOCERCIASIS

(1) *Onchocerca volvulus.* Infections with *Onchocerca volvulus* occur in West Africa and throughout the Congo basin, and have been recorded from Liberia, Uganda, Nigeria, the Cameroons, Senegal and French Guiana. Adults are much more commonly affected than children ; it is very rare in Europeans. In 10 per cent. of cases the unsheathed embryos are demonstrable in the blood and after ingestion by the black fly, *Simulium damnosum*, undergo development in the thoracic muscles ; from here they migrate to the head and on being reinoculated into the tissues of man gain access to the peripheral subcutaneous lymphatics.

Pathology. As a result of the inflammation set up by adult onchocerca worms in the subcutaneous lymphatics, cellular reaction followed by fibrosis ensues and hard, cystic tumours form, in the interstices of which male worms and embryos are found embedded in viscous material ; the female worms embed themselves in tunnels in the stroma so that their removal is impossible.

Symptoms. The subcutaneous cystic nodules, over which the skin is freely movable, vary from 1 to 10 c.m. in diameter and are particularly frequent in the vicinity of the elbows, knees, ribs, iliac crest and great trochanter. Dermal lesions characterised by achromia, xeroderma and pseudo-ichthyosis may be caused by the irritation set up by embryos in the skin (Laigret) (**74**), and eye lesions have also recently been recorded. Some authorities have also described enlargement of the testicles, elephantiasis of the scrotum and hydrocele in

onchocerca infestation, embryos being demonstrable in the hydrocele fluid and œdematous, lymphatic tissue.

Diagnosis. The condition may need to be differentiated from dermoid cysts, fibromata, molluscum fibrosum, and juxta-articular nodes associated with syphilis and yaws. Biopsy and subsequent section of the nodule may be necessary to establish a diagnosis or embryos may be demonstrated in the aspirated fluid or in the adjacent skin.

Treatment. Excision of the nodules under novocaine anæsthesia can be carried out, especially in the vicinity of joints where they may give rise to considerable pains and discomfort.

(2) *Onchocerca cæcutiens*, which is considered by some to be the same as *O. volvulus*. In Guatemala infection with *Onchocerca cæcutiens* occurs in coffee-producing areas at a height of from 2,500 to 5,000 feet, where coffee flies abound. Three species of Simuliidæ transmit the disease—*S. metallicum*, *S. mooseri* and *S. ochraceum*. These flies bite out of doors between the hours of 8 a.m. and 6 p.m. and as many as 58·6 per cent. of the inhabitants of some districts have been found infected in Guatemala, and as many as 90 per cent. in Mexico. Children as well as adults are commonly affected. The adult worms are white opalescent nematodes, the female measuring 33·5 to 50 mm. in length and the shorter male 19 to 32 mm. The sheathless micro-filariæ are rarely if ever found in blood, and vary from 150 to 360 μ in length and 6 to 8 μ in breadth.

Pathology. Fibrous tissue nodules form as a result of irritation by the male and female onchocerca worms which become completely encapsulated in a fibrous tissue matrix ; the nodules are firm, greyish-white in colour with softened centres and contain milky, gummous material in which embryos can be readily demonstrated. The microfilariæ, according to Strong (75) move about freely in the nodules, penetrate the capsule and reach the corium; similarly they invade the tissues of the eye, especially the conjunctiva, iris and cornea. An eosinophile leucocytosis is the rule, 25 to 75 per cent. of cells in the differential count being eosinophiles.

Symptoms. The clinical manifestations of American onchocerciasis include nodules, skin lesions and ocular complications. (1) *Guatemala nodules :* these are firm nodules affecting the scalp and face, measuring as a rule from 0·5 to 2·0 cm., and occasionally attaining dimensions of 5·0 c.m. (2) *Cutaneous lesions :* in the majority of cases where embryos are found in the dermis no skin lesions are found, but occasionally pruriginous and xerodermatous conditions result from their irritation. A peculiar form of erysipelas confined to the head, neck and face, known as " erisipela de la costa," has been attributed to this cause, but Strong, who has recently investigated the question, suggests it is probably secondary to streptococcal infection of the skin from scratching in a case where the corium is heavily infected with microfilariæ. (3) *Ocular lesions :* these occur both in Guatemala and South-West Mexico in about 5 per cent. of cases and consist of conjunctivitis, punctate iritis, keratitis and choroiditis; microfilariæ have been found in sections of the pericorneal conjunctiva, cornea, iris and choroid. The onset is generally insidious ; conjunctival hyperæmia and small areas of opacity in the cornea may be present and photophobia complained of. Blindness commonly results.

Diagnosis. This is made by demonstrating the unsheathed microfilariæ in the milky fluid aspirated from the nodules, or in the adjacent skin, a thin piece being shaved off and teased up in saline for microscopical examination. An eosinophile leucocytosis is the rule. There is little danger to life.

Prevention. The eradication of black fly, the use of fish for the destruction of its larvæ and pupæ and of repellants are important, but specially so is the surgical removal of all nodules in the head, face and shoulder which constitute a focus for disseminating the disease.

Treatment. Removal of the nodule under novocaine anæsthesia should

be practised whenever possible. Plasmoquine, tartar emetic and fouadin are worthy of trial to remove filariæ from the skin.

DRACONTIASIS (*Plate 68, 16, p. 1066*)

(*Guinea-worm Disease*)

Guinea-worm disease is caused by *Dracunculus medinensis* (*Fuellebornius medinensis*) and is found in certain parts of Africa, India, Persia, Arabia, Turkestan and Brazil. It is specially common in countries like the Deccan in India, where step-wells are used as a source of water supply. The adult female is a thin, cord-like worm, with a rounded anterior end and recurved tail, measuring 40–80 cm. in length by 0·5–1·5 mm. in breadth. It inhabits the subcutaneous and interstitial tissues, especially of the lower limbs, and when ready to discharge its embryos secretes some toxic substance under the dermis, resulting in blister formation and ulceration. On contact with water or on cold applications to the limb, there is a reflex discharge of embryos from the prolapsed uterus which is constantly found perforating the ulcer base. After the embryos escape into water, they must be swallowed by a certain species of Cyclops which acts as the intermediary host. They burst through the stomach into the cœlom and undergo a series of developmental changes which take seven to nine days. Man becomes infected by drinking water containing infected cyclops; on reaching the human stomach these are killed by its acid secretion but the larvæ escape unharmed, invade the gut, and the gravid female appears in the subcutaneous tissues some ten to fourteen months later. The fate of the male worm is unknown.

Pathology. The blister itself is composed of (1) a layer of elevated dermis; (2) a layer of fibro-gelatinuous exudate containing entangled larvæ; and (3) a granulation tissue base with a central eschar through which the filmy uterus of the female worm protrudes; the worm lies in a tunnel in the subcutaneous tissue surrounded by a fibro-cellular layer. Three factors are responsible for the pathological lesions observed in man, namely, the female worm, the embryos, and bacteria. The toxic substances responsible for blister formation may, if absorbed, lead to anaphylactoid symptoms, while premature ejaculation of embryos into the deeper tissues may produce a sub-acute sterile abscess. Secondary bacterial invasion by such organisms as *Staphylococcus aureus*, streptococci and *Bacillus coli*, etc., cause acute abscesses, cellulitis, suppurative buboes, synovitis, arthritis, septicæmia and even death.

Symptoms. Anaphylactoid symptoms similar to those encountered in ruptured hydatid may occasionally be observed just prior to, or simultaneously with, the appearance of the vesicle; they consist of an itchy, urticarious eruption which is noted in 40 per cent. of cases, and which in certain instances may be associated with vasomotor collapse, tightness of the chest, asthmatic dyspnœa, vomiting, diarrhœa and a high eosinophilia (**76**). The lower extremities are involved in 86·5 per cent. of cases and less frequently the arms, trunk, buttocks and scrotum. The septic complications previously referred to may give rise to severe fever and permanent deformities due to the contracture of tendons, and fibrous ankylosis of joints may result. Rheumatic-like muscular pains and neuritis may be caused by the pressure and irritation set up by calcified worms, and cases presenting such symptoms coming from endemic areas should be X-rayed; their convoluted, moniliform shadow has been shown by Connor to be pathognomonic of guinea-worm disease. An eosinophilia accompanies dracontiasis, but on secondary bacterial infection neutrophile polymorphonuclears increase at the expense of the eosinophiles.

Diagnosis. Little difficulty is experienced in diagnosis once the worm appears at the surface of the body, but previous to that, eosinophilia and a history of residence in an endemic centre may be the only features suggestive of infection.

In doubtful cases the application of cold water or spraying the affected part with ethyl chloride will be followed by a discharge of larvæ.

Prevention. Water in step-wells and ponds becomes infected through contact with the limbs of guinea-worm cases, and measures such as the covering of wells or building cemented kerbs round ponds should be taken to prevent this. Filtering water through muslin is an effective procedure as this keeps back the cyclops.

Treatment. Urticaria and other anaphylactoid symptoms are best treated by injections of adrenalin (♏ x of a 1 in 1,000 solution), and if the case is seen before the blister has ruptured it should be painted with iodine and aspirated. Secondary bacterial infection almost invariably results if the worm be broken during efforts to extract it. Being elastic it retracts into the subcutaneous tissues, carrying with it the bacterial flora of the sinus and ulcer. For this reason every effort should be made to sterilise the ulcer base and sinus through which the worm protrudes before extraction is attempted. The worm may be extracted either by intermittent traction and massage, as is the custom amongst Vaidya in India, or by outlining the worm with a flesh pencil and making multiple incisions under novocaine anæsthesia. Sometimes the worm is closely convoluted on itself, and under these circumstances the whole area may be excised. A localised abscess must be treated surgically by inserting a probe through the sinus and slitting up the fibro-cellular tunnel in which the worm lies. Other septic complications require treatment as they arise. The old method of gradually extracting the worm by daily douching and winding it around a stick or match is still practised in the Orient.

TRICHINIASIS

(*Trichinosis, Trichinelliasis*)

Trichiniasis is a disease produced by the embryos of *Trichinella spiralis* (*Trichina spiralis*) during their migrations from the human intestine to the voluntary muscles. The disease, though rare in England, is not uncommon in America and Germany. The host reservoirs are the black and brown rat, and pigs, dogs, cats and other animals which feed on them contract the disease in this fashion. Man becomes infected by eating raw or underdone pork in which the larvæ have encysted. The cyst walls are digested by the gastric juice and the embryos are liberated, attain maturity, attach themselves to the intestinal mucosa and breed in the small intestine. The males soon die, but the impregnated females bore deeply into the villi and deposit the viviparous young in the lymphatics and possibly in the mesenteric veins. Liscard estimated that 1,500 larvæ were deposited by each female. The viviparous larvæ, which measure 100 $\mu \times 6\ \mu$, are capable of passing through the capillary bed of both the liver and lungs in their migrations, and appear in the arterial circulation from the seventh to the twenty-third day. They are deposited in muscle from the ninth day onward, and continue invading the blood stream for a period of five or six weeks, *i.e.*, as long as the female worms survive in the gut. Throughout this period they may be demonstrated in the blood.

Pathology. During the invasive stage there may be a catarrhal or hæmorrhagic inflammation of the small intestine. Once the larvæ become deposited in the muscles, they cause local inflammatory reaction leading to the formation of a fibrous tissue capsule which is oval in shape with blunt ends; in the centre the tightly coiled larva is located. These capsules always lie with their long axis parallel to the muscle fibres. Microscopic examination shows degeneration in surrounding muscle fibre, loss of transverse striæ and an increase in the number of the nuclei. Calcification, beginning at the poles, may occur within six to nine months, and later the worms themselves sometimes become impregnated with lime salts. Encysted larvæ, however, have been known to survive thirty-one years (**77**). The diaphragm, intercostal and abdominal muscles and those of the tongue and larynx are particularly affected.

Symptoms. Three stages may be recognised: (1) invasive stage by the female worms; (2) the period of larval migration; (3) the period of larval encystment in muscle. In the first week during the *invasive stage* gastro-intestinal symptoms develop with nausea, vomiting, diarrhœa, perhaps associated with blood and mucus in the stools, and colicky abdominal pain; lassitude, sleeplessness and depression may be present. The tongue is red and slightly furred, and later becomes dry. In the *second stage* myositis of the tongue, laryngeal and intercostal muscles and diaphragm result, and swallowing, speech and breathing become difficult. Where the muscles of the arms, legs, abdomen and jaws are involved local stiffness and pain ensue and the affected muscles become extremely painful, tender and hard to the touch. Urticaria, œdema of the face, eosinophile leucocytosis and prolonged remittent fever associated with sweating are characteristic. The electrical reactions of nerve and muscle are diminished. Trismus may occur. The implication of respiratory muscles causes shallow and interrupted breathing, making coughing, sneezing and yawning difficult, if not impossible; this inability to cough up pulmonary secretions may lead to lung complication. Movement of the eyelids becomes painful and the power of accommodation is also temporarily lost. During the *third week* cachexia and subcutaneous œdema may develop, and in hyper-infections headache, stupor, delirium and coma supervene. Death may take place in the fourth week or earlier through toxæmia, pneumonia or bronchitis, and if the patient recovers convalescence is slow and hindered by muscular pains, muscular atrophy and persistent œdema.

Diagnosis. During the first week trichiniasis may be confused with ptomaine poisoning, enteritis or dysentery, and subsequently with rheumatic fever, typhoid or nephritis. The liability of trichiniasis to occur in groups or in several members of one family and the high eosinophilia may suggest the diagnosis; during this stage the embryos may be demonstrated in the blood stream by the method introduced by Stäubli of mixing the blood with 10 parts of 3 per cent. acetic acid and subsequently examining the centrifuged deposit. Not infrequently this method gives positive results from the twelfth to the twentieth day. Later, biopsy on an affected muscle such as the deltoid at its insertion, the masseters, triceps and gastrocnemii, may reveal precystic or encysted larvæ; specimens of muscle may be rapidly excised under novocaine anæsthesia. If calcified the elliptical cysts may be visible with the X-rays.

Prognosis. The mortality rate varies in different outbreaks from 1 to 30 per cent., and depends largely on the intensity of the infection. Hyper-infected patients frequently die from toxæmia or pulmonary complications, but after five weeks there is a reasonable chance of recovery.

Prevention. This depends on inspection of meat at *abattoirs* and the adequate cooking of pork. Such methods of curing pork as smoking and salting are ineffectual, but refrigeration at 5° F. for twenty days or longer is effective. Pathologists may acquire the disease during autopsy.

Treatment. No specific drugs are known, and treatment must proceed along palliative lines. Muscular pains may be treated with narcotics, aspirin, phenacetin and caffein citrate internally and belladonna applications externally.

Œsophagostomiasis. *Œsophagostomum apiostomum* is a nematode found in anthropoid apes in West Africa and monkeys in the Philippines and China. Some 4 per cent. of prisoners in gaols in Northern Nigeria are said to harbour the parasites. The larvæ undergo development in the wall of the intestine enclosed in fibrous nodules. As they approach maturity they erupt into the lumen, often leaving an ulcerated area, attach themselves to the mucosa and attain maturity. Here they have been occasionally mistaken for hook-worms. Clinically, colonic diarrhœa with the passage of blood and mucus may result, and occasionally peritonitis or even septicæmia ensue. Microscopic examination of the stools reveals ova resembling ankylostome eggs, and only an examination of the adult worms enables the species of helminth to be recognised. Various anthelminthics

effective for ancylostomiasis like thymol, oil of chenopodium and carbon tetrachloride cure the disease.

There is another closely related species known as *Œsphagostomum stephanostomum*, from South America; only one case has been recorded. Here nodules occurred in both the small intestine and large bowel.

ANCYLOSTOMIASIS (*Plate 68, 6-11, p. 1066*)

(*Hook-Worm Disease. Uncinariasis*)

Ancylostomiasis is caused by infection of the duodenum and jejenum with two small nematode worms, *Ancylostoma duodenale* and *Necator americanus*, which may give rise to severe microcytic, hypochromic anæmia. From an economic viewpoint ancylostomiasis is, next to malaria, the most important disease in the tropics. It has been estimated that 45 million wage earners in India alone are subject to this infection, while employers of labour in tea plantations have stated that when freed from the parasite the labourer is worth 25 to 50 per cent. more as a wage earner. *Ancylostoma brasiliense* of cats and dogs on rare occasions infects man, while that of larvæ of *Ancylostoma caninum* may cause creeping eruption.

Ætiology. *A. duodenale*, known as the "Old World hook-worm," is, according to Faust (**78**), the common human ancylostome of the north temperate zone of the Eastern Hemisphere; the adult males measure 8–10 mm. × 0·4–0·5 mm. and the females 12–18 mm. × 1 mm. The ova found in the fæces are elliptical, thin-shelled and transparent, containing two to eight segmented sphericles and measuring 55–65 μ × 32–45 μ. *N. americanus*, on the other hand, is the common species in the Eastern Hemisphere south of 20 degrees north latitude, as well as the prevalent form in the Southern United States, Central and South America. It is the smaller parasite, the males measuring 7–9 mm. × 0·3 mm. and the females 9–12 mm. × 0·4 mm. The eggs resemble those of *A. duodenale*, measuring 64–75 μ × 36–40 μ. The adult worms of the two species differ in their buccal armature: the capsule is smaller in *N. americanus* and has an irregular border instead of the four ventral hook-like teeth characteristic of *A. duodenale*.

Life Cycle. One to two days after fæces containing ova are deposited on moist ground the rhabditiform larvæ hatch out; rarely, where patients were very constipated, they have been passed in the fæces. After moulting twice filariform larvæ emerge which may remain viable for three or even four months. When they come in contact with the human skin they bore through the tissues into the vessels and pass to the right side of the heart and lungs, subsequently travelling *viâ* the trachea, rima glottidis, œsophagus and stomach to the duodenum and jejenum—their natural habitat. Subsequently mature male and female worms develop, eggs appearing in the excreta in about five weeks. In Europe ancylostomiasis has occurred amongst miners; the heat and moisture of the mines, combined with defective sanitation, lead to infection through the naked bodies of the workers.

Pathology. The ancylostomes, which engulf the mucosa in their buccal cavity, are true blood suckers, causing local bleeding and blood loss, and at autopsy the small intestine may show petechial hæmorrhages at their points of attachment. In fatal cases the heart is dilated and its muscle shows fatty degeneration which also involves the liver and kidneys.

Symptoms. Following invasion of the skin the larvæ may produce ancylostome dermatitis, also known as "ground itch" or "cooley itch." It commences with itching following by œdema, erythema, a papular eruption and vesicle formation. The condition clears up within a fortnight unless secondary bacterial infection occurs, when pustules and furuncles result. In coolies the feet and legs are commonly affected. In Cornish miners, who call the eruption "bunches," the

hands and forearms were mainly involved. Similar eruptions may be caused by larval hook-worms of the dog and cat, which fail in man to become adult.

Symptoms may come on in six to eight weeks in severe infections; they are dependent on gastro-intestinal dysfunction and anæmia which is chlorotic in type. The Price-Jones curves show microcytosis, a decrease in the average diameter of the corpuscle and displacement to the left. The colour index is low (0·5 to 0·8) and hypochromia marked. Hypochlorhydria or achlorhydria is often present.

Whether the infection remains subclinical depends not only on the intensity of infection, but also on the response of the red marrow which undergoes compensatory erythroblastic hypertrophy. Many factors may affect this response adversely such as faulty nutrition, vitamin-deficient diets and intercurrent disease. Children fail to respond more readily than adults and women than men, and in consequence are more prone to anæmia. Those with compensated blood loss show no symptoms or anæmia; often their infection is a mild one. Partially compensated cases tire readily, develop mental lethargy, epigastric pain, discomfort, fullness of the abdomen, and flatulence. Palpitation and shortness of breath also begin to appear and "pot belly" is a common sign in children. Where the hæmopoietic response definitely fails mental and physical inertia increase; the severe case now shows a very earthy skin, a yellow discoloration of the alæ nasi and forehead, pallor of the mucous membranes and gastro-intestinal features associated with constipation or diarrhœa. Geophagia or earth-eating is not uncommon. Dyspnœa, palpitation, pulsating cervical veins, hæmic murmurs, retinal hæmorrhages, œdema of the feet and serous effusions develop; the anæmia is really severe, the red cell count varying from 700,000 to 2,000,000 cells per c.mm., the hæmoglobin from 10 to 25 per cent. and the colour index from 0·5 to 0·7. The leucocytes are normal or slightly increased in number and eosinophilia is frequent. Untreated patients may die from anæmia, cardiac failure or intercurrent disease such as pneumonia and dysentery, while in survivors detrimental defects are widespread. Mental and physical development is impeded in children and puberty delayed, while in adults the economic loss to the community cannot be computed. Mental sluggishness amongst the backward whites in the tropics and subtropics is often traceable to this cause (**79**).

Diagnosis. Dyspeptic disturbances, physical and mental inertia and a microcytic, hypochromic anæmia should arouse suspicion of ancylostomiasis, especially if there be an associated eosinophilia. In all cases coming from endemic areas the stools should be examined microscopically for ova—preferably by the Clayton Lane flotation method.

Prognosis. Hook-worm disease is specially serious in children, in time of famine and in those suffering from intercurrent infection like malaria, dysentery and pneumonia to which it predisposes. Appropriate treatment is almost invariably successful if not too long delayed.

Prevention. This consists in wearing good shoes and boots, in the appropriate care of fouled ground and the proper disposal of night-soil. Carriers should be treated and latrine accommodation substituted for promiscuous defæcation so common in the East. Proper sanitation should be instituted in mines.

Treatment. Several drugs with a special lethal action on ancylostomes are available. Preliminary treatment consists of a light diet, combined with saline purgatives and the administration of 30 grains of well triturated thymol in cachets, or 0·5 c.c. of oil of chenopodium at 6, 8 and 10 p.m., followed by magnesium sulphate (ounce i) at mid-day. Oil of chenopodium is of special value if there be an associated ascariasis, and some advocate its administration as a routine one week after a course of thymol. Solvents of thymol like alcohol, butter, milk, castor oil, ether, glycerine and chloroform must be avoided as they lead to excessive absorption with dizziness, headache, muscular inco-ordination,

vomiting and burning in the epigastrium resulting. The drug is contraindicated should there be fever, hepatic disease, nephritis, pulmonary or cardiac disease. Carbon-tetrachloride is given in doses of 3 c.c. in liquid form or in gelatine capsules ; preliminary starvation is not advisable. An effective procedure is to combine carbon tetrachloride (3 c.c.) with oil of chenopodium (1 c.c.); a light supper but no breakfast is allowed and the combined drugs are administered at 7 a.m. followed by a saline purge at 9 a.m. At noon a light meal is permitted. During and after treatment the stools are collected and examined for ova and parasites and re-examined in a week's time. Should ova reappear, a second course of treatment with a different drug is indicated.

The anæmia is important and, in addition to eradicating infection, the patient should be given iron in large doses, *i.e.*, as ferri et ammon. cit., grains xxx., t.d.s., or four Blaud's pills thrice daily after meals. In addition, where there is defective acid secretion, acid hydrochlor. dil. (B.P.) should be administered in doses of 1 drachm in diluted orange juice after meals. The diet should be nourishing, well balanced and rich in vitamins.

ASCARIASIS (*Plate 68, 17–19, p. 1066*)

(*Round Worm*)

Ætiology. In shape the adult *Ascaris lumbricoides* resembles the ordinary garden worm, the male measuring 17–25 cm. × 3 mm. and the female 20–40 cm. × 5 mm. ; it tapers anteriorly and has a blunt conical end. The eggs are yellow and oval, possess a thick transparent shell and sometimes a mammillated covering. They measure 45–75 μ × 35–50 μ. The unfertilised eggs are more elliptical and may be passed when only female worms are present.

Life Cycle. Ova passed in human fæces mature in the night-soil and are influenced by temperature, moisture and oxygen supply. The rhabditiform larva develops within nine to thirteen days and ova in contaminated soil may remain viable for many months or years. Upon being swallowed, the fully developed ova pass through the stomach and the rhabditiform larvæ hatch out in the intestinal juices, penetrate the intestinal wall, worm their way into the lymphatics or venules and proceed *viâ* the heart or the thoracic duct to the lungs ; here they are filtered out in the capillary bed and bore their way into the alveoli. Subsequently they migrate to their normal habitat, the small intestine, *viâ* the trachea, œsophagus and stomach. The worms attain maturity some two to two and a half months after human infection, and the females begin to lay their eggs about this time.

Pathology. During migration the larvæ may produce inflammation associated with small hæmorrhages and œdema. There is pathological exudate in the respiratory passages and local eosinophilia. In hyper-infections patches of consolidation may result in the production of " ascaris pneumonia."

Symptoms. Symptoms of pulmonary involvement begin from two to five days after swallowing ascaris ova. There is fever, cough, dyspnœa and signs of consolidation resembling lobar pneumonia. Generally the temperature subsides in four or five days, but in hyper-infected patients ascaris pneumonia may prove fatal. Occasionally during migration the larvæ get into abnormal situations such as the liver, heart, muscles, kidneys and central nervous system ; acute nephritis has been described associated with larvæ in the urine. Urticarial manifestations, œdema of the subcutaneous tissues and intense eosinophilia are characteristic of this stage of the disease. The adult worms may produce symptoms by toxic, reflex and mechanical means ; patients sensitised to ascaris protein may develop itchy, urticarial rashes and œdema of the subcutaneous tissues, especially of the face, while in children nervousness, enuresis and even convulsions occur. Dyspepsia, flatulence, abdominal discomfort, pain and diarrhœa with or without blood, may supervene, the latter condition being known as " ascaris dysentery."

In hyper-infected cases complications are not uncommon; they include (1) intestinal obstruction which is found in the vicinity of the ileocecal valve and caused by "balling" of ascaris worms; (2) perforation of the intestine with peritonitis or localised abscess, with possibly sinus formation and discharge of worms through the abdominal wall; (3) appendicitis; (4) obstruction of the pancreatic and bile ducts leading to jaundice, cholangitis, cholecystitis or even liver abscess; (5) œdema of the glottis due to vomited worms lodging in the trachea; if impacted in this situation they may cause suffocation; (6) involvement of the accessory sinuses, such as the antrum, through entry of worms during vomiting.

Diagnosis. The diagnosis of ascaris pneumonia is difficult, though it may be suspected from the associated eosinophilia and confirmed by the appearance of ova in the excreta subsequently. Intestinal ascariasis is diagnosed by the demonstration of fertilised or unfertilised eggs in the stool or the passage of adult parasites.

Prognosis. Prognosis is good except in hyper-infections where ascaris pneumonia or mechanical complications of different types may ensue.

Prevention. Undoubtedly human ascariasis is acquired from uncooked food or by contamination of the hands with infested soil. Contaminated night soil should not be used on vegetable gardens as in China, since there is no satisfactory method of sterilising it.

Treatment. Santonin, 3 to 5 grains, on consecutive or alternate days on three occasions generally proves effective. A period of preliminary starvation should precede treatment and castor oil be given as a purge. In children the dosage is proportionately less. Oil of chenopodium (1 c.c.) and carbon tetrachloride (3 c.c.) are also effective remedies; they may be administered in combination as in ancylostomiasis. Certain complications referred to above may call for immediate surgical intervention.

Trichuriasis. This is an infection of the large bowel by the whip-worm *Trichuris trichiura* or *Trichocephalus dispar*. The adults measure 4–4·5 cm. × 0.5 cm. The anterior two-thirds is extremely fine like a hair, but the posterior third is thicker. The eggs are brown in colour and barrel-shaped with terminal knobs, measuring 50 μ × 23 μ. Infection is conveyed to man through swallowing fertilised eggs in food or water contaminated with infected fæces. On reaching the cæcum the larvæ escape and attach themselves to the mucosa; occasionally the appendix, ileum and colon are implicated (Plate 68, 4, 5, p. 1066).

Pathology. Occasionally a worm perforates the submucosa or even the peritoneal cavity. Occlusion of the lumen of the appendix may lead to appendicitis.

Symptoms. In the Orient infections are common, at least 25 per cent. of the population being infected. The condition is generally subclinical, but reflex disturbances, anæmia, urticaria and eosinophilia may occur in children.

Diagnosis depends on demonstrating the characteristic eggs in the fæces.

Prevention. Care should be taken to cleanse the hands before eating where there is a possibility of coming in contact with infected soil, while raw fruit and vegetables should be covered with boiling water for a few seconds before consumption.

Treatment. No absolutely specific treatment is available, but hexylresorcinol in a dosage of 0·6 to 1 gram in tablet form may be given on an empty stomach (Lamson) (**80**) with beneficial results. Oil of chenopodium is at times successful in man, and Hall found mercurochrome given by the mouth in capsules dislodged 88 per cent. of whip-worms in the dog.

Oxyuriasis. This is caused by infection with the thread- or pin-worm known as *Oxyuris vermicularis* or *Enterobius vermicularis*. These worms are more commonly encountered in women than in man, and in children than in adults. Multiple infections in members of the one family are frequent and auto-infection is common. The adults, which live in the cæcum, appendix and adjacent parts

of the large and small bowel, attach themselves to the mucosa. The male measures 3 to 5 mm. and the female 10 mm. The ova, which measure 50 $\mu \times 20\,\mu$, are thin-shelled, colourless, plano-convex in shape and contain coiled embryos; they are rarely found in the fæces. The gravid females produce intense itching in the vicinity of the anus where they often dry and burst liberating ova; on scratching the patient's finger-nails become contaminated and re-infection occurs from this source. If swallowed, the egg hatches out on reaching the duodenum and the rhabditiform larvæ are set free (Plate 68, 1–3).

Pathology. Inflammatory reactions may occur in the mucosa around the attachment of the worms, and when present in the appendix a verminous, catarrhal appendicitis may result. In the peri-anal region small hæmorrhages, subcutaneous tumours and erosions of the mucous membrane with the development of a cutaneous eczema may be produced.

Symptoms. Intestinal worms may lead to reflex symptoms, and at night after the patient has got in bed their migration out of the rectum may produce considerable discomfort and itching. Pruritus ani and eczema may develop, which may result in sleeplessness, sexual disorders and neurasthenia. Vesical irritability, frequency of micturition, mucoid secretion from the rectum and prolapsis ani may be induced, and vaginal discharges sometimes result in young girls. Occasionally the worms migrate into the stomach, œsophagus and other areas.

Diagnosis. In patients with a history of pruritus, microscopic examination of scrapings from the peri-anal region may reveal the eggs, and if the patient be examined shortly after going to bed the adult worms may be found. Not infrequently there is a mild eosinophilia.

Prognosis. The prognosis is good. Severe neuroses sometimes develop in patients with nervous instability, and systemic infection with bacteria may possibly result through the lesions induced by the worms.

Treatment. Children who are infected should sleep alone, have the nails cut short, and wear cotton gloves and sterilised pyjamas. The hands must be carefully washed after defæcation. The gravid females in the cæcum may be killed off by the administration of oil of chenopodium, santonin, thymol and filix-mas. The bowel may be washed out with a hyper-tonic saline solution (4 drachms to a pint) and followed by an enema composed of $\frac{1}{10}$ infusion of quassia, the foot of the bed being raised or, alternatively, a simple soap enema may be employed. Another effective measure consists of a preliminary bowel wash-out with bicarbonate of soda, followed by the administration of Yatren (8 ounces of 2·5 per cent. solution), which is retained up to eight hours. Unguent hydrarg. ammon. B.P. may with advantage be applied to the peri-anal region. Surgical intervention is necessary if symptoms of appendicitis exist.

Diseases due to Larvæ

MYIASIS

Myiasis results when larvæ of certain of the dipterous insects invade human tissues.

Ætiology. In the tropics, wounds and cavities discharging pus or fœtid material should always be protected as there are many flies which deposit their eggs or larvæ in such a medium. Such larvæ have been recorded in the ear, nasal cavities, skin, vagina, urethra or in the intestine itself, and the fly *Wohlfartia magnifica* sometimes deposits its eggs in the conjunctival sac with serious consequences. Dermal and intestinal myiasis constitute the two chief types.

(1) ***The Screw-Worm*** (*Chrysomyia macellaria*). This fly measures 9–10 mm. in length and is common in most parts of tropical and sub-tropical America, being distinguished from the ordinary blue-bottle by three black, linear, dorsal markings on its thorax. It deposits its eggs upon discharging foul wounds. The larvæ hatch out in a few hours and when mature measure 2–3 inches in length. In

appearance they resemble a screw—hence their name. They are formed of twelve segments, each armed with a series of spines, and they burrow into and eat the tissues, producing great destruction. Once the nose is implicated the larvæ gain access to the accessory sinuses, bore their way through adjacent bones and may even penetrate the base of the skull, fatal meningitis following. When the external auditory meatus is attacked the middle ear may be destroyed.

Prevention. This consists in covering wounds and discharging orifices and sleeping under a mosquito net.

Treatment. The larvæ can generally be removed from polluted wounds by the application of antiseptics, while injections of chloroform or diluted carbolic acid are useful in nasal involvement. Operation may be necessary where sinuses are implicated.

(2) ***The Mosquito-Worm*** (*Ver macaque*, beef-worm) (*Dermatobia hominis* vel *cyaniventris*). The mosquito-worm is common in Central and adjacent parts of South America. It possesses a yellow head with brown eyes, a grey-coloured thorax and dark, metallic-blue abdomen. It measures 14–16 mm. in length. The larvæ are conveyed to the human skin from eggs which have become glued to the ventral surface of certain species of mosquitoes, biting flies and ticks, and after undergoing development invade the tissues *viâ* the puncture wound. A sort of boil, known as a warble, results, which contains a central opening through which the maggot respires, eliminates its black excreta and later escapes. It then proceeds to develop into a chrysalis and finally a fly. Bruce described a remarkable and sometimes fatal anaphylactic reaction in oxen and sheep infected with warble larvæ (*Hypoderma bovis* and *Oestrus ovis*) following natural trauma of the cyst. The syndrome has not been described in man, but not unlikely it occurs.

Treatment. The opening of the warble should be enlarged with a bistoury, the maggot removed and the cavity treated antiseptically. Tobacco juice is used to kill the larvæ by natives.

(3) ***Ver du Cayor or Tumbu Disease.*** This disease, common in Central and West Africa, is due to the larvæ of the Tumbu fly (*Cordylobia anthropophaga*). It measures 8·5–11·5 mm. in length and is yellow in colour with black spots on the abdomen. The eggs are laid on clothing or on the ground and the emerging larvæ, which possess mouth hooks, bore their way into the tissues; a pricking sensation develops and subsequently a warble or boil. These warbles affect the scalp, thighs and buttocks of children and may become inflamed and sometimes suppurate; they mature in about a fortnight and escape through the central hole by means of which their fæces were previously excreted.

Treatment. The maggot is squeezed out of the aperture which should be enlarged if necessary; the cavity is subsequently treated antiseptically.

(4) ***The Congo Floor Maggot.*** The adult fly (*Auchmeromyia luteola*), which is found throughout tropical parts of Africa, deposits its eggs on the floors of huts and in outhouses, and, after hatching out, the larvæ suck the blood painlessly from the tissues of people sleeping on the ground. The larvæ are about 15 mm. in length, consist of eleven segments and show considerable motility, while the adult fly is yellow in colour with longitudinal stripes on the back of the thorax; its length varies from 10–12 mm. The disease can be prevented by sleeping on raised beds.

(5) ***Intestinal Myiasis.*** Fly larvæ are not uncommonly observed in human fæces. Generally they are deposited after defæcation, but sometimes where the eggs are swallowed in food, larvæ may develop in the intestinal canal of man. *Fannia canicularis* accounts for most cases in Europe, but several species of other genera such as *Sarcophaga*, *Apiochæta* and *Anthomyia* may be responsible. Malaise, vomiting, diarrhœa, colicky abdominal pains, fever, rigors, headaches, vertigo and convulsions may result. The bile ducts may sometimes be invaded, with serious consequences.

Treatment. Patients should be purged with castor-oil. Thymol, filix-mas, santonin and turpentine may prove useful.

TONGUE-WORMS (*Plate 71*)

The adult tongue-worms, which superficially resemble tape-worms, are really degenerated, segmented arachnids which live in the nostrils or lungs of certain carnivora or snakes and deposit their eggs on vegetation; when these eggs are eaten, the larvæ encyst in the viscera of the intermediary host. Two species have been reported in man, *Linguatula serrata*, the larvæ of which encyst in the human liver; cases have been reported from Brazil and parts of Europe; the second species, known as *Porocephalus armillatus*, encyst in the mesentery, liver, lungs and other organs, and cases are not uncommon in the negroes of the Belgian Congo. Inflammation of the lungs and peritoneum may result and pulmonary signs and symptoms may follow; at autopsy larval forms are found in the peritoneal cavity. The parasites move about in the abdominal cavity over the surface of different viscera and become encysted in the liver, lungs and small intestine. X-ray in a case recently described by Low and Cordiner (**81**) showed the presence of peculiar shadows in the liver and other parts of the abdomen, which from their shape and size could only be cysts of *P. armillatus*; many of these presented quite clearly the crescentic appearance taken up by the nymph-forms of the parasites within the cyst during life, and which through having undergone calcification were clearly visible in the X-ray picture.

Bites and Stings

Quite apart from the transmission of filterable viruses, rickettsia bodies, and various pathogenic bacteria, protozoa and helminths, man may suffer severely in consequence of bites and stings by certain arthropods. It is essentially with the latter that the present section deals.

Insect Bites. The insects which are particularly troublesome to man from this view-point are (1) the biting midges (*Chironomidæ*); (2) the buffalo gnats (*Simuliidæ*); (3) the sand-flies (*Psychodidæ*); (4) the mosquitoes (*Culicidæ*); (5) the biting flies (*Tabanidæ*); (6) the blood-sucking *Muscidæ* including the stable-fly (*Stemoxys calcitrans*) and the tsetse-flies (*Glossina palpalis* and *Glossina morsitans*); (7) the blood-sucking lice (*Pediculidæ*); (8) the blood-sucking bugs of the families *Cimicidæ* and *Reduviidæ;* (9) members of the *Hymenoptera* such as bees, ants and wasps.

Symptoms. Localised inflammation results from the irritant action of insect venoms which may occasionally exert both hæmolytic and neurotoxic effects. The clinical manifestations may be the outcome of allergic reaction in a sensitised person and under these circumstances the type of local reaction appears to depend on the site of the inoculation. If the irritant is injected into the dermis, a large urticarial wheal rapidly forms, as Boycott (**82**) found in the case of people sensitised to midge bites, and on reaching the deeper tissues, as in the case of the stable-fly (*Stemoxys calcitrans*), a delayed reaction associated with œdema of the subcutaneous tissues ensues. The bitten part becomes puffy and swollen, the surrounding skin is stretched over it, giving a sensation of tightness, and it may be either pallid or scarlet-red according to the reaction of the more superficial vessels. Apart from a sense of heaviness and itchiness the condition is not actually painful and swelling generally subsides in from thirty-six to seventy-two hours. In severe cases, intense itching is common and superficial vesiculation may occur. Another serious result of bites with such insects as mosquitoes and stable-flies, etc., consists of the inoculation of virulent bacteria such as streptococci into the tissues, or the introduction of specific organisms like anthrax, tetanus and gas gangrene.

With the blood-sucking Muscids, such as the stable-fly and tsetse-fly, imme-

diate pain results from the bite. Sand-flies bite exposed parts such as the hands, wrists, ankles and neck, particularly from sunset onwards, and give rise to almost intolerable itchiness which may recur for several days. Only the female mosquito sucks blood, some species biting painlessly, others causing much discomfort. The intensity of local reaction varies in different individuals; in susceptible people much swelling, erythema and even vesiculation may result. Blood-sucking lice commonly affect man; *Phthirus pubis*, the crab-louse, is found on the pubic hair and is often acquired during coitus; its bite may result in a considerable degree of irritation, fever and a bluish discoloration of the skin. Body lice produce erythema and itchy rose papules; vesicles may form and sometimes a bronzing of the skin, known as vagabond's disease, results; secondary sepsis may follow scratching, while head lice produce eczema of the scalp, adenitis and insomnia in children. Urticaria and itching wheals follow the bite of the ordinary bed bug, *Cimex lectularius* of temperate climates, and *C. hemiptera* of tropical climates; the latter has been found in the cork lining of sun-helmets in the tropics. The stings of bees and wasps (*Hymenoptera*) are always painful, and the intensity of local and general reaction following them is dependent on sensitisation resulting from a previous bite. Where people are bitten in the mouth, respiratory obstruction may result if the tongue and fauces be involved, while œdema of the glottis has occasionally led to death by asphyxia. In a sensitised individual profound vasomotor collapse, syncope, coma and occasionally death may follow the sting with great rapidity, while in more moderate cases one observes the development of a rapidly spreading wheal with surrounding erythema and generalised urticaria within twenty minutes. Conjunctival injection, lachrymation and chemosis follow, accompanied by headache, faintness, nausea, vomiting, vasomotor collapse with hypotension and dyspnœa of asthmatic type. Gradually the condition passes off, but next day where the bite is on a limb there may appear a large, puffy swelling in subcutaneous tissues while the surrounding skin is scarlet-red, often intensely itchy and perhaps associated with vesiculation. In extreme cases the whole limb may be greatly swollen.

Prevention. Every effort should be made to destroy insect pests, including their breeding places, while the screening of bungalows and use of mosquito nets at night are very helpful. The application of such essential oils as citronella and eucalyptus are also useful and may be applied either to the clothing or directly to the skin as ointment.

Treatment. Iodine should be applied at once in the case of bites by stable-flies and other insects likely to convey bacteria, and subsequent itching is best relieved by the application of an aqueous solution of carbolic acid (1 in 20) or an alcoholic solution of menthol (1 per cent.), or lotio calaminæ to which has been added liquor carbonis detergens and liquor plumbi subacetatis fort.

In stings by bees and wasps, pressure must not be applied to the part as otherwise the contents of the poison sac are squeezed into the tissues. The sting should be gently removed or scraped out. Subsequently, diluted liquid ammonia, powdered bicarbonate of soda or methylene blue may be applied locally for bee stings, and mild acids like vinegar for alkaline wasp stings. The appearance of anaphylactic symptoms calls for the injection of ℿ x of $\frac{1}{1000}$ adrenalin injected subcutaneously. Sepsis is treated along usual surgical lines, while specific antisera should be immediately given in streptococcic infections associated with lymphangitis, or in anthrax, gas gangrene and tetanus.

Arachnid Bites. The arachnida include the mites, ticks, spiders and scorpions, and their bites may give rise to considerable disability.

(1) *Mites.* There is a very troublesome form of dermatitis acquired in handling such raw materials as sugar, grain, etc., known as "Grocer's itch" (*Glycyphagus domesticus*), "grain itch" (*Pediculoides ventricosus*), "water itch" in tea plantations (*Rhizoglyphus parasitious*) and "copra itch." In temperate climates the harvest mite may give rise to considerable itching and erythema.

Treatment. Gloves are the best protection against mite dermatitis. Talc powder and flowers of sulphur sprinkled in the stockings, or washing the legs with green soap or benzene are useful for the ordinary harvest mite.

(2) *Ticks.* Ticks bite man as a rule by accident. Tick paralysis in man may follow the bite of several species, including *D. venustus* and *D. andersoni.* Bites generally occur on the nape of the neck, which becomes swollen, painful and œdematous. Later, paralysis of the lower motor neuron type follows, the legs being first involved and subsequently the arms.

Treatment. In removing ticks, carbolised oil or paraffin should be applied prior to attempting extraction, as this results in withdrawal of the head and so prevents its being broken off.

(3) *Spiders.* Most spiders are not particularly dangerous to man, but some, especially *Latrodectus*, are very deadly. The *Araneida* or true spiders possess poison glands and inject venom into their prey.

Ætiology. Spider venoms possess a predominantly neurotoxic action affecting the neuro-muscular juncture as well as the medullary centres. Guinea-pigs which are naturally bitten may die with tetanoid spasms of the muscles and bronchial spasm. Some venoms contain a hæmolysin. The red-backed spider of Australia and New Zealand (*L. hasseltii*) and the " black widow " of California (*L. mactans*) both spin their webs across the seats of dry earth closets in the country districts where sewage does not exist, and man is generally bitten on the genitals during the act of defæcation. Erysipelas, cellulitis and septicæmia, tetanus, anthrax and gangrene may follow.

Pathology. Local inflammation and even gangrene may follow the bite, but often there is little naked-eye change. At autopsy visceral congestion, petechial hæmorrhages, pulmonary œdema and with some species renal changes associated with hæmoglobinuria may be found.

Symptoms. The outstanding clinical symptoms are pain and muscular spasms of various sorts. On being bitten the patient may instantaneously develop severe pain, though in other cases its onset is delayed for one or two hours. Frequently it is intense, radiating to the limbs, testicles and the abdomen, the walls of which may be held so rigidly that an acute abdominal crisis is suspected. Vasomotor collapse follows with pallor, vomiting, sweating and low blood pressure. Dyspnœa with respiratory stridor occurs. The pupils are generally contracted and in the late stages fail to react to light. The reflexes are sluggish, weakness appears early and dysphagia and priapism may occasionally supervene. At first the temperature is subnormal, but rises later, and where secondary bacterial infection ensues, fever may persist for many days. Dilatation of the right heart, cyanosis, pulmonary œdema and coma may follow in severe cases. With some species including the " cross spider," *Epeira diadema* and *G. gasteracanthoides*, hæmoglobinuria develops.

Prognosis. The prognosis in most cases is good, but with *Lactrodectus* and certain species of *Atrax*, the death rate reaches 6 per cent. or higher. In cases which recover, pain in the limbs and sleeplessness may persist for some time after acute symptoms have subsided.

Diagnosis. Where the spider is seen and there is an immediate onset of acute pain, the diagnosis is easy. When there is a latent interval and local inflammatory lesions are absent considerable difficulty may be experienced, and such divers conditions as food poisoning, cardiac failure and acute abdomen may be suspected.

Prevention. The danger of *Lactrodectus* bites would be largely eliminated by careful inspection of dry earth closets before use.

Treatment. Where the extremities are bitten, immediate ligature, incision and mechanical suction should be employed, while locally iodine is a useful application to prevent secondary infection. Morphia may be necessary to alleviate pain, while laryngeal and muscular spasm may be benefited by intra-muscular

and intravenous injections of calcium gluconate (10 c.c. of a 10 per cent. solution). Circulatory failure should be combated by saline (0·9 per cent.) and glucose (5 per cent.) solutions given intravenously and by injections of coramine, pituitrin and adrenalin. Pulmonary œdema calls for the administration of atropine and immediate venesection. If convalescent serum be available it is worth a trial.

(4) *Scorpions.* Scorpions have a partially segmented body with strong, pincer-like pedipalps and paired poison-glands situated in the post-anal segment of the spined tail. When attacking, this is plunged forward into its prey, there being immediate ejaculation of the contents of its poison sac. Scorpions of the genus *Buthus* are well-known in the tropics, and others such as *Euscorpius italicus* and *Centrurus exlicauda* are dangerous.

Symptoms. The sting is exceedingly painful and severe toxic symptoms may follow, including nausea, vomiting, diarrhœa, sweating, cramps and fever. Trismus, stiffness of the neck, muscular paresis of different types, coma and respiratory failure may supervene. Children not infrequently die from direct toxic effects and severe sepsis may occasionally follow in adults.

Treatment. Local treatment similar to that outlined for spider bite should be instituted. The application of strong ammonia and the local injection of novocaine and adrenalin may ease pain, though morphia is at times required. A specific scorpion antivenene has been successfully prepared from horses inoculated with the contents of the poison sacs, and is widely used in Upper Egypt, where a great reduction in the mortality amongst children has been observed. The usual dose for children is 5 c.c. intravenously.

Centipede Bites (*Myriapoda*). The small centipedes in temperate climates may inject venom and cause considerable local inflammation and symptoms associated with an erysipelas-like eruption. In the tropics there is a larger centipede known as *Scolopendra gigantea*; this causes more profound local inflammation, necrosis, lymphangitis and toxic features such as generalised pains, headache, vomiting and fever. In children coma and death may follow.

Treatment follows the lines outlined for scorpion bite, but no specific antiserum is available.

Biting Leeches (*Hirudinea*). Leeches are members of the Hirudinea—a branch of the Chætopod worms and are specially troublesome in the tropics, in leafy forests, marshy jungles, streams and rivers.

The Asiatic Land Leech (*Hæmadipea zeylanica*) measures about 1 inch in length. It occurs in India, Ceylon, Japan and the Philippines and travellers often find their socks soaked in blood at the end of a march through leech-infested forests, while people sleeping out have actually died from severe biting occurring at night. Sepsis is another danger complicating leech bite.

The Aquatic Leech (*Limnatis nilotica*) is larger and is found in the Near East. On being swallowed it fastens itself to the mucosa of the mouth, pharynx, larynx, glottis or nasal cavities of man and animals, producing severe hæmorrhage which may prove fatal unless the leech be removed. During the World War this leech caused considerable trouble in Gallipoli and Palestine.

Prevention. Gum-boots are necessary to keep leeches out, but as they may drop from the leaves of trees on to travellers in forests, a search should be made for their presence during trek. At night, if sleeping in the open, a fine mosquito net should be used. The aquatic leeches can be removed by passing drinking water through a piece of muslin or through a sieve.

Treatment. Salt or vinegar should be applied to the leeches, as these measures cause them to relinquish their hold. Traction without this will probably break off the head of the leech, leaving its suction apparatus behind and local inflammation and suppuration is liable to result. After removal tincture of iodine should be applied to the bite.

SNAKE BITE

Symptoms of snake poisoning result when a sufficient quantity of venom derived from a member of the proteroglyphous colubridæ has been inoculated into the tissues. These snakes all possess poison glands and grooved fangs (*Elapidæ*) or completely canalised fangs (*Viperidæ*) which are situated anteriorly in the upper jaw. The only snake dangerous to man with posteriorly situated fangs is the boomslang (*Dispholidus typus*).

Ætiology. Snakes are carnivorous and their venoms are merely the specialised salivary secretion of the poison gland, which is the homologue of the parotid gland of mammals. This gland is situated behind the upper jaw and the laterally compressed venom duct passes forward along the upper lip margin to open at the base of the fang which is surrounded by a fold of mucous membrane known as the *vagina dentis*. The vipers have long fangs which are completely canalised and capable of considerable forward rotation, whereas the elapine colubrids possess much shorter fangs which are grooved and possess only a limited power of elevation. It is easy to determine whether a snake is venomous or not by examining the mouth parts and ascertaining whether there are anteriorly situated fangs in the upper jaw; then by inspecting the fangs and noting whether they are grooved or canalised one can determine whether the snake belongs to the elapins or vipers respectively. The *Elapidæ* include the sea snake (*Hydrophiidæ*) which have valved nostrils and vertically flattened tails, as well as all the terrestrial elapine snakes (*Elapinæ*). The *Elapinæ* comprise the most deadly of all known snakes and include the king cobra (*Naia bungarus*), the spitting cobra (*Naia nigricollis*), the ordinary cobras of Asia and Africa (*Naia*), the Indian Kraits (*Bungarus*), the dreaded Mamba (*Dendraspis augusticeps*), the deadly Australian death adder (*Ancanthopis antarticus*) and tiger snake (*Notechis acutatus*), and the coral snakes (*Elaps* and *Micrurus*) of Central and South America.

The Viperidæ are subdivided according to the presence of absence of a loreal pit into the Viperinæ and the Crotalinæ. The Viperinæ include the formidable Gamboon viper (*Bitis gabonica*), the puff adder (*Bitis arietans*), the horned viper (*Cerastes cornutus*) of Egypt, the *Echis carinatus* and the Daboia (*Vipera russellii*) of India, as well as the European vipers (*V. berus*, *V. aspis* and *V. ammodytes*). The Crotalinæ comprise the rattlesnakes and pit vipers and include various species of *Crotulus* such as *C. horridus* and *C. adamanteus*, various species of *Agkistrodon*, the Bushmaster (*Lachesis mutus*) and the Fer-de-Lance (*Bothrops atrox*), etc.

The Mechanism of Bite. When a snake strikes it throws itself forward with great speed over a distance not generally exceeding one-third of its length and as it nears its objective the jaws swiftly open and the fangs are elevated and rotated forward. Powerful closure of the jaws drives the fangs into the tissues, and simultaneously venom is expelled under pressure through the venom duct and canalised or grooved fangs into the tissues. Fixation of the jaw is important with elapine colubrids like the cobra, and such snakes bite like a dog, often hanging on to the bitten part so that occasionally they have to be forcibly evulsed from the victim. With vipers, owing to a different arrangement of the muscles acting on the poison glands, expulsion of venom is instantaneous and independent of fixation of the jaw. So rapidly do vipers strike that the onlooker is sometimes left wondering whether the snake has actually bitten, or not.

Venom and Venom Constituents. The certainly lethal dose of venom varies with different species of snakes, as does also the venom yield. Many factors such as captivity, disease and starvation affect the yield adversely. Viperine venoms contain a toxic depressor substance producing peripheral circulatory failure, a powerful thrombase and a constituent known as hæmorrhagin, which digests the vascular endothelium and causes hæmorrhages throughout the tissues of the body.

Elapine colubrid venoms contain a neurotoxin having a curari-like action at the neuromuscular juncture which causes extensive paralysis of different muscles, including those of respiration. Hæmolysins and anti-coagulins are also present in many of these venoms. Certain species of the Australian colubrids possess venom of mixed type. The elapine colubrids generally possess an inferior inoculating apparatus, but more highly toxic venoms which kill by producing a curari-like paralysis of the respiratory muscles. The vipers, on the other hand, have an excellent biting apparatus and kill by peripheral cardio-vascular shock and internal hæmorrhage; their venom is less deadly though the local digestive action on the tissues is much more intense.

Pathology. In fatal cases of elapine colubrid bites, the mode of death is congestive, resulting from paralysis of the respiratory muscles; there is fluid blood in the vessels, dilatation of the right heart and swelling, congestion and œdema round the site of the fang punctures. In fatal viper bites multiple hæmorrhages are found in the viscera, serous and mucous membrane and the skin, but unless the inoculation has been made into a vein fluid blood is generally found in man. In the vicinity of the bite there is congestion and a gelatinous, hæmorrhagic exudate infiltrates the tissues, producing an appearance not unlike red-currant jelly. Adjacent vessels are often thrombosed, and in the later stages extensive suppuration and local gangrene is found.

Symptoms. The signs and symptoms of snake bites are dependent first on the species of snake, secondly on the quantity and site of injection of the venom, and thirdly on the body weight of the patient. Snake bite is particularly dangerous in small children.

Local Manifestations. The local lesions caused by the colubrids include numbness at the site of the bite, congestion and swelling. With the vipers there is much local pain, far greater swelling and considerable oozing of blood from the fang punctures, which are surrounded by hæmorrhage and generally separated by a distance of 1 to 3 cm. Though two is the rule, one, three or even four fang marks may result from one bite, the extra ones being produced by reserve fangs. Local suppuration and gangrene may follow, especially in viper bites, and chronic ulcers, extensive necrosis and actual gangrene of fingers, hands, feet and limbs may ensue. Some 56 per cent. of patients are bitten on the lower extremities, and the upper extremities account for another 42 per cent., body, neck and face bites being fortunately rare.

Systemic Manifestations. The interval between the bite and the appearance of systemic manifestations is determined by the quantity and nature of the venom injected and the rate of its absorption. Symptoms may appear as early as fifteen minutes; in other instances they may be delayed for many hours. The onset is characterised by nausea, faintness, vomiting, headache and signs of vaso-motor collapse, with cold extremities, low blood pressure, rapid thready pulse, blanched skin and extreme prostration. Psychical shock is a real factor in snake bite, and authentic cases are reported in natives who have died from fright after having been bitten by snakes which have subsequently been proved non-poisonous.

Elapine Colubrid Bites. In elapine colubrid bites, as typified by the cobra, muscular weakness of the limbs, ataxic gait, paresis of the ocular muscles and frequency of micturition set in early; the speech becomes blurred and indistinct, and if palatal paralysis ensues a nasal quality is added to the voice. Ptosis and double vision are frequent and sensory disturbances are sometimes superadded. Ultimately, swallowing becomes difficult, the tongue swells and saliva dribbles from the mouth. The breathing, which was at first excessive and laboured, becomes shallow and slow. Cyanosis begins to appear, coma and convulsions of asphyxial origin develop, and death results from peripheral respiratory failure.

Viperine Bites. Vasomotor collapse is profound, extensive hæmorrhagic extravasations are found in the skin, blood may ooze from the gums, while

epistaxis, hæmoptysis, hæmaturia, hæmatemesis and mælena may ensue. Red blood corpuscles may appear in the urine before other hæmorrhagic phenomena become manifest.

Complications. Extensive local suppuration and gangrene frequently results from viperine bites, while with elapine bites blunting of the cough reflexes and paresis of the muscles of deglutition may terminate in septic pneumonia. In Krait bites acute ascending paralysis of the spinal cord is recorded some ten days later.

Course and Prognosis. Prognosis depends on the body weight of the patient, the quantity and quality of venom injected and the availability of specific antivenene. Most local treatment is ineffective as it is applied too late. Death may occur in from fifteen minutes to three days.

Diagnosis. Whenever possible the snake itself should be examined to determine whether it is poisonous. The clinical syndrome of blurred speech, stumbling gait and double vision has occasionally led to the suspicion of alcoholic intoxication. It is well to remember that in the Orient alleged cases of snake bite may be due to criminal poisoning.

Prevention. Much can be done by wearing strong boots with puttees or leggings, and at night lanterns or electric torches should be used to illuminate roads when walking in snake-infested country. Beds, bedding and sleeping bags should be examined, and, if camping out, a mosquito net is a safeguard.

Treatment. Two questions always arise in treatment: (1) has a lethal dose of venom been injected into the tissues ? (2) has a lethal dose been absorbed into the circulation ? Where large quantities of venom have been inoculated the absorption time is extremely rapid, varying from two to ten minutes with really deadly snakes, but where smaller quantities of venom have reached the tissues this period may be lengthened.

Local Treatment. The most essential procedure is the application of a ligature. A piece of rubber tubing, 1·5 cm. in diameter, makes an excellent tourniquet, or, failing this, strips of clothing may be loosely knotted around the limb and subsequently tightened by twisting with a stick as a first-aid measure. The ligature must be applied without delay around a single bone such as the arm or thigh proximal to the bite. It must be tight enough to obliterate the arterial circulation and be left in position for at least twenty minutes in the first instance ; subsequently it may be loosened for a half to one minute until the limb has become flushed with blood, after which it is immediately re-applied for a similar period. Where necessary the procedure may be repeated. Early ligature decreases the dosage required to save life, and by increasing the death time sometimes enables antivenene to be given to otherwise fatal cases.

Surgical Procedures. The skin is washed with potassium permanganate solution if available, or other fluid, to remove any inspissated venom. Incision of ½ inch in length by ¼ inch in depth over each fang mark may reveal the presence of broken fangs. It permits the subsequent application of mechanical suction by a breast-pump or Bier's suction glass, and affords an index to the efficiency of ligature, but is of doubtful value as a means of draining away venom from the fang tracks. Early free excision of the bitten tissues has more to recommend it ; if ligature has been applied early, the extent and depth of the area excised varying with the species of snake implicated. Mechanical suction can subsequently be applied with benefit.

Local Injections. Different solutions are advocated, including a 1 to 5 per cent. solution of potassium permanganate or gold chloride, and the application of a ligature must precede the injection. Unfortunately necrosis and gangrene often result from these irritant chemicals and their value is doubtful.

Specific Antivenene Treatment. As a general rule, each antivenene is only antidotal to its one particular venom, and most countries where snake bite is common now produce antivenenes locally against the prevailing species of snakes.

They may be monovalent, bivalent or multivalent in type, and dosage varies with the concentration and titre. In the case of colubrid bites injections must be given intravenously, and this route is preferable in viper bites also, though concentrated antivenenes are being given intramuscularly with apparently good results in the United States. Should time and circumstances permit, the patient may be tested for hypersensitiveness to horse serum and subsequently desensitised if necessary. Antivenene should be given at the earliest possible moment, remembering that the longer it is delayed and the smaller the body weight of the patient the larger the dosage required. Children for this reason need several times the dosage which would be life-saving in an adult. Patients must be carefully watched for at least twenty-four hours after antivenene has been administered, as paralytic symptoms may reappear, requiring subsequent injections.

General Measures. The patient should be reassured, given stimulants such as black coffee and caffein citrate, and put to rest in bed with hot bottles. Strychnine and alcohol are better avoided and morphia is contra-indicated. Circulatory shock is treated by the abundant administration of warm fluids by the mouth and *per rectum*, and intravenous injections of 5 per cent. glucose where there is difficulty in swallowing. Injections of coramine, pituitrin and adrenalin may be helpful; the foot of the bed should be raised and the limbs bandaged from below upwards. Respiratory failure may be treated with coramine injections and artificial respiration and oxygen. It is important to keep the mouth and naso-pharynx as free from mucus as possible, and to prevent food from entering the larynx should vomiting occur.

POISONOUS FISHES

In the tropics man is not infrequently attacked by fish, the bite or sting of which may lead to serious consequences. In some cases fish venoms such as that of *Trachinus draco* resemble snake venom in producing hæmorrhage and local necrosis when injected subcutaneously, while on intravenous injection a primary rise, followed by a fall of blood pressure with cardiac and respiratory paralysis, has been noted. A few of the more common poisonous fishes are referred to below.

(1) ***Jelly Fish*** (*Medusæ*), of which the Portuguese man-o'-war (*Physalia pelagica*) is the best known example, may sting very severely, producing urticarial wheals, local œdema, numbness and pain extending up the limb, itching, burning and erythema; vesicular dermatitis, ulceration, and even necrosis of tissue may follow. Systemic manifestations include fever, generalised muscular pains and spasm of the abdominal muscles, lachrymation, constriction of the chest, dyspnœa and cardio-vascular shock; deaths have occasionally resulted. Probably anaphylactic shock in previously sensitised individuals is responsible for the severer manifestations.

(2) ***Tropical Eels*** (*Murænidæ*) are also dangerous, as they possess powerful, non-grooved teeth between which venom flows from poison pouches situated above the membrane of the palate. Severe local effects and cardio-vascular shock may follow the bites.

Other poisonous fish possess grooved or channelled spines or barbs connected with poison glands; the Scorpion Fish (*Scorpænidæ*), the Sting-rays (*Raii*) and the Cat-fish such as *Cridoglanis bostockii* and *Trachuris draco* may be cited as examples.

Symptoms. Locally there may be severe pain of stabbing type associated with numbness and tingling; swelling and inflammation follow, and in extreme cases purulent discharges, extensive sloughing and gangrene ensue. Amputation may be necessary. With the sting-rays, paræsthesias and paralyses of the limbs, fever, gastro-intestinal symptoms, cardiac weakness, vasomotor collapse, restlessness,

delirium and syncope may be produced. Death sometimes follows from cardiac failure or septicæmia. Tetanus has been recorded.

Treatment. The local treatment is similar to that outlined for snake bite. Morphia should be freely used for the pain. Cardio-vascular shock and respiratory failure are treated along similar lines to those already outlined. Local complications such as suppuration, abscess and gangrene require surgical treatment.

TROPICAL SKIN DISEASES

Certain skin diseases are peculiar to warm climates, while others occurring in Europe are modified by such factors as racial immunity, social customs and skin pigmentation. Thus leucoderma (vitiligo) produces great disfigurement in dark-skinned people, and may be confused with the depigmented patches of nervous leprosy. Keloid, which occasionally complicates surgical scars and burns in Europeans, is purposely produced amongst primitive peoples in connection with certain tribal customs. Keloid development involving the ears, back, thighs and chest, are especially common amongst Central African negroes. Malignant changes are rarely observed.

CHIGGER DISEASE

Chiggers are found in parts of Africa, tropical America and India, as well as in the West Indies and Madagascar. It is a common source of invalidity amongst coolies and other natives. The chigger (*Tunga penetrans*) is a reddish-brown flea, inhabiting dry, sandy soil, and readily attacks warm-blooded animals. After the female has become impregnated, she burrows obliquely into the skin and rapidly increases in size; on maturing the eggs are expelled through a small opening in the skin.

Pathology. The impregnated female causes considerable irritability and local tissue reaction; the parts become inflamed, pus forms and a pea-like elevation follows; subsequently the skin ulcerates and the chigger is expelled, leaving a small sore which may be secondarily infected with bacteria.

Symptoms. The feet are most commonly affected, since they come in contact with the ground, a favourite situation being the skin between the toes, the root of the nails and the soles. The legs, thighs, hands, face, scrotum, penis and perianal skin may also be implicated, and in severe cases hundreds of chigger sores may be present; in hyper-infection the tissues are honeycombed by the process. Severe local sepsis, septicæmia or even tetanus may follow the infection, which occasionally proves fatal.

Treatment. Where chigger is endemic the floors should be frequently swept and treated with suitable antiseptics, and walking barefooted must be avoided. The feet may be rubbed with a mixture composed of 5 drops of lysol in 1 ounce of vaseline. Careful search should be made for chiggers, which appear as black dots in the tissues; they should be removed as soon as they have fastened themselves to the skin. The orifice of entrance is enlarged with a sterilised needle, the insect enucleated and the part subsequently dressed antiseptically.

Craw-Craw (*Nodular Dermatitis*). The term craw-craw is applied to any itchy papular or pustular eruption involving the skin—particularly that of the limbs. It occurs in parts of tropical Africa, Ceylon, India, South China and the West Indies. Filarial embryos were found in the exudate by O'Neill, but they were probably *Microfilaria streptocerca*, which MacFie has since demonstrated in the skin of many West African negroes.

Symptoms. The condition orginates as a papular dermatitis, the papules being hard and horny and very itchy. Scratching results in secondary infection, and a pustular dermatitis with enlargement of adjacent lymph glands may follow. Pustulation of the feet and legs is frequent.

Diagnosis. The condition must not be confused with acari dermatoses, coolie itch or scabies. No acari or other mites are demonstrable and no burrows are seen.

Treatment. Infected stockings and foot-wear should be destroyed. If pustules are present they should be opened, the crusts removed, the ulcers scraped and subsequently disinfected with 1 in 1,000 sublimate solution and then dressed with boric acid ointment on lint. Bathing in carbolic lotion (1/20) may prove beneficial.

Veldt Sore. Veldt sore is met with in South Africa, and is a chronic septic ulcerated lesion involving the exposed, hairy parts of the body. It has a wide-spread geographical distribution in the tropics and subtropics and is known as Barcoo Rot in Australia and Desert Sore in both Sinai and Mesopotamia, where it affected troops during the Great War. It is most common in hot, sandy or desert country, and occurs specially where people have to live on restricted dietaries deficient in fruit and vegetables. Streptococci, staphylococci and diphtheria bacilli have all been isolated from the lesions.

Symptoms. There is first a painful vesicle which occurs especially on the back of the hand, the fore-arm, elbows and knees. It contains a yellow fluid, and after rupturing produces a punched out, circular or oval ulcer with a tough, grey base and bluish indurated edges. It may take many months to heal, leaving a thin scar when it does so. In Sinai instances of diphtheritic paralysis of the limbs and palate were noted: the Klebs-Lœffler bacillus was found in the sores, but whether it was merely a secondary invader is unknown.

Prevention. Vitamin reinforcement of the diet with orange juice, marmite, etc., is important, and abrasions should be treated antiseptically and covered. Horse manure may constitute a source of infection.

Treatment. The ulcers should be protected by sterile dressings and ammoniated or nitrate of mercury ointment applied. A high vitamin diet and iron and arsenic tonics are advisable. Anti-diphtheria serum must be given if diphtheria bacilli be present, and may be followed by dramatic cure. Autogenous streptococcal vaccines are worthy of trial.

Tropical Ulcer (*Ulcus tropicum; tropical sloughing phagedœna*). This is a gangrenous, sloughing ulceration of the skin and subcutaneous tissues, resulting in the formation of chronic ulcers which are often very resistant to treatment. The disease differs from the Veldt sore in originating in damp, humid parts of the tropics—especially in the jungle. Generally there is a history of trauma, followed by the appearance of lesions in the lower limbs. It occurs especially in the debilitated and those suffering from other diseases. People of any age and either sex are susceptible, and occasionally outbreaks assume epidemic proportions amongst the coolies in tea plantations. According to Smith (**83**), the condition can be directly transmitted by inoculation of ulcer material from man to man. Different views are held regarded its ætiology, some suggesting deficiency disease, while others hold that a fusiform bacillus and the spirochæte, *Treponema schaudinni*, are causative. Hypochlœmia is not uncommon.

Symptoms. The disease originates as a bleb containing serous or sanguineous fluid. Rupture leaves a dirty grey slough which rapidly extends into a foul, sloughing ulcer, causing considerable pain and sometimes fever. Considerable areas of tissue may be affected and deep ulceration may involve tendons, muscles, nerves, blood vessels, periosteum and even joints. The dorsum of the feet and front of the legs are most commonly affected, the hands and fore-arms occasionally. The acute stage of sloughing and spreading is followed by one of tissue equilibrium, when the growth of granulation tissue balances the area of tissue destroyed. Still later healing occurs. As a rule the ulcers persist for many months and, in extreme cases, for years; inadequate epithelial proliferation is generally responsible for delay in healing.

Diagnosis. A variety of different ulcers, such as those associated with

varicose veins, yaws, syphilis, Leishmania and fungoid granulomata of the skin, may need to be differentiated. The history of trauma and residence in a jungle area are important.

Prognosis. Most cases heal, given proper treatment and time, but occasionally in intractable cases amputation may be necessary to save life. Death occasionally results from toxæmia, inanition and septicæmia.

Prevention. The use of puttees, leggings and strong boots in the jungle is advisable to prevent trauma.

Treatment. General measures include rest and a nutritious, high vitamin diet, reinforced with cod-liver oil, calcium and parathyroid extract where hypocalcæmia exists. Injections of salvarsan may prove of value. Local treatment varies with the stage of the ulcer. In the rapidly progressive stage, sloughs should be excised and antiseptic lotions of permanganate or carbolic applied. Curettage of the ulcer base and daily dressing with B.I.P.P. may have good results. Some observers have reported healing following the application of adhesive elastic strapping or elastoplast bandages. Where epithelial proliferation is slow, healing can be greatly accelerated by skin grafting.

PEMPHIGUS CONTAGIOSUS

(*Pyosis mansoni*)

This is a contagious coccal infection of the dermis, characterised by inflammation with vesicles and bullæ which ulcerate and become covered with scabs. Cultures from the lesions show *Staphylococcus aureus* and *albus*, and occasionally streptococci. European children are specially affected. The disease is common in Ceylon, Malaya and parts of Africa.

Symptoms. The initial lesion is a minute, red fleck which develops into a vesicle, a bulla, and ultimately a pemphigus-like vesicle containing fluid which at first is clear but later thick and purulent. After rupture the ulcers generally dry up and heal, not infrequently leaving pinkish, glazed scars on the skin. In children the eruption may have a widespread distribution, the whole body, except the face, being sometimes involved, but as a rule the eruption is mainly confined to the axilla and crutch.

Diagnosis. The disease may need to be differentiated from impetigo contagiosa, chicken-pox, early small-pox and ring-worm.

Treatment. The avoidance of auto-infection is important. The lesions should be washed with a 1 in 1,000 solution of perchloride of mercury and a dusting powder of zinc oxide, boracic acid and starch in equal parts subsequently applied. Ung. hydrarg. ammon. is of distinct value.

TINEA

Ring-worm infections of the skin and nails abound in the tropics. The two most common ones—dhobie's itch and Hong-kong foot—are due to the *Epidermophyton inguinale;* they occur in Europe and are described elsewhere (*see* p. 881).

Tinea Unguium. This is a mycotic infection of the nails which is not infrequent in Europeans in the Far East, and is often associated with Tinea infection elsewhere. The nails become discoloured, lose their lustre, are brittle, grooved and pitted, while material composed of epithelial cells, tissue debris and fungus accumulate under the nails. The nail bed is definitely involved and paronychial inflammation present in varying degrees. Diagnosis is made by demonstrating *Epidermophyton inguinale* in scrapings mounted in 20 per cent. potassium hydrate solution. Treatment consists of local applications containing salicylic

acid (3 per cent.) and benzoic acid (5 per cent.). X-ray is of value, but in severe cases surgical removal of the nails may be necessary.

Tinea Imbricata (Tokelau). Ring-worm affects chiefly the face, trunk and limbs, and is caused by a fungus, *Endodermophyton concentricum*, which is readily demonstrable in the epithelial scales. It occurs mainly in the Eastern Archipelago and South Pacific, being characterised by rosette-like, brown spots which give rise to flaky, tissue-paper scales, free centrally, but attached at their peripheral bases. The circular lesions are about $\frac{1}{4}$ inch in diameter, and being close-set give rise to a festooned appearance.

Tinea Flava. This ring-worm is common in the tropics, involves the face, neck, chest and arms, and manifests itself as a yellowish-brown, scurfy patch on the black, negroid skin. According to Castellani, the causal fungus is *Malassezia tropica*. There is a black variety called Tinea nigra which is caused by *Cladosporium mansoni*.

Pinta (*Caraate ; Mal del Pinto*). This is a group of dermatomycoses found in tropical Amercia, characterised by patches of pigmentation in the skin. The disease is contagious and attacks either sex at any age. A variety of fungi are implicated, including *Penicillium, Aspergillus* and *Monilia.*

Symptoms. The back of the hands are first involved, with patches of pigmentation which are rough, dry, raised and vary in colour. Red, violet, white and black types are associated with different types of fungi. Gradually the condition may spread to other parts of the body, and when the scalp is involved the hair becomes white. Itchiness is marked in the skin lesions which may be of an offensive character.

Diagnosis. The patches may resemble leprosy or leucoderma; anæsthesia is not present and microscopic examination of material in 20 per cent. caustic soda reveals the fungus.

Treatment. This is the same as for ordinary ring-worm of the skin.

Piedra (*Trichosporosis*). This disease occurs in British Guiana and Columbia. It is caused by the *Trichosporon giganteum*, which produces hard, gritty nodosities around the hair of the scalp.

Creeping Eruption (*Larva migrans ; Myiasis linearis*). This is a raised, linear, red eruption, which gradually extends in a sinuous fashion or as a straight line, the posterior portion fading as it progresses. It may result from the wanderings of *Gastrophilus* or other fly larvæ under the skin, but much more commonly is caused by nematode larvæ such as *Ancylostoma braziliense, A. canium, Uncinaria stenocephala* and *Gnathostoma hispidum.*

Symptoms. Sharp smarting pain and intense itching often occur at the site of the lesion, which may develop small, round, red papules or pustules.

Treatment. If the disease is due to *Gastrophilus* larvæ, surgical removal under local anæsthetic is the best treatment. For *Ancylostoma* larvæ *oleum chenopodii* diluted with three parts of castor oil should be applied locally. Spraying with ethyl chloride for two minutes at the anterior end of the larva is helpful in the case of canine ancylostomes. Blisters and pustules may be treated with mercurochrome solution or other appropriate antiseptics.

Cercarial Dermatitis. This is an inflammatory condition of the skin due to the passage through it of cercariæ. It was first described by Cort in 1928, *Cercaria elvæ* being implicated. Taylor and Bayliss noted a similar condition in England with another species of cercariæ. It may also occur as the first indication of Bilharzia infection in man.

Symptoms. These consist of itching and smarting of the skin, and the appearance of erythematous red spots, urticarial wheals and papules; occasionally pustules follow.

Treatment. This is merely palliative, consisting of the application of cooling lotions like calamine lotion combined with lead acetate, and liquor carbonis detergens to reduce itching.

TROPICAL DISEASES OF UNKNOWN ORIGIN

Ainum. This is a disease of the toes, characterised by ring-shaped constriction culminating in spontaneous amputation of the affected phalanx. The condition is found amongst adult natives and Hindoos on the West Coast of Africa, in Brazil, British Guiana, the West Indies, the Southern United States of America and India. The cause is unknown.

Pathology. The ring of fibrous tissue generally implicates the little toe. The epidermis is thickened, and there is an increase of adipose tissue associated with rarefaction and absorption of the underlying bone.

Symptoms. Clinically a groove or furrow first appears on the inner and plantar side of the base of the little toe ; this gradually deepens, extending round the toe adjacent to the swelling. There is little pain, even in the early stages, and both feet may be involved. Occasionally the fourth toe is affected, but rarely the others. The fibrous tissue band may constrict to such a degree that the toe hangs on by a thin pedicle ; it either drops off or is amputated by the patient.

Prognosis. The disease may last from one to ten years, but life is never endangered.

Treatment. In the early stages vertical incision through the constricting band, or, later, surgical amputation, is advisable.

Big Heel (*Endemic hypertrophy of the os calcis*). This is a peculiar hypertrophic condition of the os calcis encountered in natives on the West Coast of Africa and Formosa. Possibly it has an ætiological connection with yaws.

Symptoms. At onset there is fever associated with pain and tenderness of the heel ; this gradually gets worse for the first four or five weeks and thereafter slowly diminishes ; there is unilateral or bilateral swelling of the os calcis. If the condition becomes chronic, a permanent thickening of bone results.

Treatment. Surgical removal of the hypertrophic bone is indicated if enlargement be excessive and it interferes with walking.

Onyalai (*Chipola*). Onyalai is a disease of unknown origin affecting natives in Central Africa, characterised by the appearance of blood-filled vesicles implicating the mouth and other mucous membranes. Severe hæmorrhage may result when these burst.

Ætiology. Patients of any age or either sex may be affected, but young males appear particularly prone. It is found in Portuguese West Africa, in the Belgian Congo, Northern Rhodesia and East Africa. Mense suggested that it was due to poisoning by *Euphorbiaciæ* : Gilkes (**84**) believes it to be a vitamin deficiency.

Pathology. Hæmorrhages may involve the skin, subconjunctival tissues, alimentary tract, the serous sacs, retroperitoneal tissue, pelvis of the kidney and bladder. The inside of the cheeks, lips and palate present numerous umbilicated oval or circular vesicles of about 1 cm. diameter.

Symptoms. The condition commences with headache, vague pains in the chest, and a moderate rise of temperature, and is followed by a discharge of blood from the nose and mouth. The tongue becomes painful and swells, and there may be swelling of both parotid glands ; vesicles which form inside the mouth increase to about the size of a small pea and subsequently burst, leaving a raw surface which bleeds intermittently. The breath becomes evil-smelling, the patient rapidly develops anæmia and listlessness from blood loss, and in severe cases is so weak that he cannot feed himself. In severe cases bleeding may start from the gastro-intestine, rectum or bladder, and blood appear in the stools and urine. The red cells are reduced to 500,000 to 1,000,000 per c.mm. in severe cases, and the hæmoglobin correspondingly decreased. There is a slight leucopenia, with a relative lymphocytosis of 30 to 40 per cent. The urine contains red blood corpuscles and casts.

Diagnosis. The condition has to be differentiated from viper bites, purpura hæmorrhagica, Henoch's purpura, and *Euphorbiaciæ* poisoning. There are no painful swellings of the joints and the gums are not spongy, so that the condition should not be confused with scurvy.

Prognosis. The mortality rate varies from 25 to 50 per cent. Cases which show a temperature of 103° to 104° F. often do better than those with a subnormal temperature. Relapses are not infrequent.

Treatment. The patient is put to bed, given a high vitamin diet, including fresh milk, marmite, orange juice, fruit and green vegetables, and the anæmia treated by blood transfusion, iron and arsenic. Gilkes states that calcium lactate is beneficial.

Chiufa. This is an acute proctitis of unknown origin which starts at the anus and involves the rectum. The inflammation may involve the whole of the descending colon up to the splenic flexure. The condition affects natives in Northern Rhodesia, especially during the hot weather and rains, though it may occur at all times of the year.

Symptoms. The onset of chiufa is sudden and the disease runs an acute course which may end fatally within a few days. According to Gilkes (**85**), a white powdery condition appears around the anus, while in women the vulva and vagina may be implicated. This powdery appearance disappears after a few days, and the patient becomes acutely ill with a high temperature, pain in the back and neck, excessive sweating and weakness. By this time the skin round the anus appears indurated and reddened, the sphincter becomes relaxed, the anal canal dilated and gaping and throbbing pain is complained of. Constipation at this stage is the rule. As the inflammation proceeds upwards, diarrhœa and vomiting set in, the stools become mucoid and watery in type, the breath foul, and food and drink are refused. There is rapid loss of weight, urine is passed involuntarily, and the patient may die rapidly.

Diagnosis. The condition differs from the epidemic gangrenous rectitis of South America in the absence of gangrene, and is only likely to be confused with rectal schistosmiasis by those not having experience of this disease.

Treatment. No definite treatment is known, the condition having been inadequately studied. Natives apply powder containing tannic acid to the rectum, blowing it up by means of a willow reed pipe.

Chappa. This is a peculiar affection of the joints, associated with nodules in the subcutaneous tissues which may break down and ulcerate. The disease is met with in Southern Nigerian natives, and nodules as large as a pigeon's egg may form in the subcutaneous tissues; joints may be destroyed and bones attacked.

Symptoms. At onset there is severe pain in the limbs, muscles and joints, and subsequently nodules appear which increase in size and break down and form ulcers, which may remain unhealed for years.

Diagnosis. The nodules have to be distinguished from onchocerca nodules, and the ulcers from those of tropical ulcer and yaws.

Treatment. Surgical treatment includes scraping the ulcers and the application of antiseptic dressings. Salvarsan, mercury and iodides have been used without very beneficial results. The prognosis is by no means always good.

Mossy Foot. This is an infectious papillomatous condition of the feet and legs encountered in natives inhabiting the Amazon Valley. The causative agent is not known with certainty, but some attribute it to the fungus *Phialophora verrucosa*, while others regard it as a form of skin tuberculosis. It has been described in Brazil, Honduras, Costa Rica and Guatemala. The disease is infective and may spread by auto-inoculation from one part to another.

Pathology. Granulomatous, warty masses composed of vascular tissue are found on the feet and legs; there may be yellow crusts, but sinuses do not occur.

Symptoms. The disease commences as a vesicle on the dorsum of the foot, extending upwards until the whole of its surface, as well as the skin of the leg, is covered with vascular, warty lesions, which are very painful. The sole of the foot is not implicated. Sometimes it attacks people with elephantoid legs. Many years may elapse before the disease is fully developed.

Diagnosis. Verruga nodules, Madura foot and ulcers of tertiary yaws and syphilis may need to be differentiated.

Treatment. This consists in excision by means of a cautery; X-ray treatment has been used in some instances with success.

ULCERATING GRANULOMA

(*Granuloma venereum. Granuloma inguinale. Ulcerating Granuloma of the Pudenda. Serpiginous Ulceration of the Genitals*)

A venereal disease occurring in many parts of the tropics characterised by a chronic progressive ulceration involving the genitals, perineum and groins of both sexes.

Ætiology. The disease was first noted in British Guiana and the West Indies, but is now known to occur in Porto Rico, Brazil, Northern and Central Africa, India, China, the Pacific Islands and Northern and Central Australia. After puberty both sexes are affected, and natives races as well as Europeans are susceptible. Several different ætiological agents have been implicated, including spirochætes, a capsulated organism—the *Microbacterium capsulatum granulomæ*—present in plasma cells and recorded by Flu as related to the Friedlander group, and an oval bacillus described by Donovan and others, contained in endothelial cells which is present in scrapings from the ulceration. Probably none of these organisms is of ætiological significance. The disease is definitely venereal and contracted during coitus.

Pathology. From the pathological viewpoint the disease is allied to the infective granulomata; microscopic section reveals vascular tissue containing an abundance of round and plasma cells and clumps of intracellular bacilli. The older areas undergo fibrosis as the active ulceration extends peripherally without involving the lymphatics.

Symptoms. The disease begins on the penis or labia as a vesicle or flat papule; the covering epithelium undergoes desquamation, exposing granulation tissue which bleeds readily and soon becomes covered by a creamy, offensive pus. Where the glans is involved a fungating growth resembling epithelioma may form. The ulcerative process extends by direct continuity to the groins and thighs, while in the female the vagina, perineum and peri-anal skin may also be involved and recto-vaginal fistula result. In the skin lesions cicatrisation occurs in older areas as the ulceration slowly extends peripherally, but healing never follows in mucous membranes, where the extension takes place much more rapidly. Similar ulceration has been stated to involve the face, neck and mouth. Outstanding clinical features are the chronic nature of the ulcerative process, the tendency to scarring in the skin, the absence of lymphatic involvement, the mild degree of pain and discomfort complained of and the satisfactory state of the general health. Complications include urethral stricture, septic cystitis, pyelitis and vesico-vaginal fiatulæ.

Diagnosis. Syphilis or tubercular ulceration may be suspected or lupus vulgaris simulated, and when the glans penis be involved a fungating epithelioma may be the diagnosis until biopsy reveals a different pathology.

Prognosis. The disease naturally runs a very chronic course extending over many years and often lasting for life. Where the mucous membranes are involved progress is more rapid. Modern treatment has greatly improved the outlook.

Prevention consists in the avoidance of sexual connection with infected people.

Treatment. In the early stage where the ulceration is still superficial surgical incision of the ulcerated area, preferably with the electric cautery, results in cure. Where the ulceration has extended more deeply surgical intervention may be impractical, and here intensive treatment with tartar emetic should be given intravenously as in schistosomiasis; a total amount of 60 grammes is generally necessary, though in intractable cases more than twice this dosage may need to be administered. Non-specific protein therapy may also stimulate healing and is worth a trial in sluggish cases; the best procedure is to give T.A.B. vaccine intravenously, commencing with 50,000,000 per c.mm. and gradually increasing to 300,000,000 per c.mm. in a series of six injections given at three or four daily intervals.

REFERENCES

1	C. Singer	1928	*A Short History of Medicine*, Clarendon Press, Oxford, p. 282.
2	S. M. Burrows, R. J. Matthews, and C. Wilcocks	1935	*Studies of Tuberculosis among African Natives*, John Bale, Sons & Danielsson Ltd., pp. 1–87.
3	C. J. Martin	1930	*Lancet*, **ii.**, pp. 561, 617 and 673.
4	W. W. Hall and E. G. Wakefield	1927	*Journ. Amer. Med. Assoc.*, **89**, p. 179.
5	F. Marsh	1933	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **27**, p. 255.
6	D. H. K. Lee	1935	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **29**, p. 7.
7	L. A. P. Anderson, A. Howard and J. L. Simonsen	1925	*Indian Journ. Med. Res.*, **12**, p. 613.
8	H. H. Scott	1915	*Reports on Vomiting Sickness*, Jamaica Government Printing Office, Kingston, p. 22.
9	L. Wills	1933	*Lancet*, **i.**, p. 1283.
10	N. H. Fairley	1930	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **24**, p. 131.
11	N. H. Fairley	1932	*Ibid.*, **25**, p. 297.
12	F. W. Harvey and A. G. McKendrick	1923	*The Practice of Medicine in the Tropics* (W. Byam and R. G. Archibald), **3**, p. 2197.
13	R. Remlinger	1919	*Annales de l'Institut Pasteur*, **24**, p. 28.
14	M. Theiler	1930	*Ann. Trop. Med. & Parasit.*, **24**, p. 249.
15	W. A. Sawyer and W. Lloyd	1931	*J. Exper. Med.*, **54**, p. 533.
16	L. Rogers and J. W. D. Megaw	1935	*Tropical Medicine*, J. & A. Churchill Ltd., 2nd Ed., p. 167.
17	R. Daubney, J. R. Hudson and P. C. Garnham	1931	*J. Path. & Bact.*, **34**, p. 543.
18	H. S. Stannus	1933	*A Sixth Venereal Disease*, Baillière, Tindall & Cox, London, p. 119.
19	L. Rogers and J. W. D. Megaw	1935	*Tropical Medicine*, J. & A. Churchill Ltd., 2nd Ed., p. 182.
20	E. Weil and A. Felix	1917	*Wien. klin. Woch.*, **30**, p. 1509.
21	L. Rogers and J. W. D. Megaw	1935	*Tropical Medicine*, J. & A. Churchill Ltd., 2nd Ed., p. 197.
22	C. J. Martin and F. E. Williams	1918	*Brit. Med. Journ.*, **i.**, p. 447.
23	J. Cunningham	1918	*Indian Journ. Med. Res.*, **6**, p. 68.

24	R. Koch	1886	*Recent Essays by Various Authors on Bacteria in relation to Disease, New Sydenham Soc.*, 1935, p. 327.
25	L. Rogers and J. W. D. Megaw ..	1935	*Tropical Medicine*, J. & A. Churchill Ltd., 2nd Ed., p. 271.
26	G. A. Hansen	1874	*Norsk. Mag. f. Lægevidensk.*
27	L. Rogers and J. W. D. Megaw ..	1935	*Tropical Medicine*, J. & A. Churchill Ltd., 2nd Ed., p. 314.
28	A. Whitmore	1913	*Journ. Hyg.*, **13,** p. 1.
29	A. T. Stanton and W. Fletcher ..	1921	*Trans. 4th Cong. Far East Assoc. Trop. Med.*, **2,** p. 196.
30	A. T. Stanton and W. Fletcher ..	1932	*Melioidosis*, John Bale & Sons, London, p. 36.
31	W. G. Liston	1924	*Brit. Med. Journ.*, **i.,** pp. 950, 997.
32	A. W. Bacot and C. J. Martin ..	1914	*Journ. of Hyg.*, Plague Supplement, **3,** p. 423.
33	F. P. Mackie and B. P. B. Naidu ..	1931	*Lancet*, **ii.,** p. 893.
34	Sir D. Bruce	1887	*Prac.*, **39,** p. 161.
35	B. Bang..	1897	*Z. f. Thier*, **1,** p. 241.
36	P. W. Bassett-Smith	1922	*Brit. Med. Journ.*, **ii.,** p. 902.
37	G. W. McCoy	1911	*Pub. Health Bull.*, No. 43, p. 53.
38	G. W. McCoy and C. V. Chapin ..	1912	*Journ. Inf. Dis.*, **10,** p. 61.
39	J. C. G. Ledingham and F. K. Fraser	1924	*Brit. Med. Journ.*, **i.,** pp. 950, 957.
40	Lee Foshay	1935	*Journ. of Allergy*, **6,** p. 360.
41	Lee Foshay	1934	*Amer. Jour. Med. Sc.*, **187,** p. 235.
42	H. Noguchi and T. S. Battistini ..	1926	*Journ. Exper. Med.*, **43,** p. 851.
43	E. Rixford	1894	*Med. Times*, **8,** p. 704.
44	A. Castellani	1905	*Journ. Ceylon Branch Brit. Med. Assoc.*, **2,** p. 38.
45	F. P. Mackie	1907	*Brit. Med. Journ.*, **ii.,** p. 1706.
46	P. H. Ross and A. D. Milne.. ..	1904	*Brit. Med. Journ.*, **ii.,** p. 1453.
47	W. Schüffner	1934	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **28,** p. 7.
48	G. Buchanan	1927	*Special Report Series No.* 113, *Med. Research Council*, p. 1.
49	N. H. Fairley	1934	*Brit. Med. Journ.*, **ii.,** p. 10
50	H. C. Brown and L. J. Davis ..	1927	*Brit. Journ. Exp. Path.*, **8,** p. 397.
51	K. Fataki, *et alia*	1916	*Journ. Exper. Med.*, **1,** p. 447.
52	C. M. Wenyon	1926	*Protozoology*, Baillière, Tindall & Cox, **2,** p. 945.
53	N. H. Fairley and R. J. Bromfield..	1934	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **28,** p. 156.
54	G. R. Ross	1932	*Researches in Blackwater Fever in Southern Rhodesia*, London School of Tropical Medicine and Hygiene, p. 223.
55	C. M. Wenyon	1926	*Protozoology*, Baillière, Tindall & Cox, London, **1,** p. 399.
56	H. Noguchi	1924	*Proc. Internat. Conf. on Health Problems in Trop. Amer.*, Boston, Mass., p. 455.
57	H. A. Penna	1934	*Brasil-Medico*, No. 46, p. 949.
58	L. E. Napier	1927	*Kala-azar*, Oxford Medical Press, 2nd Ed., p. 91.
59	L. Rogers	1912	*Brit. Med. Journ.*, **i.,** p. 1424.
60	L. Rogers	1921	*Bowel Diseases of the Tropics*, Henry Frowde, Hodder & Stoughton, London, p. 302.
61	T. P. Kilner	1931	*Proc. Roy. Soc. Med.*, **25,** p. 242.
62	A. C. Fischer	1934	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **28,** p. 277.

63	E. Brumpt	1927	*Précis de Parasitologie,* Masson et Cie, Paris, p. 530.
64	W. P. MacArthur	1934	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **27,** p. 348.
65	F. Dévé..	1913	*Compt. Rend. Soc. de Biol.*, **75,** p. 100.
66	K. D. Fairley	1923	*Med. Journ. Austral.*, **2,** p. 37.
67	N. H. Fairley	1922	*Quart. Journ. Med.*, **15,** p. 244.
68	H. R. Dew	1928	*Hydatid Disease : Austral. Med. Pub. Co.*, 1st Ed., pp. 153, 184, 230, 338.
69	C. D. de Langen	1928	*Meded. Dienst. d. Volkesgezondheit* in Nederl. Indie, **17,** p. 1.
70	J. W. S. Macfie and J. F. Corson ..	1922	*Ann. Trop. Med. Parasit.*, **16,** p. 465.
71	S. L. Brug	1927	*Geneesk. Tidjschr. Nederl-Indie,* **5,** p. 750.
72	A. H. McIndoe	1935	*Proc. Roy. Soc. Med.*, **28,** p. 45.
73	N. H. Fairley	1931	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **24,** p. 635.
74	J. Laigret	1929	*Bull. Soc. Path. Exotique,* **22,** p. 499.
75	R. P. Strong, *et alia*	1934	*Onchocerciasis,* Cambridge Howard Medical Press, p. 63.
76	N. H. Fairley and G. W. Liston ..	1924	*Indian Journ. Med. Res.*, **12,** p. 351.
77	E. C. Faust	1929	*Human Helminthology,* Lea & Febiger, Philadelphia, p. 326.
78	E. C. Faust	1929	*Ibid.*, p. 369.
79	C. A. Kofoid and J. P. Tucker ..	1921	*Amer. Journ. Hyg.*, **1,** p. 79.
80	P. D. Lamson and C. B. Ward ..	1932	*Journ. Parasitol.*, **18,** p. 173.
81	G. C. Low and G. R. M. Cordiner ..	1935	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **28,** p. 535.
82	A. E. Boycott	1928	*Univ. Coll. Hosp. Mag.*, **13,** p. 200.
83	E. C. Smith	1932	*An Atlas of Skin Diseases in the Tropics,* John Bale, Sons & Danielsson Ltd., London, p. 44.
84	H. A. Gilkes	1935	*Trans. Roy. Soc. Trop. Med. & Hyg.*, **27,** p. 491.
85	H. A. Gilkes	1935	*Ibid.*, p. 495.