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CHEMICAL DISINFECTION AND STERILIZATION

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PREFACE

MODERN science becomes daily more specialized—a factor unavoidable, owing to the enormous growth which this child of the mind has made during the last fifty years, yet one to which serious objections may be found.

The control of growth of micro-organisms is a problem which enters into many diverse and separate compartments of present-day science. The methods discussed and elaborated in one field are rarely introduced into another, although in a few cases the effect of environment on some original stock method may be readily discernible. For example, the whole problem of osmosis, originally a problem of interest to biochemists and botanists, is now the subject of much polemic discussion amongst physical chemists. The determination of P_H or the hydrogen-ion activity in solutions, originally a method devised and elaborated by electrochemists, is one of the chief corner-stones of modern physiological research.

The scientific principles underlying disinfection are simple and well known, but their application into the many diverse spheres in our private and corporate life has effected what appears at first sight to be an extraordinary transmutation of method. Closer investigation, however, reveals the fact that such changes are not only to be depicted, but are also necessary.

In the pages of this book an effort has been made to collect and summarize some of the more important applications of general methods which have interested the authors from time to time. Some apology is needed for the method of presentation. Although some of the problems which are briefly discussed are already dealt with *in extenso* in a wide and varied literature, others, equally important in their respective fields, are scarcely mentioned in current textbooks, and it was felt that the inclusion of even a brief summary between the covers of one volume would appeal to those whose interests cover this wide field, but who have neither access to, nor leisure to study, the very scattered literature on the subject. In addition, it is the hope of the authors that readers may be stimulated

to explore that fascinating but mysterious country wherein lie the secrets of the laws which govern the actions of germicides on micro-organisms.

Our best thanks are due to Mr. R. Orchard for his kind assistance both in proof-reading and in summarizing the laboratory data.

S. R.
E. K. R.

July, 1921.

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CHEMICAL DISINFECTION AND STERILIZATION

CHAPTER I

INTRODUCTION

Bacteria and Public Health.—Bacteria were discovered over two centuries ago by the Dutch naturalist Leeuwenhoek, but the first demonstrations of the causal relation of micro-organisms to disease were those of Pasteur in relation to silkworms and of Davaine on the bacillus of anthrax in 1863.

The relationship between bacteriology and Public Health in its widest sense has now been more fully developed, and at the present time the ramifications of the science stretch into every compartment of our daily life. The monumental work of Robert Koch, chiefly devoted to the study of organisms producing disease—*i.e.*, the pathogenic bacteria—has led to a closer study of the methods by which certain bacteria gain access to the body and there cause these zymotic diseases, and has indicated the way to preventive measures against infection. The bacteria given off by a diseased person may find their way into the systems of healthy people by a great number of paths. Occasionally this is brought about by direct contact, all the more dangerous in the case of the disease "carriers" who exhibit none of the usual disease symptoms, but have the power of transmitting it. Air currents may carry atmospheric dust or particles of water containing the germs. Certain diseases are transmitted through the air by means of insects which act as intermediary hosts, especially mosquitoes, flies, gnats, and fleas. These carry not only pathogenic bacteria, but many kinds of animal parasites, notably protozoa, which give rise to specific diseases. Animals, such as rats, are frequent transmitters of plague. Cats and dogs have been shown to carry diphtheria. Water is a frequent vehicle of certain disease germs, such as typhoid, cholera, and dysentery, which get into water-supplies from sewage contamination. Unlikely but occasionally, dangerous sources of infection are found in the soil, contaminated food, even bank-notes, tram and train tickets, hides, and rag flock.

Not only do certain micro-organisms produce diseases in the human system, but others may make food unsuitable for consump

tion by the production of by-products of a poisonous nature; this is especially true of " ptomaine " poisoning. Others cause diseases in plants and wood. Certain bacteria are of course used for technical purposes: in making alcohols and vinegar; again, in the tannery, bakeries, breweries, and dairies; other and minor applications are adopted for retting flax, fermenting coffee and cocoa fruits, and curing tobacco. Partial sterilization of soil has been known to increase the growth of crops. For many of these industries pure cultures of organisms must be used to produce the desired results. " Wild " cultures produced by infection frequently cause the loss of much valuable material.

It is evident that the chief methods of control of bacterial life are to be found in tracing the method of infection if it has arisen, and killing the organisms when found. Ideal disinfectants should be able to kill germs which act injuriously on higher forms of life without having any marked action upon such higher forms. A disinfectant must likewise be efficient in destroying the spores of pathogenic organisms, which as a rule are more resistant than the germs which form them. From this definition it will be evident that a disinfectant must do much more than prevent decomposition and remove the noxious smells which often emanate from putrefying matter. A disinfectant really goes to the source of the trouble and by killing the organisms prevents the spread of epidemic disease or the occurrence of the other evil effects of bacterial life which have already been alluded to. An antiseptic, on the other hand, prevents animal or vegetable substances from undergoing bacterial decomposition, and a body is said to be aseptic when it is in a condition of sterility. A substance which has the property of absorbing the unpleasant odours which are emitted from matter undergoing decay is called a deodorant, and such substances must be carefully distinguished from true disinfectants. Some disinfectants are deodorants; but a deodorant, unless of a permanent character, is not an antiseptic. It is true that in most cases a noxious smell accompanies decay, and therefore any substance which permanently removes the smell must necessarily cause the cessation of the decay; but in other cases in which there is no appreciable odour a deodorant would not be required. Charcoal is an example of a body that will absorb any unpleasant smell which may arise from organic matter, but which does not kill the germ producing the decay. Although commonly called a disinfectant, it should be more properly classed among the deodorants.

Natural influences are at work correcting and retarding any extensive growth of organisms. In tropical countries, strong sunlight is a most efficient germicide; recent investigation has shown

that it is the ultra-violet portion of the spectrum which is the most effective, and special apparatus has now been designed for sterilization by irradiation with artificial light of short wave lengths. By bacterial sedimentation during storage and dilution natural purification takes place in lakes and artificial reservoirs, while the washing away of organic matter and decomposing filth by rain-storms removes much of the pabulum which the bacteria need for thriving on. Pathogenic germs are frequently destroyed by the putrefactive or other products of the life of micro-organisms which are not directly deleterious to the human organism. Professor Metchnikoff's lactic acid bacillus is an organism of this nature. Desiccation in dry climates and severe cold in northern latitudes do much to restrict bacterial outbreaks, but are not, strictly speaking, natural disinfectors, but rather antiseptics.

Very early in the history of the human race we find the use of aromatic substances used to mask the presence of noxious odours. **Sulphur** has been employed from the earliest times, and many descriptions of its uses are given. Ulysses (Odyssey) says to his old nurse: "Old woman, bring me sulphur and fire in order that I may free the air of its poison and purify this palace." In the time of Hippocrates, sulphur was regarded as an antidote against plague. Ovid makes mention of the fact that sulphur was employed by the shepherds of his time for bleaching fleeces and for purifying their wool from contagious diseases. During the plague of Athens, Acron, according to Plutarch, stayed the spread of epidemic by lighting fires in the middle of the public places and in the streets where deaths had occurred, and the lighting of fires during times of plague has been customary until quite recent times.

H. Henriet asserts that he has proved the presence of traces of formaldehyde in the air, and considers that it plays an important part in the purification of the atmosphere. He finds that the quantity of formaldehyde varies between one and five parts by weight in 100,000 of air, and is proportional to the temperature.[1] The formation of sugars in the plant cell has been thought by Bayer to take place through the intermediary formation of formaldehyde, and lends some support to Henriet's investigations. In pine forests the gradual oxidation of the turpentine and other terpenes yields quite appreciable quantities of various peroxides, all of which have quite marked germicidal properties.

Ozone is found in the upper strata of the atmosphere. Its formation has been attributed to the photo-chemical action of the easily absorbed ultra-violet light of the solar spectrum.[2]

[1] *Compt. rend.*, 1903, **138**, No. 4; 1904, **139**, No. 1.

[2] E. K. Rideal, "Ozone." Constable, 1920.

The use of **copper** for sterilizing water is of an early date. The Sanskrit "Śuśruta Saṃhita," about 800 B.C., gives the following directions for storing water: "It is good to keep water in copper vessels to expose it to sunlight, and filter through charcoal"; while in the "Atharva Veda," probably of about the same date, it is stated that foul water may be cleansed by insolation and dipping hot copper into it. The Mosaic law, with all its minute instructions as to the purification of the people and their belongings, shows the same combination of religious ceremonial and sanitary precautions; this law undoubtedly contributed to the permanency of the Jewish race during its early history.

Almost contemporary with these hygienic requirements of very early times grew the knowledge of preserving food from bacterial decomposition. Probably the oldest form of preserving was by desiccation, and although the preserved flesh now extant in the form of the Egyptian mummies is preserved by desiccation with the aid of preserving chemicals and the exclusion of air, the preparation of meat dried and pounded with fat, as the South American "charqui," North American "pemmican," and South African "biltong," and the use of dried fruits such as raisins, figs, herbs, and notably hay, are very early examples of drying used as a preservative. It has been stated that sealed jars of preserved figs were discovered during the excavations of Pompeii. They still preserved "their delicate flavour and freshness."

The first discovery of the preservative use of **salt** was, no doubt, accidental, and due to the finding of carcasses embedded in the incrustations of the many saline deserts of Asia. Pliny describes salt as "defuncta etiam a putrescendo vindicans, ut durent ita per secula,"[1] and refers to "carnes sale adservatæ," flesh preserved with salt.[2] Columella (de Re Rustica) has "muriâ condire," to preserve with brine.[3] But at periods when fresh food was easily obtained, preservation was not so much a matter of importance, and therefore there are few early allusions to the use of salt, vinegar, and allied substances except as medicines or condiments.

The difference between various salts was confused, and the names given are difficult to identify. Thus in Jeremiah ii. 22, and in Pliny, **nitre** signifies crude carbonate of soda, since called **natron,** and later in Spain **barilla,** and although the real nitre or saltpetre was collected in India before the Christian era; the beginning of its use for reddening salted meats is of a very early date.

The Greeks and Romans made great use of salted fish, but mainly as an incentive to the consumption of wine. It was not

[1] *Hist. Nat.*, **33**, 9. [2] *Ibid.*, **33,** 10.

[3] The word *condiment* originally means a preservative, from this word *condire*.

likely that salting would be employed popularly, since salt was by no means plentiful, as shown by the word "salary" (salarium), or allowance of salt, coming to mean the payment of officials (Trench). Wine was frequently salted, or made with sea-water, with the object of keeping. Olives, samphire, and other vegetables were preserved in brine. Pickles of various kinds, ταρίχη, were used (Julius Pollux, book vi.).

Alum was known to the Egyptians as a drug, and its astringent and preservative action on flesh is mentioned. The effects of sulphur in fumigation are described by Homer.

Boric acid and borax were confused by the ancients with other salts, and valued only as fluxes in the arts. Asiatic borax was first refined at Venice. Boric acid was named by the alchemists "sal sedativus," but without reference to its preservative effect.

Aromatics, on the other hand, from being used for embalming, were eventually extended to food. These generally owed their properties to benzoic or cinnamic acid or to essential oils. Turpentine from *Pistacia terebinthus* (not from pines) was added to wine in Palestine, and is several times mentioned in the Bible. Among the Romans, **myrrh,** the gum-resin of *Balsamodendron myrrha,* which grew throughout the East, had a great reputation for preventing the souring of wine. Pliny[1] says: "Lautissima apud priscos vina erant murræ odore condita." Essential oils, aloes, and other bitters were also used.[2]

Bitter herbs were used from the first, and owed their virtues in preventing change partly to their tannin, which coagulated albuminous substances, and partly to essential oils and to alkaloids, which acted as antiseptics. Mugwort (*Artemisia vulgaris*), alecost (*Chrysanthemum balsamita*), and alehoof (*Nepeta glechoma*) derived their Saxon names from their preserving beer; wormwood (*A. absynthium*) was much used for vegetable juices on the Continent. Camomile, quassia, gentian, and hop are all bitters of the kind. Acrid substances like pepper were early employed as preservatives, particularly from insects. All these imparted their own strong flavour, and therefore their application was limited. "Cassaripe," the inspissated juice of the root of *Manihot utilissima,* is used by the natives of Brazil and the Antilles as a meat preservative.[3]

In northern climates the smoking of meats and fish was always practised, and oak or beech wood smoke was preferred, as these yield more of the preserving agents, acetic acid and creosote. The formation of an "empyreuma," or tarry liquor, from wood was early known, and to hasten the process the flesh was dipped

[1] *Hist. Nat.,* **14,** 13. [2] *Ibid.,* **13,** 15; *Palladius,* **11,** 14.

[3] *Zeitsch. oest. Apoth. Ver.,* 1900, 217.

in it before smoking, but in this way an inferior product was obtained.

With the growth of bacteriological science these older methods of preservation and sterilization have given way to newer ideas and practice, especially in the means of preservation employed for food, and the efficient sterilization of infection carriers, with a due appreciation of the means by which infection is carried, and very proper precautionary measures both in the sick-room and outside it.

The problem has resolved itself into a struggle for existence between man and inimical micro-organisms, which are known to have great vitality, powers of endurance, and facilities for penetration, accompanied by a stupendous fecundity. That a complete extermination of all microscopic life would not be desirable is evident from the industrial importance of some applications of mycology, while M. Schottelius,[1] as a result of his experiments on hatching sterilized eggs, is of the opinion that life itself is impossible without micro-organisms. On the other hand, from a study of technical mycology, one is driven to the conclusion that the enzymes secreted by the organisms, and not the organisms themselves, are the all-important bodies, and therefore Schottelius' contention is not strictly valid.

The means at our disposal for dealing with this problem are:

1. **Exclusion.** The rough methods of quarantine and sanitary cordons have not proved a success, since the ways of ingress are so many and wide, and the intolerable oppressiveness of these regulations leads certainly to their frequent evasion. The English methods of inspection and temporary closure of certain routes have proved much more effectual. Cholera killed many people, but it did an immense service to England by forcing us to protect our water supplies. The last, or personal, line of defence lies in the care and precautions taken by the individual. Cleanliness, fresh air, light, and good water are the chief.

In recent years it has always been shown that many, if not all, zymotic diseases may be excluded from the person by the introduction of special *toxins* into the individual, a process which renders him immune from the attacks of the organisms that produce the disease. These toxins are produced by the pathogenic organisms themselves, and, as already mentioned, are usually inimical to the growth of the organism, and may be regarded as their natural disinfectants. In view of these facts, Pasteur and his successors have cultivated the pathogenic organisms in broth and other media, and after sterilization have injected the liquid products as prophy-

[1] *Nat. Weis.*, 1912, 92. See also Guyenot, *Bull. Biol. Fr. et Belg.*, **51**, 1917; and Peters, *Jour. Physiol.*, Cantab., 1920.

lactics against various diseases. The virus can also be attenuated by passing it through different animals, or by special methods of taming, until, whilst still producing the toxins, it can be introduced into man without producing any dangerous symptoms, and thus can render him immune from fresh attacks, or place him in a position to develop the natural disinfectant sufficiently rapidly to kill off the pathogenic organisms, even after they have gained access to the blood. Roux, at Vienna in 1894, was one of the first to report a large number of cures of diphtheria by injecting a quantity of serum from the veins of a horse previously inoculated with Loeffler's diphtheria bacillus. Under the name of antitoxin, this diphtheria antidote is now a commercial article, and may be regarded as a special disinfectant for dealing with the organisms of this disease; whilst during the war success has attended the antitoxin treatment of tetanus, pneumonia, and influenza, and similar treatment is now of common practice for plague and typhoid.

2. **Removal.** Under this heading may be included the natural processes which obtain in a healthy individual, and artificial methods for improving his environment. It is now well established that the blood by its white corpuscles, as "phagocytes," or by its enzymes, has the power of assimilating and destroying bacteria and spores that find their way into it. If vigorous health be maintained, experience proves that a human being or animal may enjoy immunity for a time, even when in an infectious area. The limit to this protection may be reached when the micro-organisms overcome the phagocytes or other defensive substances in the blood. Many natural processes external to the individual, such as the self-purification of rivers, aid the higher organisms in this combat. Man, by artificial methods of subsidence, mechanical precipitation by inert matters, filtration, and chemical precipitation, supplements these efforts of nature to purify the water supplies.

3. **Destruction.** This is the office of real disinfectants, of which the physical agent heat is the most important. Next come the multitude of chemical disinfectants, many of which have been highly vaunted, but few of which are of actual value. A knowledge of the chemical constitution and relative position of these compounds throws considerable light on their mode of action; and recent progress in synthetical organic chemistry has been of great assistance in furnishing compounds of known purity and constitution, which have, at the hands of the bacteriologist, been shown to possess antiseptic and disinfectant properties of ascertained value. The number of these compounds is constantly on the increase, but at present it is difficult to predict, except in some few special cases,

in what direction the constitution of a compound influences its bactericidal behaviour. Pathogenic organisms have been proved to differ in their susceptibility to chemical agents, so that, for personal disinfection at any rate, some of the newer compounds may eventually be proved to be definite specifics.

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CHAPTER II

THE DISINFECTION OF AIR

In the early days of the development of the science of disinfection it was considered necessary to disinfect air, since at that time the air was regarded as the natural vehicle of disease germs. It is now generally realized that air-borne infection is extremely rare, non-contact cases being, however, occasionally observed, probably due to particles of dust or spray inhaled during coughing acting as vehicles for the disease germs. Although organisms in virtue of their small size can remain suspended in the air for long periods of time, being wafted about by the slightest air current, yet they rapidly die unless surrounded by some protecting coating such as a water or mucus film, when their rate of subsidence naturally increases. Light and the small quantities of naturally occurring germicides in the air, such as ozone and hydrogen peroxide in the country and acids in town air, are concomitant causes for rapid destruction.

The early experiments of C. Flügge[1] drew attention to the dangers attached to speaking loudly, sneezing, or coughing as an aid to the dissemination of germs. This work has been confirmed by numerous investigators, notably by P. Frankland.[2] In ordinary respiration, however, it has been shown by numerous observers that bacteria are arrested by the mouth, interior of the nose, and expelled by the ciliary membrane in the mucus to such an extent that expired air is almost free from organisms, while few of those inhaled reach the lungs.

In our laboratory at Westminster in 1914 we found 38 organisms in suspension per cubic foot, and they fell out of the air at the rate of 538 per square foot per hour. On another day, we found 110 organisms falling per square foot per hour, and 20 organisms in each cubic foot. The maximum variation was from 840 to 110 falling per square foot per hour. The number condensing with moisture on a vertical cooled plate varied from 95 to 135 per square foot per hour.

Winslow and Browne[3] undertook a very comprehensive bacterial

[1] *Zeitsch. Hyg.*, **25**, 1. [2] Eastbourne Health Congress, 1901.
[3] *Monthly Weather Review*, July, 1914, **42**, 452.

analysis of different sorts of airs, and came to the following conclusions:

1. The number of microbes developing at 20° C. from outdoor air in suburban districts is generally under 50 per cubic foot, and rarely over 100. The count at 37° C. for such air is about half that at 20° C., and rarely over 50 per cubic foot. The number of mouth streptococci in such air is small, averaging 10 per 100 cubic feet. The air from still more remote regions would no doubt show smaller numbers.

2. The air of city streets shows a slightly higher number of microbes, but the general relations are much the same in all the respects noted above.

The air of occupied spaces shows, as might be expected, larger average numbers of bacteria and much greater fluctuations. The number of organisms growing at 20° C. may average over 100 microbes per cubic foot, as in the factories studied, and may reach 700 or more, as in some offices. The 37° C. count averages over 50 both in factories and offices, and was nearly as high as the 20° C. count in the latter case. A few very high 37° C. counts were obtained, two between 1,000 and 2,000 in offices, and one of 5,200 in the country, the latter clearly abnormal. Mouth streptococci are much more abundant in indoor air, varying from 20 to 40 per 100 cubic feet of air, and the results bear out the conclusion that the number of these organisms furnishes a good measure of mouth pollution due to concentration of population in confined spaces.

Preliminary methods of air purification may be conveniently classified under the following heads:

1. **Heat.** When polluted air has simply to be got rid of, it can be passed through a furnace if care be taken that it all comes in contact with the heated surfaces. Experiments with refuse destructors have established that, although a comparatively low temperature is sufficient for killing micro-organisms, a temperature of at least 680° C. is essential for destroying organic noxious vapours. Heated channels are open to the following objections:—(*a*) If the air passes rapidly, there is danger that the central parts of the current will escape without being sterilized, on account of the bad conducting qualities of air; (*b*) the air so treated is rendered unfit to breathe; (*c*) the coils, if narrow, become clogged and coated; (*d*) they are uncertain in action, depending on the working of the stove; (*e*) if made of firebrick flues or fireclay tubes, instead of iron, they are easily broken in stoking, stirring, or cleaning; (*f*) they have been known to cause fires by passing near woodwork. Nevertheless, a method of this kind is cleaner, cheaper, and more effectual than any chemical disinfection for constant use.

2. **Washing with water,** with or without disinfectants. Numerous apparatus have been designed, with screens, bead-tubes, plates, fans, or bubbling-through arrangements. Screens constructed of vertical cords interlaced with horizontal copper wires, over which water trickles, are useful in dusty factories and in cases of dense fog; the air so purified is bright, clear, and free from odour, but dust is not entirely arrested.

3. **Air Filters.** Cotton-wool strainers are used at the Houses of Parliament; they can be made efficient, but require considerable motive power to impel the air. Asbestos filters can be renewed by burning, but are only practicable on a small scale. Sodium peroxide has been proposed for removing carbonic acid and renewing oxygen in confined spaces and in sick-rooms, but there is no disinfecting action.

It has already been indicated that infection is not, strictly speaking, air-borne, since in those cases where aerial contamination was indicated it has been shown to be due to the passage of organisms on floating dust or drops of water. Nevertheless, the air in rooms is frequently used as a vehicle for diffusing vaporous disinfectants on to the surfaces and into crannies and chinks in the walls of the room. In many cases the settling of organisms on drops of water and the adherence to wet wall surfaces is augmented by the injection of a spray into the room, together with the gaseous disinfectant.

4. **Sterilization of Air by Chemical Methods.** The chief volatile germicides used for this purpose are formaldehyde, sulphur dioxide, and more rarely chlorine and ozone.

(i.) Formic Aldehyde or Formaldehyde.

H.CHO is only known in solution, "Formalin," and in a state of vapour, since, if an attempt be made to condense it, it polymerizes to a white crystalline solid, paraformaldehyde or trioxymethylene, $C_3H_6O_3$. Formaldehyde is readily soluble in water, giving, if perfectly pure, a neutral solution; commercially it is always slightly acid, from the presence of a little formic acid.[1] The odour is pungent, causing irritation to the eyes and nose; beyond this action it is not poisonous. The aqueous solution is stable when kept in well-closed bottles, but loses some of the gas on exposure. Loew and Fischer, in 1886,[2] discovered that it possessed powerful antiseptic properties; Trillat, in 1888, showed

[1] G. Bruni states that the acid solutions are much more fatal to micro-organisms than the neutral ones (*Chem. Zentr.*, **51**, 1900).

[2] *J. pr. Chem.*, **33**, 221.

that the presence of a minute quantity of this substance in urine effectually preserved it from putrefying. In a further paper he remarks that " hitherto it has been thought that the most powerful antiseptic bodies belonged to the hydroxyl compounds of the aromatic series of hydrocarbons (the phenols) and to the metallic salts. Formaldehyde is, however, a very powerful antiseptic, being actually superior to bichloride of mercury in this respect. The result is quite unexpected, as acetic aldehyde does not possess this property."[1] It is prepared by passing methyl alcohol vapour mixed with air over a red-hot platinum spiral or heated platinized asbestos, condensing and purifying the vapours.[2]

Buchner,[3] Aronson,[4] and F. Cohn,[5] have investigated the properties of formaldehyde, while Lehmann, Gegner, and Blum[6] have examined its value as a general disinfectant, and Stahl,[7] Hauser,[8] and Liebreich[9] have reported on its suitability for special purposes. All these writers are agreed in attributing to formaldehyde powerful antiseptic and deodorant properties. Blum, however, points out that micro-organisms are only killed in somewhat strong solutions (2 per cent.). In 1894 C. Slater and the author confirmed Blum's statement.[10]

Cambier and Brochet showed that the vapour of formaldehyde produced by heating paraformaldehyde effects the complete sterilization of household dust.[11] Slater and Rideal[12] examined the action of the vapour evolved at 19° C. from a 40 per cent. solution by exposing to it glass slips of dry bouillon cultures under a bell jar. *B. typhosus*, *B. coli*, *M. prodigiosus*, and *Sp. cholerœ* were killed in less than ten minutes; *S. pyogenes aureus* in twenty; *B. pyocyaneus* in thirty minutes. As to the disinfection of rooms, 1½ ounces of 40 per cent. formaldehyde were evaporated by a spirit lamp in a room of 1,548 cubic feet (about 11½ feet side). The dust was disturbed by vigorous sweeping, then examined bacteriologically. After four hours' exposure to the vapour, the dust was again disturbed, and a sample examined. In other experiments threads soaked in various cultures were suspended at different heights and at about 3 to 5 feet from the source of the vapour. The results were not decisive, but showed marked effects from the vapour There is no reason why much larger quantities of the antiseptic should not be used. The air before disinfection contained 429

[1] *Moniteur Scient.*, 1892, 490.
[2] Trillat and Berlioz, *Compt. rend.*, **114**, 1278; **115**, 290; **119**, 563.
[3] *Münch. Med. Woch.*, 1889, No. 20.
[4] *Berlin. Klin. Woch.*, 1892, 749.
[5] *Botan. Centr.*, 1894, 573.
[6] *Münch. Med. Woch.*, 1893, 32.
[7] *Pharm. Zeit.*, 1893, 22.
[8] *Münch. Med. Woch.*, 1893, 567, 655.
[9] *Therap. Monatsch.*, **4**, 183.
[10] *Lancet*, April 21, 1894.
[11] *Compt. rend.*, **119**, 607.
[12] *Lancet*, April 21, 1894.

organisms for 10 litres, afterwards only 71. The threads after disinfection in all cases produced more scanty cultures, which grew more slowly. Some of those impregnated with *B. typhosus* and *B. coli* were sterile.

An important observation frequently lost sight of is that *Formalin* is an active germicide only in the presence of water vapour sufficient to prevent polymerization. This point has been investigated by A. Walker.[1]

Disinfection with formaldehyde has now become widely used, and a large amount of experimental work has been done on this subject.

In the Slater and Rideal investigation just recorded the quantity employed corresponds to 0·4 ounce formaldehyde per 1,250 ounces of air, or 0·032 per cent. by weight. As formaldehyde has practically the same density as air, this is also 0·032 per cent. by volume. There have since been introduced three distinct methods of applying formaldehyde to room disinfection, which possess advantages over the method then adopted. They are:

(1) **Mechanical Methods.** (*a*) Vaporizing paraformaldehyde by means of heat in the presence of water vapour; (*b*) spraying the walls, ceiling, and floor with the solution. (See Room Disinfection.)

(2) **Chemical Methods.** Vaporizing paraformaldehyde by mixing it with sodium peroxide or potassium permanganate.

(3) Methods attempting to increase the efficacy of the formaldehyde vapour by the addition of chemicals.

As a precaution to be noticed in adopting any method, it is necessary to efficiently seal up the room before disinfection. Paper should be pasted over the cracks round the doors and windows, and an efficient block placed up the chimney or in front of the grate aperture to prevent undue waste of the vapour. It is also important to ensure that the temperature of the room is sufficiently high to ensure proper sterilization; frequently the room is well ventilated before disinfection, and in cold weather the temperature may easily sink to 40° or 45° F. temperatures, at which the germicidal power of the vapour is very weak. About 60° F. is a convenient temperature for the purpose.

1. (*a*) Mechanical Vaporizers.

Trillat observed that, when heated under a pressure of two or three atmospheres, nearly the whole of the formic aldehyde in a solution may be evolved as gas without the polymerization that occurs when heated in the ordinary manner, and that the production

[1] *New York Med. J.*, October 19, 1912.

of the active gas is assisted by the addition of neutral mineral salts such as calcium chloride. His apparatus consisted essentially of an ordinary steam autoclave heated by means of gas or a Swedish petroleum lamp. "Formochloral," which is formalin of 40 per cent. containing in solution about 10 per cent. of calcium chloride,[1] is placed in the body of the apparatus, 1 pound being said to be sufficient for "an ordinary-sized room"—say 1,500 cubic feet. When a pressure of 35 to 40 pounds has been reached, corresponding to a temperature of 135° to 140° C., which takes about thirty minutes, the gas can be introduced into the sealed room by means of a fine copper tube or jet passing through the keyhole of the door, and controlled by the valve on the top of the autoclave, which is worked outside the room. According to the amount of the charge, from twenty minutes to one hour is required to discharge the gas, the pressure being maintained throughout the operation.

Dr. Kenwood obtained perfect sterilization of diphtheria swabs with this apparatus, and observes in his Leeds paper:

"(1) When the air is charged with from $\frac{1}{2}$ to 2 per cent. of formaldehyde, the disinfection of all surfaces is complete and rapid, and this holds good under the ordinary conditions of temperature and moisture obtaining in living-rooms.

"(2) The vapours possess a certain and variable amount of penetrating power into loose fabrics, especially when these are dry. This penetration is largely due to the circumstance that when produced in a warm state the vapour is of a low specific gravity and mixes well with the air.

"(3) That the vapours do not affect the colours of textile materials, etc., or (with the exception of iron or steel) metallic surfaces.

"(4) That the room and articles exposed can be cleared of the vapours readily by sufficient aeration, and the vapours are not so irritating but one can always enter the room and unseal at the first attempt (an advantage over SO_2 and Cl_2).

"(5) That the disinfecting properties of the aldehyde are greater than those of SO_2 or Cl_2.

"(6) That there is no danger in entering the room, either from the aldehyde or from the CO which is formed at the same time. This is proved from the fact that the men employed in the works and exposed to considerable quantities enjoy good health, and also from many experiments with animals in atmospheres heavily charged with the vapours generated as in room disinfection."

[1] Rosenau states that in similar apparatus in America 20 per cent. of calcium chloride, "or some other neutral salt, such as borax or common salt," is used, and that not less tha 10 ounces of the solution is allowed per 1,000 cubic feet.

Formaldehyde Lam s. It has already been shown that good results cannot be obtained by the simple evaporation of a concentrated solution of formaldehyde, as, owing to various causes, the maximum amount of the gas is not obtained. R. G. Wilson,[1] from experiments in railway carriages, concluded that the suspension of sheets moistened with undiluted formalin (40 per cent. formaldehyde) was wholly inefficient. The dry heated air caused further concentration and polymerization, so that the formaldehyde lost its volatility. A similar observation was made by Dr. Lübbert when working in tropical Africa.[2]

Many lamps for aerial disinfection have been proposed upon the principle that formaldehyde can be generated when the combustion of a mixture of methyl-alcohol vapours and air takes place over red hot platinum (Hoffmann). Such lamps have been devised by, among others, Tollens, Bartel, Robinson, Trillat, Broche, Schweinertz, and Dieudonné.

The objections to the use of the methyl-alcohol lamps are that the oxidation of the methyl alcohol to formic aldehyde is far from complete, the rate of generation and amount of the gas varying considerably with the same apparatus in different hands, and also that quantities of poisonous carbon monoxide are evolved in the room equal to 3 to 5 per cent. of the alcohol used. It is satisfactory, however, to notice that Dr. Kenwood has found that under proper conditions sufficient formaldehyde can be generated from 1½ litres of alcohol to disinfect a room of 2,000 cubic feet.

"It is most generally recommended that with these lamps about 2 litres of alcohol is sufficient for rooms of 3,000 cubic feet, and about six hours' exposure should be given."

The difficulties attending the direct production of formaldehyde from methyl alcohol *in situ* has led other investigators to endeavour to obviate the production of paraformaldehyde when using the formaldehyde solution. In America, the Chicago Board of Health uses a special spray producer devised by Dr. Behm, and has, therefore, given up all attempts at using lamps. The Massachusetts State Board uses a kind of autoclave, and this apparatus has been used by many of the Boards of Health in the States. It resembled very closely Trillat's autoclave, and the formaldehyde was first mixed with calcium chloride solution, which is meant to facilitate the retention of the water when the gas is generated. It would seem, from our own experiments, that formaldehyde to act as a disinfectant requires some water vapour, and, therefore, care must be taken not to generate the gas too dry; whilst, on the other

[1] *New York Bull. Med. Sciences*, October, 1901.

[2] *Therapist*, October 15, 1901.

hand, thorough penetration seems to be retarded when too much water is present.

Holzine is a 35 to 60 per cent. solution of formaldehyde in methyl alcohol, with 5 per cent. of menthol "to prevent formation of methylal." It was used in the Oppermann-Rosenberg apparatus, being evaporated from an asbestos plate by a few pieces of red-hot coke, and is also employed as a spray. K. Walter found that polymerization of the aldehyde was not prevented.[1] Krell's patent, 23,886 of 1900, rapidly pouring formaldehyde solution into a vessel in which a sufficient mass of heated metal had been placed to evaporate the liquid, is open to the same objection of waste by polymerization.

Paraformaldehyde was used, compressed into tablets, under the name of "paraform," by the Formalin Hygienic Company in their Alformant or "Schering" lamp. This was an ordinary spirit lamp with a large metal chimney supporting a perforated metal cup at about 4 inches over the flame. Some "paraform" tablets, weighing about 1 gramme each, are placed in the cup, and the moist products of combustion from the spirit pass up through the perforations, when the paraformaldehyde is volatilized chiefly as active formaldehyde. The directions given are to use at least ten tablets or 10 grammes of paraformaldehyde to every 1,000 cubic feet with six hours' exposure.

Dr. Kenwood succeeded in sterilizing swabs infected with *B. diphtheriæ* by using twenty-one paraform tablets in a room of 2,004 cubic feet with four hours' exposure.

One of the authors has had considerable experience with the paraform lamps, and details of his experiments were published in *Public Health*, November, 1897. A room of 1,500 cubic feet was first used to find the minimum quantity of paraformaldehyde which would disinfect, and it was found that:

(*a*) One gramme per 1,000 cubic feet did not kill *B. coli communis* when the room was sealed for four hours.

(*b*) Four grammes per 1,000 killed *B. coli communis* and *Staph. pyog. aur.* exposed on silk thread, but not when the cultures were soaked into paper slips, the room being sealed for six hours.

(*c*) With 8 grammes per 1,000 *B. coli communis* and *Staph. pyog. aur.* were killed on paper slips.

(*d*) Fifteen tablets per 1,500 cubic feet (10 grammes per 1,000) succeeded in killing *B. coli communis*, *B. typhosus*, *B. diphtheriæ*, *Staph. pyog. aur.*, when the room was sealed for twenty hours and the organisms exposed on silk threads, paper slips, and inside rolls

[1] *Chem. Zentr.*, 1896, ii., 119.

of linen which had been dipped into the cultures. *B. anthracis* and *B. subtilis* exposed in the same three ways were not killed in this experiment.

(*e*) Twenty tablets, equal to 13·3 grammes per 1,000, with *B. anthracis* and *B. subtilis*, both containing spores, failed to sterilize the silk threads or paper slips when they were exposed in the centre of the room on the same level as the lamp, but the *B. anthracis* exposed on a linen slip near the wall was found to be sterile. Room sealed twenty hours.

(*f*) With 20 grammes per 1,000 cubic feet, silk threads infected with *B. anthracis*, and exposed (1) 6 feet over the lamp and (2) near the wall, were sterilized. A dry paper slip similarly infected near the wall gave growths on subculture, but those from a wet slip were much attenuated and did not appear until the fourth day. An infected fold of dry linen similarly placed was not sterilized, but the organisms in another fold, wetted and then infected, were killed. Room sealed twenty-four hours.

In further experiments to determine whether it was necessary to remove infected fabrics from the room—in other words, to ascertain the penetrating power—it was found that, with 10 grammes per 1,000 cubic feet, pieces of damp linen infected with *Staph. pyog. aureus* culture, and placed in test-tubes plugged with cotton-wool, were not sterilized when they had been enclosed within eight folds of a heavy blanket, and when buried in the centre of a feather pillow; on the other hand, when 13·3 grammes per 1,000 cubic feet were tried, infected linen sealed in a sterile paper envelope exposed on a table in the room was sterile, and the infected linen from similar envelopes placed inside the pillow and between eight folds of the blanket did not give any growth of the staphylococcus after subculture, although in the last two cases the broth of the subculture became turbid from some other adventitious organism. Room sealed twenty-four hours.

In the above experiments there were obtained sufficient good results with 10 grammes per 1,000 cubic feet to warrant this quantity being used in all cases of ordinary disinfection, and if in special cases the walls and floors are in addition sprayed with a 0·5 per cent. formalin solution before using the lamp, we believe that disinfection will be ensured.

In a report to the London County Council dated February 10, 1902, on their experiments with paraform lamps, using 20 grammes of the tablets per 1,000 cubic feet for five hours, Drs. Klein, Houston, and Gordon state that "in cases where wood flooring, unpainted or unvarnished articles of furniture, or similar absorbing materials and cloth fabrics are to be submitted to disinfection on account of

their being possibly polluted with tubercular sputum, or highly resisting microbes like the spores of anthrax or other spores (*e.g.*, tetanus), the disinfection with formalin alone (in the method mentioned) will not suffice." It will be noticed that the time is not even that given in the directions for the use of the lamp in ordinary cases.

To disinfect goods like books and boots which were liable to be injured by steam, Dr. Charles Porter, at Stockport, placed them with an alformant lamp containing five tablets in the chest of a "Nottingham" steam disinfector of 200 cubic feet capacity. Dr. Symons, of Bath, used, either in spray or liquid form, 3 to 6 ounces formalin, followed by 2 ounces water, in a steam disinfector of 70 cubic feet, from which about two-thirds of the air had been exhausted, closing for at least one hour, then exhausting partially again and passing in 1 ounce of liq. ammoniæ a short time before opening.[1]

Most of these lamps relied upon the water obtained in the combustion of the spirit used for heating the solid paraform for supplying the necessary amount of moisture, but methylated spirit gives somewhat too small a quantity for the best results. This defect has been remedied in what is called the Hydroformant lamp, in which an annular vessel holding 12 ounces of water is fixed, and this water is converted into steam at the same time as the tablets are gasified. A somewhat more cumbersome apparatus, known as Flügge's, embodies the same idea, and is used largely in Germany. In connection with this apparatus, a second generator is employed, which is used for passing ammonia into the room seven or eight hours after the development of the formaldehyde, the ammonia combining with the latter to form hexamethylene tetramine, which is free from odour, before the room is opened.

Harrington states that the gas penetrates through dry pervious fabrics, but not always sufficiently to ensure germicidal action, and that when the fabrics are damp there is practically no penetration. He concludes that formaldehyde should only be resorted to for surface disinfection. Inasmuch as the vapour is so soluble in water, one would expect that materials previously moistened would absorb more of the gas than dry fabrics, and therefore show greater efficiency.

K. Walter made a series of observations in the Research Department of the 10th German Army Corps on the strength of formaldehyde solutions fatal to common forms of pathogenic bacteria. "With anthrax, cholera, typhoid, staphylococcus, and diphtheria 1 in 10,000 arrested growth, and slightly stronger solutions sufficed

[1] *J. San. Inst.*, January, 1900, 675.

to destroy. Fæces were deodorized and rendered aseptic by a 10 per cent. solution in ten minutes."[1] With regard to the vapour, although he concludes that it acts efficiently as a disinfectant on germs near the surface, he failed to secure sterilization of those more deeply situated.[2] Remarking that "steam in motion is more efficacious in penetrating objects than steam not in motion," in later experiments he passed formaldehyde vapour, together with steam, under pressure through a cylinder 130 centimetres long and 0·5 metre high containing the articles to be disinfected; by this method it was found that the formaldehyde penetrated to the interior. The mixed vapours were afterwards condensed, giving a solution adapted for washing floors and walls. He is still of opinion that the disinfection of a room and its entire contents *in one action* cannot be carried out by the vapour, "no matter by what method it is evolved, but that dresses, uniforms, and the like may be disinfected entirely and without injury by means of a current of formaldehyde vapour."[3]

In our own experiments we had already remarked the superior energy of a current and of moisture, bearing in mind that the convection current passes up from the lamp and down the walls; in fact one of the advantages we have indicated for formaldehyde is its ready diffusibility and solubility in water, so that if the room is properly sealed it is only a question of time and quantity when the formaldehyde shall have completely diffused through the air and impregnated all the moisture in the chamber. These experimental details are conditions of every species of disinfection; they are easily attained, but not often observed. At the same time, if the fabrics are considerable in number and volume, since the surfaces absorb a correspondingly greater amount of vapour, it will be necessary to employ a larger quantity of the reagent, or it may be even desirable to specially disinfect them in an apparatus such as Walter recommends.[4]

A formaldehyde diffuser, known as the Kalzen, consists of a thick tube which is made inflammable, and burns with a smouldering flame sufficient to vaporize a paraformaldehyde charge placed in the container. Provision is made for evolution of steam at the same time.[5]

[1] *Zeitsch. Hyg.*, **21**, 421.

[2] *Chem. Zentr.*, 1896, ii., 119.

[3] *Zeitsch. Hyg.*, **26**, 454-475; *Chem. Zentr.*, 1898, i., 306; *J. Soc. Chem. Ind.*, April 30, 1898.

[4] *Münch. Med. Woch.*, 1899, **46**, 1535.

[5] *J. Soc. Chem. Ind.*, June, 1907, 626; *Public Health*, August, 1905, 704; *Sanitary Record*, March, 1911, 257.

2. **Chemical Methods.**

(*a*) **Formalin Permanganate Method.** A method simpler in operation than the process of vaporization in lamps or spraying is the chemical method originally suggested by Evans and Russell. The method consists in mixing crystalline potassium permanganate with a certain quantity of formalin. A part of the aldehyde is oxidized to formic acid, usually about one-fifth; there is a considerable heat evolution which vaporizes the formaldehyde and water. The success of the operation depends chiefly upon the relative amounts of formaldehyde permanganate and water in order to ensure the proper vaporization of the formaldehyde. Kenwood describes the method by which he has obtained good results: 142·5 grammes of potassium permanganate are placed in a metallic dish (which should be about 7 inches in diameter and from 3 to 4 inches deep), and twice the weight of formalin is then poured upon the permanganate. Dorr and Raubitschek advise using per cubic yard of room space $\frac{3}{8}$ pint of formalin (40 per cent.), $\frac{3}{4}$ ounce of potassium permanganate, and $\frac{3}{8}$ pint of water. Lockemann and Croner[1] modify the mixture by using for the same space $\frac{7}{8}$ ounce of permanganate, $\frac{1}{2}$ pint of formalin, and $\frac{1}{4}$ pint of water. We have found the ratio of 40 grammes of permanganate to 100 c.c. of formalin an effective mixture. Lockemann and Croner have also advocated a mixture of paraform and permanganate with bicarbonate of soda; this mixture requires simply the addition of water to generate the formalin vapour. Major Munson has obtained up to 86 per cent. formalin vaporized by this method, but in general practice not more than 50 to 60 per cent. is generally obtained.

(*b*) **Formalin Peroxide Method.** This method, originally introduced by Eischengrun,[2] is known generally as the "Autan" method. The mixture consists of about 30 per cent. paraformaldehyde with 10 to 15 per cent. sodium bicarbonate, to which is added about 60 per cent. barium peroxide. About 50 grammes of the mixture are used per cubic metre of room space. On mixing with water, the oxidation of part of the formaldehyde proceeds energetically, and the rest of the formaldehyde is vaporized with large quantities of water. According to Auerbach and Pluddemann, 3 parts of formaldehyde must be oxidized to vaporize 1 part with the necessary quantity of water (about 6 parts of water to 1 part of formaldehyde).

(*c*) (i.) The addition of quicklime has been suggested for evolving formaldehyde from its solution, but in experiments with

[1] *Desinfektion*, 1909, 11-12.

[2] See also R. P. Crandall, *U.S. Naval Med. Bull.*, 1917, **11**, 519.

this dehydrating agent we have obtained only 8 per cent. of the theoretical yield, so that the heat evolved by the union of the lime with the water is sufficient to polymerize a large quantity of the gas.[1] Fused calcium chloride and concentrated sulphuric acid also gave very little gas. When lime is added to the formaldehyde solution, calcium formate is produced, and probably, therefore, some methyl alcohol, according to the equation—

$$2CH_2O + H_2O = CH_3OH + H.COOH.$$

(ii.) For local application an addition of glycerine seems to present advantages, on account of its remaining moist, and therefore penetrating porous materials and retaining the formalin, in addition to its own antiseptic power. R. Walther and A. Schlossmann, using Lingner's apparatus, by which a mixture of 75 per cent. formalin, 15 per cent. water, and 10 per cent. glycerine, called "glycoformal," can be sprayed into a room until a thick fog results, using about 4 pounds of mixture per 1,000 cubic feet (= 544 grammes CH_2O, or 1·4 per cent. in the air), and closing merely in the ordinary manner, reported that they succeeded in sterilizing a number of objects of the most refractory character and of considerable thickness, while live animals were not injured.[2]

(iii.) Other addition agents which have been tried and suggested from time to time are alcohol, acetone, and some organic acids, chiefly of the fatty series. The intent of these addition agents is to increase the penetrative power of the formalin itself. Fournier introduces acetone, ammonia, and water in the form of a fine spray into the room previous to the introduction of the formalin.

To obtain complete sterility of the walls and floors large quantities of formalin would be required. In general practice this aim need not be accomplished provided that the destruction of all pathogenic organisms is ensured. The experiments of Werner, Rose, Aronson, and others have shown that under normal conditions of disinfection with formalin vapour, provided that the recommendations as regards temperature, moisture, sealing of rooms, etc., are adhered to, anthrax spores and also tubercle bacilli in sputum may be rendered inactive even if the formalin be subsequently removed by ammonia or other means.[3]

[1] Bolten (*Pharm. Weekblad*, 1918, **55**, 60), on the other hand, claims the lime process to be more efficient than the permanganate process.

[2] *J. pr. Chem.*, **57**, 173, 512.

[3] *Trans. Fifteenth Int. Cong. of Hygiene*, Washington, 1913, 756.

In addition to permanganate and barium peroxide other oxidizing agents have had a limited application, such as sodium dichromate, suggested by S. G. Dixon;[1] sodium chlorate, employed by C. G. Stone,[2] and especially bleaching powder. This method has been extensively developed in America, when early experiments were conducted by D. W. Horn.[3] Hamilton[4] obtained bad results with bleaching powder as an oxidant, and states that only chlorine was evolved. Pozen and Dieter,[5] on the other hand, submitted all these chemical methods to an exhaustive bacteriological test, and came to the conclusion that under the proper conditions of operation this method was as effective as any other and more economical in operation. They confirmed the poor results obtained with the aid of lime. They give the following quantities of reagents as effective in sterilizing 1,000 cubic feet of room space:

Permanganate Method.

Formalin ..	.. 1 pint
$KMnO_4$ ..	.. 0·5 pound

Sodium Chlorate Method.

Formalin ..	.. 1 pint
$NaClO_3$ ..	.. 6 ounces

Chlorinated Lime Method.

Formalin ..	.. 1 pint
Chlorinated lime ..	$\frac{5}{6}$ pound

Barium Peroxide Method.

Formalin	.. 1 pint
Barium peroxide	$1\frac{1}{2}$ pounds

Dichromate Method.

Formalin	.. 1 pint
$Na_2Cr_2O_7$	.. 10 ounces
H_2SO_4 ..	.. $1\frac{1}{2}$ fluid ounces
Glycerine	.. $1\frac{1}{2}$ fluid ounces

(ii.) SULPHUR DIOXIDE.

Sulphur dioxide or sulphurous anhydride, SO_2, is a colourless gas of specific gravity 32 (air = 14·45), with the well-known odour of burning sulphur. One litre weighs nearly 3 grammes. It is obtained by burning sulphur or a sulphide in air—

$$S + O_2 = SO_2.$$

One kilogramme of sulphur gives 700 litres of the gas.

It is irrespirable, producing violent coughing and suffocation. About 5 per cent. in air has produced fatal results, causing acute catarrh, acid eructations, anorexia, irregularity of the bowels, and permanently impaired digestion (Hirt, Eulenberg, etc.), but $\frac{1}{2}$ per cent. can be endured for a length of time. A wet towel moistened with washing soda enables a larger amount to be faced.

One litre of water at ordinary temperature dissolves 50 litres, or 145 grammes, producing an acid liquid containing the unstable H_2SO_3—

$$SO_2 + H_2O = H_2SO_3.$$

[1] *J. Amer. Med. Assoc.*, 1915, **64**, 459.
[2] *J. Ind. Eng. Chem.*, 1918, **10**, 123.
[3] *Amer. Pub. Health*, 1918, **8**, 161.
[4] *Ibid.*, 1917, **7**, 283.
[5] *J. Ind. Eng. Chem.*, 1919, **11**, 448.

This liquid smells strongly of the gas, as, gradually at ordinary temperatures and rapidly on heating, it decomposes again into sulphur dioxide and water. Hence it rapidly loses its strength unless well stoppered. (It only slowly attacks corks, so that it can be kept in a corked bottle.) In the anhydrous state SO_2 is not disinfectant; on adding water it becomes active; hence the term "sulphurous acid" will be used throughout for this agent, as more familiar and accurate. It acts in four ways:

1. As an acid it absorbs ammonia, compound ammonias, and organic bases like "ptomaines" and the products of growth of pathogenic organisms. The salts so formed (sulphites) are much less injurious. It has this property in common with other acids.

2. It decomposes sulphides and sulphuretted hydrogen, with the liberation of sulphur.

3. It reduces organic matters, or combines with them to form compounds which are in most cases inert. This explains its bleaching action on vegetable colours, as the compounds formed are nearly colourless. But the action is evanescent, as on exposure to air it is oxidized to sulphuric acid, and the colour often reappears.

4. As a poison it kills living organisms.

The gas can be easily condensed to a colourless liquid by pressure, and preserved in strong metal vessels. About 3 atmospheres (45 pounds on the square inch) is sufficient. This liquefied gas is attainable in any quantity at a cheap rate, and is much more convenient to employ than sulphur. The vessels are opened by a lever attached to a screw. The gas will flow steadily for forty hours, a single siphon evolving 500 litres of gas, equal to the amount obtained from about 1½ pounds of sulphur. It can also be obtained in hermetically sealed tins which are sufficient for the disinfection of a small room. The gas is obtained by cutting with a knife the soft metal pipe attached to the tin. Each tin contains about 20 ounces of liquefied gas, and is stated to be sufficient for the disinfection of a room 12 feet cube (1,728 cubic feet).

The Governments of England, United States, Belgium, France, Austria, Sweden, and some others prescribe fumigation by burning sulphur for infected rooms. Hence, as Arnould says, it is the "official disinfectant *par excellence*." Germany, amongst European nations, however, does not recommend it officially, and in Berlin sulphur disinfection is not much employed. The British Local Government Board prescribed that for a moderate-sized room 1½ pounds of sulphur should be burnt over a small fire and the room kept sealed for six hours or more. (As 1 pound of sulphur yields 11·7 cubic feet of SO_2, the above quantity would give 1·75 per cent. in the air if the room were 1,000 cubic feet.) The wall paper

is then to be stripped off and burnt, and the ceiling and floors thoroughly washed, etc. The Society of Medical Officers of Health suggested also that bedding and clothes should be spread out on lines, that the sulphur should be burnt over a pail of water to supply moisture, and that the time should be twenty-four hours. Other official recommendations were: Belgium, 20 to 30 grammes per cubic metre = 2 to 3 per cent. SO_2 in the air; Paris, 20 grammes per cubic metre for forty-eight hours; American Committee on Disinfection, 1885, *at least* 4 per cent. SO_2 for twelve hours in presence of moisture, equal to $1\frac{1}{2}$ to 2 kilogrammes sulphur for every 28 cubic metres (about 1,000 cubic feet). For ships arriving in the Mississippi from infected ports, the cargo is sprayed with corrosive sublimate solution, but sulphur fumigation is used for the hold. A battery of eighteen furnaces contained in a specially constructed tug is used for heating the sulphur, and the gas mixed with air is forced into the hold at the rate of 180,000 cubic feet per hour by means of a fan. One hundred to 1,700 pounds sulphur is used for each vessel, according to size.

The sulphur flame is very liable to extinction, and various devices have been introduced to remedy this defect. Corfield and Louis Parkes burn it in an iron vessel with a little spirit. Nicholls and Billyen, and also Vallin, use 8 parts of flower of sulphur, 2 or 3 of nitre, and 2 or 3 of bran or liquorice powder. This would give a deflagration, would retain much of the sulphur in the residue as sulphate, and would result in rather too rapid an evolution, so that the inevitable leakage would be greater. Another plan is to place it on an iron tray and throw a shovelful of red-hot coals on it. When this plan is adopted, there is usually a residue of unburnt sulphur left. A chafing-dish of coals, *properly protected*, with an iron tray over it, and lumps of sulphur distributed, gives better results. Even with these devices it is almost impossible to keep up a combustion sufficiently long, and some of the sulphur is wasted by being sublimed. Mendeljeff also points out[1] that the sulphurous fumes, being given off hot, ascend to the ceiling, where they may be absorbed by the plaster, while some time is required for the gas to reach the lower portion of the room where it is most required. Hence the liquefied gas, excluding, as it does, the risk of fire, is much to be preferred.

T. A. Clayton has designed a large apparatus for generating SO_2 by combustion, and for using the gas in the hot state if required.[2] Moore and Martin's U.S. patent, 700,537 of 1902, is another large generator.

[1] *Principles of Chemistry*, 40.

[2] Patent 4,892 of 1902. *Pub. Health Engineer*, April 19, 1902.

Kingzett's sulphur candles are made in the form of a night-light, and are placed in a water-jacket as a precaution against fire. They are made of sulphur with a "powerful oxidizing agent" and a wick, and are arranged to burn two hours. They are very convenient if a sufficient number are used, and the cost is moderate.

Seabury's sulphur candles[1] also burn two hours, and differ from the above in having a large compound wick. Morse and Bourne's patent, Wade's, and Shaw's U.S. patent, 698,748 of 1902, affect various details in the candles.

There has been a great conflict of opinion on the value of sulphurous acid disinfection. Vallin[2] pronounced it perfect; Arnould[3] says that "sulphurous acid, even in the almost inapplicable dose of 10 per cent., is an uncertain means of destroying spores; even moisture does not ensure success." Dr. Cassedebat, after a research at the Marseilles School of Medicine,[4] remarks: "Even in the highest dose it is too inconstant to be recognized in the disinfection of virus." Savarelli[5] condemns it. Miquel could not kill germs in twenty days.[6] Sternberg's experiments[7] were unfavourable: "It requires special conditions rather than abundance." Dr. A. J. Martin[8] says "its efficacy is contestable, without counting its public nuisance."

Dujardin-Beaumetz,[9] who studied the behaviour of this gas with Pasteur and Roux, found that 20 grammes of sulphur, as used in the official French fumigation, did not kill *Bacillus anthracis*, though it sterilized tubes of vaccine.[10] Since Wolffhügel's experiments[11] in 1881, sulphurous acid has quite lost its reputation in Germany. Koch[12] obtained indifferent results; he spread the spores about in a room where sulphur was burnt, or laid them on boards, which were then washed or sprayed with a solution of sulphurous acid and tested by transference to culture solutions or by inoculation.[13]

Dubief and Bruhl[14] state that "sulphurous acid has the most destructive effect on aerial microbes, especially moist, acting mainly on the spores of bacteria, and when pure and acting for e long period, it may prove fatal to dry germs."

M. d'Abaddée states that of the Sicilian labourers engaged in

[1] Patent No. 6,407, 1893.
[2] *Traité des Désinfectants.*
[3] *Hygiène*, 1889, 501.
[4] *Rev. Hyg.*, 1891.
[5] *Giorn. Soc. Ital. d'Hyg.*, 1890.
[6] *Les Org. vivants de l'Atmosph.*, 1883, 289 *et seq.*
[7] *Med. News of Philadelphia*, March 28, 1885.
[8] *Soc. Med. Publique*, 1892.
[9] *Bull. Acad. Med.*, September 9, 1884.
[10] See Rochard's *Encyclopædia d'Hygiène*, 1893, **5.**
[11] *Mittheil. Kais. Gesundh.*, **1**, 188,
[12] *Ibid.*, p. 234.
[13] Wolffhügel and Proskauer, *Chem. Zentr.*, **13**, 334.
[14] *Compt. rend.*, 1889.

sulphur works only 8 or 9 per cent. suffer from intermittent fever, as against 90 per cent. of those not so occupied. The sulphur works in the marshy plain of Catania protect the people in the vicinity from an evil that causes other villages to be deserted.[1] This tends to prove that sulphurous acid is strongly antagonistic to malaria.

Dr. P. Frankland[2] found that it killed several pathogenic organisms. Baumann destroyed *B. tuberculosis* with it, and formerly cases of early phthisis were treated by burning sulphur.

Drs. Marsh and Watkins-Pitchford, from trials in an experimental room of 1,152 cubic feet at the Government Research Laboratory, Bombay, in June, 1898, reported that the contents of a cylinder of compressed SO_2 destroyed the plague bacillus in twenty hours, even when protected by one to three thicknesses of cotton or linen, or by thin coverings of earth, wool, leaves, or paper.

Klein has furnished a key to these discrepancies by showing that although "most pathogenic microbes do not thrive in an acid medium, some putrefactive and zymogenic organisms can thrive well in acid—*e.g.*, *Bacillus subtilis*, *Micrococcus ureæ* in acid urine, etc."[3] Therefore, sulphur disinfection, though generally successful, may sometimes fail. Wynter Blyth is also of the same opinion.

M. Thoinot sums up thus in his *Report to the Committee of Public Hygiene of the Seine*, 1891: "The disinfection by sulphurous acid is only a practice of waiting, but it is a good practice, and ought not to be despised."[4]

One of the authors has experimented on the disinfection of rooms, using the liquefied gas, and the results obtained may be briefly summarized as follows: Silk threads and paper slips infected with *B. coli communis* and *Staph. p. aureus* were sterilized after twenty-four hours' exposure in a sealed room of 1,500 cubic feet, into which 20 ounces of SO_2 were passed. *B. subtilis* spores were not killed. Using 10 ounces of the gas, the silk threads infected with *B. coli communis* and *Staph. p. aureus* were again sterilized, but the paper slips were not. An important point was brought out by a repetition of this experiment, exposing shallow pans of water in the room in order to moisten the air during the disinfection; the SO_2 content of the air of the room was actually lowered after the twenty-four hours, through absorption by the water, from 0·5 per cent., present in the previous experiment, to 0·2 per cent.,

[1] *J. Soc. Chem. Ind.*, **1** 515.

[2] *Proc. Roy. Soc.*, **45**, 292.

[3] *Micro-Organisms and Diseases*, 1886, p. 258.

[4] See also Klein, Lawes, and Lingard in *Report of M. Off. of Local Gov. Board*, 1884, on "Chlorine and Sulphurous Acid on Swine Fever Virus"; and Crookshank's *Bacteriology*, 1887, p. 150.

and the *B. coli* and *Staphylococcus* were not destroyed either in the paper or silk threads. Disinfection with liquid SO_2 can be used for all purposes for which burning sulphur is efficacious, and possesses the advantages over the latter of freedom from risk of fire and convenience in application. The quantity of aqueous vapour normally present in the air in England is sufficient to ensure the activity of the gas, and the above experiment shows that the exposure of large wet surfaces is to be avoided.

An objection to the use of sulphurous acid is that non-volatile sulphuric acid is left behind as a result of oxidation. This acid is liable to corrode metal work and fabrics submitted to the disinfecting process.

(iii.) Chlorine.

About the year 1800, Guyton de Morveau in France, and Cruikshank in England, proposed the use of chlorine as a disinfectant. Cruikshank suggested 2 pints common salt, 1 pint powdered manganese dioxide, with 1 pint water and $\frac{1}{2}$ pint sulphuric acid gradually added, for hospital disinfection, giving the amount required for a certain number of beds.

A similar method of generating chlorine is to gently warm 1 part of manganese dioxide in a granular form with 4 parts of concentrated hydrochloric acid (5 grammes MnO_2 and 20 grammes HCl give 1 litre of Cl_2; $\frac{1}{2}$ ounce of MnO_2 is abundance for a large room).[1] Letheby recommended one teaspoonful of powdered manganese dioxide and half a cupful of strong crude hydrochloric acid, mixed by degrees by stirring in a saucer set on a hot brick.

It should be remembered that the crude acid contains arsenic, which would be evolved as the intensely poisonous arsenious chloride; hence, at a little additional expense, pure acid only should be employed.

Each of these methods requires heat, which presents great difficulties in application. Usually, therefore, the chlorine is evolved from chloride of lime by the action of moderately diluted sulphuric or hydrochloric acid. It has been stated[2] that 1 part bleaching powder with 2 parts sulphuric acid of specific gravity 1·53, and enough water to cover the powder, evolved three times as much chlorine as when hydrochloric is used. This may be due to the heat generated by the sulphuric acid, as the amounts yielded are theoretically the same, as the following equations show:

$$CaCl_2O + H_2SO_4 = CaSO_4 + H_2O + Cl_2.$$
$$CaCl_2O + 2HCl = CaCl_2 + H_2O + Cl_2.$$

[1] Reichardt, *Desinfectionsmittel*, p. 65. [2] *Lancet*, 1888, 110.

If the insoluble, and therefore solid, sulphate of lime keeps back less chlorine than does the deliquescent calcium chloride, the difference in the yield might be explained.

Dr. Mehlhausen[1] of Berlin used 600 grammes of bichromate of potash and 3 kilogrammes of pure hydrochloric acid, of specific gravity 1·16, for generating chlorine. These weights yield on warming 130·6 litres (405 grammes) of chlorine. He traced a somewhat greater activity to the gas than when prepared by the ordinary processes; this may, perhaps, be due to some chromyl chloride (CrO_2Cl_2) evolved in addition. The cost of this method prevents it from being generally employed.

Chlorine has three possible modes of action:

1. Especially when concentrated, it can combine directly with organic matters, or replace the hydrogen in them, precipitating all albuminous substances and rendering them imputrescible, while at the same time killing microbial life by combining with and coagulating protoplasm. Many of the substituted chloro-compounds are also inimical to bacteria; some of them, such as "chloropicrin," $C(NO_2)Cl_3$, have very pungent odours. Such action would be slow, would scarcely occur at all except in sunlight, but yet would be the only possible action on dry matter. It may account for the antiseptic action of chlorine, as distinguished from its disinfecting power; the former has been questioned, but the experiments of Baxter and Sternberg on dried vaccine lymph seem to be conclusive.

2. The offensive gases of putrefaction are decomposed by chlorine, sulphuretted hydrogen being resolved into sulphur and hydrochloric acid—

$$H_2S + Cl_2 = 2HCl + S.$$

Phosphoretted hydrogen would be also decomposed. Ammonia (and compound ammonias) would give first of all ammonium chloride and nitrogen—

$$8NH_3 + 3Cl_2 = 6NH_4Cl + N_2,$$

hence the copious white fumes frequently noticed when a chlorine mixture is thrown into a dung-pit. More chlorine decomposes the ammonium chloride first formed; when this takes place, there is always a formation of intensely acrid vapours which attack the eyes and lungs, owing to the production of chlorides of nitrogen and compounds like chloropicrin. In dealing with cesspools, ash-bins, or privies this becomes strongly prominent in chlorine disinfection. Marsh gas and some other hydrocarbons are not readily attacked by chlorine, but usually also are less objectionable than the gases mentioned above.

[1] *Bericht der Cholera Commission*, 1879, **6**, 335.

3. The common and most important action of chlorine is as an oxidizing agent. In the presence of water, more especially in light, it combines with hydrogen to form hydrochloric acid, and liberates oxygen—

$$2H_2O + 2Cl_2 = 4HCl + O_2.$$

The oxygen so formed is far more active than atmospheric oxygen, and is in a condition to burn up the putrescent matters and kill the organisms which accompany the putrefaction. But there are several requirements for thorough disinfection in this way, and amongst these (*a*) **moisture** is shown by the above equation to be an essential, while (*b*) **light** is strongly assistant.

(*c*) **Quantity.** Baxter was one of the first to state that the disinfecting action of chlorine and of potassium permanganate depends much more upon the nature of the liquid than upon the specific organism present. Kuhn, Bucholtz, and Haberkorn confirmed this view. They showed that in a fluid like urine, which consumes large quantities of chlorine, even though the liquid be deodorized, the action on organisms is only feeble until the chlorine is in excess, and that it must be maintained in excess until the last germ is destroyed, otherwise the fermentation will recommence. But if the action has been completed, germs that may afterwards enter from the atmosphere find it an unsuitable medium for growth. From this it follows that the smell of chlorine must be perceptible and persistent for some time, or no good result will have been obtained. Excess of chlorine may be chemically tested for by a paper dipped in a solution of iodide of potassium and starch paste, which is turned blue by free chlorine, or the bleaching of litmus paper may be used as an indication.

Baxter in his experiments mixed chlorine with vaccine lymph, and found that the activity of the latter was not destroyed till it had become acid from the presence of free HCl. Most putrefactive organisms thrive best in alkaline solution; hence the antiseptic power of all free acids in varying degrees.

To kill pure vaccine, Baxter found the minimum proportion of, chlorine to be 0·2 per cent. (*i.e.*, soda chlorinata solution, B.P. 1 in 10; chloride of lime, 1 in 100, both acidified). Hofmann[1] gives 0·15 per cent. as sufficient for septic virus.

(*d*) **Time.** The vitality of the organisms considerably influences the length of time required for sterilization. Sternberg[2] found that 1 per cent. of chlorine in air in six hours made dry vaccine inert. This is a very large quantity, for a room of 50 cubic

[1] *Vierteljahrsschrift fur gerichtliche Medicin*, April, 1878.

[2] *Bulletin of the U.S. Board of Health*, Washington, 1881.

metres would require at this rate 5 kilogrammes of bleaching powder, even if all the chlorine were evolved, which is generally impossible. Baxter stated[1] that air saturated with chlorine by standing over the aqueous solution took thirty minutes to sterilize needles charged with dry vaccine.

These are impossible conditions in practice. Living organisms themselves contain 90 to 95 per cent. of water, hence the disinfectant entering them would be greatly diluted. Moreover, their envelopes are often tough and resisting, especially those of spores. Therefore more time must be given.

Fischer and Proskauer,[2] from laboratory experiments on spores of anthrax and various bacteria, concluded that for air fumigation at least 0·54 per cent. of chlorine must be present, and considered it more efficacious than sulphurous acid. The experiments of Jalan de la Croix[3] on the putrefying bacteria of beef-tea gave a surprisingly favourable account of the power of chlorine among the agents which are fatal to low organisms, and placed it next to corrosive sublimate as an "antivirulent."

Vallin[4] threw some doubt on these researches, and asserted that the antivirulent action of chlorine is relatively restricted, and is notably inferior to what would be presumed by the figures given.

Dr. Mehlhausen[5] made a number of experiments, of which the following is an abstract:

I. In a room of 37 cubic metres, with door and window sealed, he placed a number of insects in gauze enclosures, and two vessels of water teeming with vibrios, rotifers, and infusoria. An earthen pot containing 740 grammes (20 grammes per cubic metre) of bleaching powder with a little water, to which he added 1,100 grammes of hydrochloric acid, was also introduced and the door sealed. After nine hours the room was opened and ventilated. The animals were all living; the flies only were insensible, but recovered on the next day. The water in the vessels, originally neutral, had become acid, and gave with nitrate of silver a copious precipitate of chloride. All the bacteria were dead. The 740 grammes of chloride of lime had given 59·7 litres of chlorine—*i.e.*, 1·613 litres per cubic metre, or 0·1613 *per cent.* in the air (about the amount mentioned by Hofmann, as above given), whilst some had been undoubtedly wasted by non-evolution and by leakage.

II. With the same conditions as before, but with double the amount of chlorine. The vessel contained fermenting urine. In

[1] *Report of Med. Off. of Privy Council on Disinfectants*, 1875.
[2] *Mittheil. Kaiserl. Gesundh.*, 1884.
[3] *Arch. exp. Path.*, 1881.
[4] *Traité des Désinfectants*, 1882, 118.
[5] *Bericht der Cholera Commission*, 1879, **6**, 335.

eight hours there was much residual chlorine. Most of the higher organisms were killed; the urine had become acid, but the bacteria and spirilla were still moving.

III. Equal parts of common salt and manganese dioxide, with 2 parts of sulphuric acid and 1 part of water, were warmed together, whilst putrid urine and dysenteric stools in wide, flat dishes were exposed for twenty hours to the gas. On opening, only a feeble odour of chlorine was noticed, as it was masked by the effluvia from the stools and urine. Some of the organisms were only benumbed, and recovered their activity in fresh air. The liquids were very acid, and had not entirely lost their fœtid odour.

IV. In another room of 48 cubic metres a glass balloon was placed containing 600 grammes of bichromate of potash and 3 kilogrammes of hydrochloric acid of specific gravity 1·16; by warming, 405 grammes of chlorine were evolved, equal to 2·7 litres per cubic metre, or 0·27 *per cent.* Under these conditions all the organisms were killed, but the time required was not stated. The process is, however, long, difficult, and more expensive than the others, the cost being given as 4 centimes per cubic metre, or about 1s. 6d. for disinfecting a room 11 feet square.

Vallin maintains that fumigations with chlorine are of little advantage, and are decidedly inferior to those with sulphurous acid. The disengagement of chlorine is incomplete, unless stirred and heated constantly, which is almost impossible in ordinary practice. The facility of "sulphuring" is, on the other hand, of the greatest value, and the expense is about four or five times less.[1]

Jeannel[2] noticed that chlorine seemed to have only a temporary action on certain vibrios, as he was able by means of ammonia to restore them to activity after they had been subjected to the influence of chlorine for a long period.

The experiments of Sternberg[3] concerning the action of chlorine on infusoria and micro-organisms show that the resistance of the latter is considerable. In an experimental room of 10 litres capacity he placed 28 grammes of chloride of lime. It was an hour and a half before the movements of the bacteria contained in a drop of putrid meat infusion ceased, although the watch-glass holding the liquid was directly exposed to the gas. (If he did not acidify, the only chlorine evolved would be that liberated by the small quantity of carbonic acid in the air present—namely, about 0·071 per cent., which is too small a proportion, if we take Hofmann's minimum of 0·16 per cent., or Baxter's 0·2 per cent. to be admitted.[4] But the

[1] See Sulphurous Acid, later. [2] *Union Médicale*, September 28, 1871.

[3] *Bulletin of National Board of Health*, Washington, July 23, 1881.

[4] See later, under *Chloride of Lime*.

total amount would still be immense if it could be absorbed by the drop of fluid, as it would reach 7 grammes of chlorine in the 10 litres of air.) Sternberg did not consider the movements definitely destroyed until after an hour's exposure to fresh air they had not reappeared.

Dr. Cash[1] subsequently studied the action of chlorine, and endeavoured to determine the comparative value of the halogens and of sulphurous acid in destroying the virus of anthrax and tubercle; he concluded that the halogens do not present any great differences when employed in solutions, the strengths of which are proportional to their atomic weights, though chlorine was the least active and iodine the most. This would oblige us to use 127 parts of iodine for 80 of bromine and 35·4 of chlorine. He found that when employed in dilute solutions they did not disinfect (that is, below Baxter's limit of 0·2 per cent.). He prefers sulphurous acid if the disinfecting agent be employed as a gas, but considers it better to employ a solution of the gas if possible.[2]

One volume of water dissolves approximately 2 volumes of chlorine gas, and as 1 litre Cl_2 weighs 3·169 grammes, cold saturated chlorine water contains 0·634 per cent. of weight of Cl_2.

(*e*) **Contact.** Intimate contact between the gas and the centre of infection must be assured. Reichardt remarked that chlorine failed with large masses of putrescible matter like fæces, and must be supplemented by the addition of metallic salts, etc. For if all easily decomposable matter be not destroyed, a recommencement of putrefaction is not prevented.[3] Klein,[4] however, used chlorine fumigations in stables for disinfection from swine plague with success. Care must be taken not to give a false security by illusory means. Probably in many cases it is better to rely on purification being accomplished naturally by air and moisture than run the risk of natural decomposition being retarded by the employment of inefficient quantities of antiseptics. It must be remembered that manure that has been treated with chlorine or chloride of lime loses agricultural value on account of the destruction of its ammonium salts. On the other hand, if chloride of lime is sprinkled over fæcal matter before removal, it destroys any offensive gases that may be evolved.

It cannot be too strongly emphasized that air cannot be disinfected and still remain fit to breathe. Wernitz[5] condemns all fumigations as "illusory specifics," since "we require a body

[1] *Pharm. J.*, 1887, 485; *L.G.B. Sixteenth Annual Report.*

[2] See later, Sulphurous Acid.

[3] Reichardt, *Desinfectionsmittel*, p. 57.

[4] *L.G.B. Thirteenth Annual Report.*

[5] *Desinfectionslehre*, 1882.

which shall come in intimate contact with atmospheric dust, and act for a long time on it." Vallin says: "Disinfection of air is useless, and gives a deceitful security. To make a strong odour of phenol, or put a basin of chlorine in a corner, is, with regard to destruction of virus, an operation quite futile, as the virulent particles in air are probably protected by an envelope of dried albuminous matter."

(iv.) Ozone.

Ozone (O_3), an allotrope of oxygen (O_2), is generally produced in the form of ozonized air by means of the silent electric discharge. It occurs naturally in the atmosphere, the concentration increasing with the altitude, rarely, however, exceeding 0·5 milligramme per cubic metre in amount. Its presence in air is to be attributed chiefly to the photosynthetic action of ultra-violet sunlight of wave length $\lambda = 180\mu\mu$, and in part to its formation along with hydrogen peroxide in naturally occurring processes of slow oxidation—*e.g.*, of turpentine and essential oils. Chemically it may be produced in small quantities by the decomposition of various peroxides such as those of calcium or barium, from persulphates, permanganates, and periodates, and in relatively large quantities by the slow oxidation of phosphorus. The utilization of essential oils in the so-called disinfectors for hanging up in confined spaces is probably based upon the supposition that the minute amounts of ozone when the disinfector is operating successfully would have a marked germicidal activity in the surrounding air. The silent electric discharge, however, is the only method at hand for the convenient preparation of ozonized air. Ozone is one of the strongest oxidizing agents known, and although it generally reacts with a utilization of only one-third of its available oxygen as follows:

$$O_3 + M = O_2 + MO,$$

yet under certain conditions it may act as a whole—

$$O_3 + 3M = 3MO.$$

A great number of industrial types of ozonizers have been designed for the purification of air in lecture-halls, theatres, public lavatories, slaughter-houses, tanneries, and breweries, whilst the London underground system of railways probably represents the largest application of the system in the world. The evidence for the specific utility of ozone as a means of purifying air, however, is distinctly disencouraging. Dewar and McKendrick[1] show that by the inhalation of ozonized air the frequency of pulsation of

[1] *Pogg. Ann.*, 1874, **152**, 329.

the heart is lowered very considerably, the blood temperature sinks from 3° to 5° C., and post-mortem examination shows that the blood has become venous in appearance. Thenard[1] and Briny[2] confirmed these observations of Dewar's. Schultz[3] records several cases of chronic poisoning by ozone. Jordan and Carlson[4] confirmed the deodorant action of ozone on air, but showed that long before the concentrations reached those necessary for germicidal action, injury was caused to the respiratory tract.

The lowest concentration of ozone in air which can exert a definite disinfecting action[5] appears to lie in the neighbourhood of 13·5 milligrammes per litre. With such concentration sterilization can usually be accomplished in air, but the presence of large quantities of moisture lowers its germicidal activity, owing in part to catalytic decomposition according to the reaction—

$$2O_3 = 3O_2.$$

According to Labbe and Oudin,[6] the highest concentration which may be inhaled without deleterious effect is approximately 0·11 to 0·12 milligramme per litre. They state that beneficial results obtain by the inhalation of ozonized air of this concentration, a marked increase in the oxyhæmoglobin content of the blood taking place after an interval of from ten to fifteen minutes. It is therefore evident that there is no question of germicidal activity in ozonized air of concentrations suitable for respiration.

As a powerful oxidant, however, it removes small traces of sulphuretted hydrogen and other impurities in air, whilst the unpleasant smells associated with crowded places are amenable to treatment with ozone. Schwanz and Munchmeyer[7] investigated the deodorizing action of ozone in detail. It was noted that hydrogen sulphide and sulphur dioxide underwent oxidation, whilst the mercaptans, skatol, and amidol were oxidized to somewhat pleasant-smelling substances.

Carbon monoxide was but slowly oxidized, whilst ammonia was not affected. These observations have been in part confirmed by Riesenfeld and Egidius[8] and Frankland.[9]

In the London Tube railway system the average concentration of ozone is stated to be 1·2 milligrammes per cubic metre, occasionally varying to 12 milligrammes per cubic metre.

[1] *Compt. rend.*, 1876, **82**, 157. [2] *Med. Cent. Blt.*, 1882. **20**, 721.
[3] *Arch. f. Expers. Path.*, 1892, **29**, 365.
[4] *J. Amer. Med. Assoc.*, 1913, **61**, 1007.
[5] Schultz, *Zeitsch. Hyg.*, 1890, 75; De Christmas, *Ann. Inst. Pasteur*, 1893, **7**, 689. [6] *Compt. rend.*, 1891, **113**, 41.
[7] *Zeitsch. Krankh.*, 1913, **75**, 81. [8] *Zeitsch. Anorg. Chem.*, 1914, **85**, 201.
[9] Fourth Int. Congress on School Hygiene in 1918.

The use of ozonized air has been adopted to some extent in dairies and breweries. Will and Beyersdorfer[1] state that air containing 0·6 to 0·7 gramme per cubic metre destroys organisms inimical to the brewery. They further showed by experiments conducted in the factory that moist air was more efficacious than dry, and that the ozone underwent catalytic decomposition on the surfaces of contact substances such as filtering materials.

Frequently the fermenting tuns and the cascade coolers in breweries are enclosed in a suitable shaft, permitting the utilization of ozonized air containing a sufficiently high concentration of ozone to act as an effective germicide.

Sterile air is also very desirable in refrigerating systems such as obtain in ship-holds or railway-cars, and the combination of an ozonized air generator and a refrigerator is particularly advantageous owing to the fact that the silent discharge apparatus operates most effectively with cold, dry air.

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[1] *Zeitsch. Brauw.*, 1912, **35**, 73

CHAPTER III

STERILIZATION AND PRESERVATION OF FOOD

THE chief causes of change in food may be briefly enumerated as follows:

1. **Oxidation.**—This is comparatively rare and slow in the absence of microbes. Dilute alcohol is transformed into acetic acid by air when in contact with platinum black, but the process is quicker under the action of the vinegar fungus, *Mycoderma aceti*. As far as is known, simple oxidation never renders substances injurious.

2. **Reduction.**—Almost the only reducing agent that could naturally occur in this connection would be sulphuretted hydrogen, which would involve putrefaction in the substance or in the neighbourhood, and would therefore presuppose the presence of bacteria. It has been suggested that the peculiar taste of certain canned foods depends on the reduction of the fluids by the metal, on the ground that its degree is out of proportion with the traces of metal dissolved, and that it is caused with such extreme rapidity, as, for example, when an apple or fish is cut with a steel knife. In this latter case the taste is often imaginary, as blindfold experiments with apples and fish show that the majority of persons are unable to detect which was cut with clean steel and which with silver. Of course, if the former metal is allowed time to become acted upon, a ferruginous taste is imparted. Zinc gives a different flavour, magnesium gives none; hence the cause would seem to be the metal, not reduction. There is no evidence that a slight reduction would be at all injurious. Sulphites and formaldehyde, if used for preserving, would cause some reduction in unstable constituents of the food.

3. **Metallic Contamination.**—The injury to the taste and colour of vegetable substances coming in contact with iron led to the use of copper vessels for preparing jams and syrups, and even pickles were formerly made in copper vessels. The employment of this metal for vinegar or very acid juices is most reprehensible, as, even if the surface be clean, an unknown and often considerable amount of metal finds its way into the food. Apparatus of wood, stone-

ware, and even silver and platinum, have displaced copper in making pickles. Enamelled iron should be used for making jams. The presence of copper in preserved peas has been defended on the ground that (*a*) it improved the colour; (*b*) being antiseptic, it increased the keeping properties; (*c*) it was not poisonous in small quantities, but acted as a beneficial tonic. The best authorities regard it as irritant; it is cumulative, and it should certainly be prohibited. Lead may be present from the solder, and Hehner has drawn attention to the fact that almost all canned provisions contain tin in solution.[1] Superior goods are put up with oiled paper linings, so as not to come in contact with the metal. The irritant effects of some tinned goods have been attributed to chloride of zinc, which had entered in the soldering; this, and also the dropping in of particles of solder containing lead, have been since prevented by a guard-plate underneath the hole, or by the use of resin for soldering instead of zinc chloride. W. Reuss[2] noticed the presence of lead in preserves contained in tinned iron canisters. The latter were constructed by bending some sheet-metal together, thereby avoiding contamination with lead by means of solder, and hermetically sealed by india-rubber bands. He subsequently traced the lead to these bands, which owed their colour to red lead. On examining red india-rubber bands of French, German, and English manufacture, he found them to contain as much as 60 per cent. of red lead. Many of the india-rubber bands used for sealing pickles, jams, meats, and preserves owe their red colour to sulphide of antimony, and are free from lead, but antimony has not been found in the food itself. In New York, glass vessels have been tried to overcome these difficulties, but, owing to the expense, breakage, and unsightly appearance of some forms of soups and meats, they have not met with much success. For brawn and potted meats earthenware is used. Its weight and fragility are the only disadvantages.

Attempts have been made to coat the inside of the tin with varnish, paraffin, etc., but have not been successful.

If the inside of the tin be much discoloured, or if tinned fruits show a strongly marked crystalline appearance on the interior surface, they are unsafe to be eaten. Any discoloration of the contents, or any peculiar odour or taste, should also be distrusted.

4. **Organisms.**—Yeast, moulds, and bacteria can be carried in the dust of the air on to the surface of any exposed food, and there develop fermentative and putrefactive changes. It would be

[1] H. Beckurtz (*Apoth. Zeit.*, 1897, **1**, 584), in his analyses of tinned peas, beans, celery, asparagus, truffles, etc., detected tin to the amount of 0·2 to 0·6 gramme per kilogramme. [2] *Chem. Zeit.*, 1891, 1522, 1583.

supposed, therefore, that exclusion of air and dust would suffice to preserve changeable bodies, and with this object receptacles exhausted by an air-pump and afterwards hermetically sealed have been patented. But the food must be previously collected so as to exclude organisms, or must be sterilized by sufficient heat. It is practically impossible, however, to preserve most alimentary substances in the raw state without the addition of spices or chemicals. Eggs can be preserved for months by keeping them in a pan of lime-water, or by dipping them in a cream of slaked lime and water; in each case the shell is rendered impervious by a coating of carbonate of lime, and the albuminous inner lining of the shell is coagulated and rendered aseptic, as can be proved by breaking and examining. Smearing with fat or varnishing gives a bad flavour. Paraffin wax easily peels off, and is expensive. An immense number of processes have been suggested, but the most successful are lime-water, or excluding the air by a coating of vaseline. See an account of extensive trials in Germany, United States Consular Reports, September, 1901. Sodium silicate (water-glass) also gives fair results.[1] Fruit has been kept from decay by a coating of melted wax, when gathered fresh and not quite ripe.[2] B. Ehrlich cites[3] a number of instances in which diseases were conveyed by fruit gathered, marketed, or handled under insanitary conditions, and points out that micro-organisms adhere readily to the surface of fruits. Experiments were therefore undertaken to determine the number and kinds of such micro-organisms. The smallest number were found on blueberries and plums, and the largest number on currants and cherries. It was found to be possible to remove the greater number of micro-organisms by washing.

Five strawberries from a pound bought in the open market in Covent Garden in 1914 were carefully washed in 20 c.c. of water. On cultures being prepared from this solution, coliform organisms were found present in 0·2 c.c., while anaerobic milk-clotting organisms were found present in 1 c.c.

Jams are usually covered with parchment paper sealed down by white of egg; this membrane does not necessarily exclude air, but its tiny holes must be small enough to arrest bacteria and spores of mould. Generally a disc of tissue paper is laid on the jam, when hot, as an additional precaution. It will be found sometimes that mould has grown on the top of this, but has not penetrated to the preserve.

[1] *Chem. and Drugg.*, **52**, 704; Strutt, *Chem. News*, 1901, **83**, 268.

[2] Also see use of formaldehyde, p. 52.

[3] *Arch. Hyg.*, 1901, No. 2.

Coating with glue, gelatine, or melted fat has been tried for meat, with only partial success. Meat is preserved to a certain extent by membranes such as sausage-skins. Electrical methods have been suggested,[1] but have little effect on bacteria except through the heat that may be produced.

The flour moth (*Epheste Kühniella*) has long been a trouble in army stores, as it infests the biscuits. These biscuits, while being baked, are at a high temperature for a long time and consequently the eggs in the flour from which they are made cannot remain living, but as the biscuits cool, these moths enter the mills and deposit their eggs. The remedy is to clean out the mills periodically with carbon disulphide or steam on the walls, floors, and machinery, and to cover all the open windows with fine netting. The biscuits can be packed in air-tight metal boxes until needed.

Poisonous Products of Decomposition.—It must not be forgotten that as, in the first instance, micro-organisms settle on the surface, unsafe food may present a normal appearance, and consequently be passed by inspectors and others as suitable for consumption, a point in favour of the judicious use in certain cases, and under restrictions, of approved preservatives. Very slight evidences of decomposition in fish are sufficient to indicate the possible presence of toxic products of bacteria, so that fish can never be trusted in the same way that high game and mutton sometimes are. Van Ermengen states that the toxic ptomaines sometimes found in preserved meats originate from a specific organism, *Bacillus botulinus*. The soluble ptomaine, *botuline*, which it excretes, is said to be intensely poisonous. The ptomaine is destroyed at 60° to 70° C., and the bacillus at 85° C., so thorough cooking is capable of removing the danger. This anaerobic organism, *B. botulinus*, may be taken as the type of one group, the conspicuous symptom of which is the disturbance of nerve functions which they give rise to. In the other group, gastro-enteric symptoms are produced by coliform organisms.

Milk has been shown to be a frequent source of danger, and many epidemics have been traced to its pollution, either through the water supply of the cows, carelessness in the dairy, or in the conditions obtaining between the time when it is supplied by the farmer and when it reaches the house of the consumer. Vaughan has further shown that, in addition to the danger of milk containing pathogenic organisms, under certain conditions *tyrotoxicon*, a ptomaine produced by a little-known species, has caused several outbreaks of summer and infantile cholera. As the poison is

[1] As in patents 7,851 and 8,301 of 1902.

destroyed by boiling, its absence may be assured by this precaution. Vaughan also demonstrated its presence in cheese, ice-creams, and stale fish.

Preservation of Meat.—As we have previously indicated, drying is one of the oldest methods of preserving meat; the expression of the water and desiccation leaves the fibre and dried juices incapable of putrefaction, but the flavour and digestibility are much impaired.

Smoking dries the surface, and also impregnates it with acetic acid, wood spirit, and creosote. Although the two former eventually volatilize from the food, the surface retains a good deal of the creosote, and undergoes little change except that the fat in time may become rusty or rancid. A great part of this rankness may be removed by putting about half a dozen lumps of freshly burnt or reheated charcoal in the water in which the meat is boiled. The charcoal removes the odour, but does not thereby render the article wholesome, hence the change must not have gone too far. Smoking has only a surface preservative action, and does not reach the interior, so that the ova of trichina, tape-worm, etc., remain undestroyed. In countries like Germany, where smoked sausages are consumed raw, or nearly so, the ravages of these parasites are frequently severe. In England, where thorough cooking is the rule, such epidemics are very rare; still, it must be remembered that neither drying, smoking, nor salting secures safety against the ova of parasites. To save time, hams, haddocks, etc., are often cured by dipping in pyroligneous acid, or crude wood vinegar, with or without brine, or even by being merely brushed over with this solution. Kippers and haddocks are often prepared under most unsanitary conditions, and as the treatment is often far from complete, may be a source of danger.

Salting.—The only inorganic salt that we intentionally and habitually add to our food is sodium chloride, which seems to be necessary for digestion and a natural instinct, as many wild animals are noticed regularly to visit salt deposits, and will lick lumps of salt. It will be noticed that these natural deposits always contain nitrates, and in many cases borax.

There seems to be no direct equivalent of our word "bacon" in the classics. "Perna,"[1] "petasio," and "laridum" or "lardum," seem to be the nearest. The word "bacon" is old French.

Salting, as commercially practised, is a process of osmosis or diffusion; a crystalloid applied externally, either as a solid or in strong solution, diffuses into the interior, while the soluble albuminous matters pass out into the brine. Soluble mineral salts and

[1] Plautus, "Curc.," ii., 3, 54; Persius, "et piper et pernæ, Marsi monumenta clientis."

sugar also act as partial desiccators by their affinity for water. The flesh is deprived of a great part of its putrescent constituents, but at the same time loses a corresponding nutritive value (Liebig estimated the loss at one-third to one-half), and leaves nearly insoluble fibrinoids, partially hardened and less digestible —"induratas sale," as Pliny says.[1]

After either smoking, salting, or drying, the characters of fresh food cannot be restored. It was not till the middle of the nineteenth century that it was discovered that small quantities of certain antiseptics would enable the original qualities to be retained, and prevent decay for a considerable period, with less influence on digestion than the old curing processes.

The quantity of mineral matter introduced in salting is considerable. A mixture of 2 pounds salt, 2 ounces saltpetre, and $1\frac{1}{2}$ ounces moist sugar is rubbed thoroughly into the meat, which is then kept in a cool place and turned daily, rubbing in fresh salt where required. When the brine, as it forms, is drained away from the meat, the process is called *dry-salting;* if it be allowed to remain on it, it is called wet-salting or pickling. A pickling brine is made with 4 pounds salt, $\frac{1}{2}$ to 1 pound sugar, and 2 ounces saltpetre in 2 gallons of water. The liquor in time becomes diluted by the meat juices, and is also apt to turn foul; therefore at intervals it is boiled down with more of the dry ingredients and skimmed, which has the effect of sterilizing it and removing albuminous matters. For a fine red colour the saltpetre is increased to about 8 per cent. of the pickling salt. In America it is usual to add to the brine about $\frac{1}{2}$ per cent. of bicarbonate of potash or "saleratus," and creosote sometimes in the proportion of one drop to the gallon.

In this way a high amount of salt and an appreciable quantity of nitre is consumed with the food. Thus, in mild-cured bacon we have found the following percentages:

	Sodium Chloride.	*Potassium Nitrate.*
Raw	4·27	0·0083
Smoked	3·34	0·0086
Smoked and boiled	2·38	0·0065
Smoked and grilled	2·24	0·0086

The antiseptic power of salt is decidedly weak, hence the need for large quantities. In many cases brine becomes contaminated with ptomaines. The meat, however, is usually washed before cooking.

Occasionally carbolic acid or phenol has been added to brine,

[1] *Hist. Nat.*, **28**, 20.

but it is an objectionable antiseptic for food on account of its odour, taste, and poisonous character. **Carbolic paper** has, however, been much used in Europe for packing meats. It is made by mixing 5 parts of paraffin wax, 5 of stearin, and 2 of phenol, and brushing in a melted state over paper.

Preservation by Heat.—Articles of food always contain moisture, so that the conditions present here are heat and steam. In frying, the oil or fat reaches 160° to 180° C. (the temperature at which bread-crumb turns brown), so that sterilization is usually effected. In canned meats a temperature of over 100° C. is used, hence it is probable that the whole of the food is heated to that degree. But in cooking joints Dr. Vallin[1] showed that the interior frequently attained only 54° to 60° C., or even less, and in long cooking only about 70° C. Dr. Fiore injected meat with anthrax bacilli, cooked it in various ways, and then tested the product by inoculating animals with the juice. He obtained, in roasting, a temperature of 60° to 65° C., and found that the bacilli were not killed unless the cooking had been very complete, and that the spores were not killed by a much higher temperature than is used in most countries for roasting meat. He concludes that prolonged boiling is the most favourable method of cooking for completely destroying pathogenic germs. Vallin agrees with Fiore as to the danger of too much reliance on cooking, and the need of great vigilance in the supervision of meat supplies.

M. Appert, of Paris, in 1810, first introduced the process of heating provisions in vessels which could be hermetically closed, so that the steam should drive out the air and a vacuum be produced. This is clearly seen by the fact that the ends of tins which are in proper condition are concave (they may even collapse), and that there is an inrush of air when they are opened. Unless these signs are observed, the tin is bad and must not be eaten. All tins are examined in the warehouse, and such as are "blown"—*i.e.*, convex at the ends—owing to gases from decomposition, are rejected. In our laboratory a "blown" sardine tin yielded 30·5 c.c. of gas, which had the following composition:

Carbon dioxide	69·7
Oxygen	3·7
Nitrogen, with a small quantity of H_2 and CH_4 ..	26·6

The contents of the tin were semi-fluid, and had a very strong fishy, but not putrid, smell. There was also present a very vigorously growing anaerobic organism, which decomposed gelatine with the liberation of gas at 22° C. in less than twenty-four hours, together

[1] *Rev. d'Hyg.*, September, 1897.

with other liquefying organisms. Collapsed or crushed tins (which are sometimes offered cheap) are also dangerous, as, in the sharp bending of the tin, holes are apt to be formed. There are several processes for canning foods:

1. *The Chloride of Calcium Process.*—The tins after being filled have the lids soldered on, leaving a pin-hole for escape of steam. They are immersed to two-thirds of their depth in a bath of calcium chloride solution, which boils at a higher temperature than water, heated to from 132° to 170° C. for one to three hours, and the hole closed by a drop of solder.

2. *The Aberdeen Process.*—The tins are placed in a bath as before, but they are entirely closed. During the heating they are raised at times by a frame, opened to let out air and vapour, so that the tin does not burst, closed again, and the heating continued. This is repeated two or three times, according to the size and substance. The pressure within is judged by the forcing out of the ends. Superheated steam is used by some firms instead of salt baths; it is rather more difficult to manage, but leaves the tins clean. This process, which is known by the tins having two or three blow-holes, presents the advantage that more of the natural moisture and flavour are retained. It has superseded the former process in Scotland, Australia, South America, and New Zealand.

3. *Jones's Vacuum Process.*—The tins are packed quite full, and soldered up except a small hole, with a little quill tube, in the top. The bath contains ninety-six 2-pound tins. Along the centre of the bath runs a tube with twelve taps, each of which carries eight stuffing boxes connected with the tubes. By a fan or pumps a vacuum is created, and the bath is heated gradually to 100° C. The fluid in the tins, under the diminished pressure, boils at about 38° C., so that the steam and air are carried off at a low temperature. After a time the exhaust taps are turned off. The tins then contain no air, and are full of steam. The cooking is continued for two hours at 121° C., letting off the steam occasionally as the pressure increases.

4. *Salzer's Baltimore Process.*—Meat is subjected to dry steam and compressed in moulds, then wrapped in paper or other material, coated with plaster of Paris, and embedded in a heated fat such as suet or lard, in a can or in metallic foil, with certain precautions.[1]

5. In Germany, and to a certain extent in Italy and France, the dangerous and objectionable custom is prevalent of eating meat in the uncooked state, simply smoked or pickled. Raw hams and bacon only smoke-dried, Gotha sausages, and even chopped raw steak with bread-crumbs and onions, are commonly

[1] Patent No. 11,988, 1892.

consumed. This practice necessitates that the meat in the markets should be rigidly inspected, and hundreds of carcasses are seized and destroyed. With the idea of saving this confiscated diseased meat for food, W. Budenberg, of Dortmund, invented a flesh sterilizer, in which the disease germs are killed by steam under pressure.

It consists of a large iron cylinder, one end of which opens on hinges and closes hermetically against packing. Steam at a pressure of half an atmosphere (112° C.) is injected at the top, circulates round the movable iron shelves on which the pieces of meat are placed, and escapes to a condenser through a tube at the bottom, or can be led into a fireplace to burn any unpleasant vapours from the meat. The temperature can now be raised to 127° C. by letting in steam of $2\frac{1}{2}$ atmospheres; after two or three hours' heating all germs of disease are destroyed. The fat and liquor are drawn off separately below. The fat can be used, the liquor is thrown away. At a higher temperature the meat is much disintegrated and dried, but is still digestible and fit for the food of animals, dog biscuits, etc. The temperature of the interior of the largest lumps of flesh, as registered by a maximum thermometer, remains steady at from 100° to 120° C. The loss of weight is from 40 to 50 per cent.

In some cases, where the apparatus is only used as a meat-steamer to save large quantities of meat from being lost by putrefaction in summer, it can be worked throughout at half an atmosphere of steam pressure. At this lower temperature the meat is as juicy and savoury as in ordinary cooking. The interior of the pieces reaches an approximate temperature of 100° C., so that it can be sold for eating without hesitation. The inventor states that the sterilization at the higher temperature was found by experiment to be perfect.

6. *G. Hartmann's Process*[1] is on the principle of fractional sterilization, and consists of three steps. The first consists in subjecting the preserves to a temperature of 100° to 120° C. for a short time; the second in keeping them for some days at a temperature of 20° to 30° C., when any germs which have not been destroyed in the primary sterilizing process develop. These are then killed by a final sterilization.

The modern processes of canning food consist chiefly in subjecting the cans to steam in autoclaves heated to 212° F. and higher;[2] careful control is exercised over the temperature, and from every batch a certain number of tins are always removed and incubated at 98° F.

[1] Patent No. 14,601, 1892. [2] R. T. Mohan, *J. Soc. Chem. Ind.*, 1913, **32**.

The following types of spoiled cans are differentiated: leaks, springers, swells, and flat sours.

In leaky cans the food is spoiled through entrance of the micro-organism through a small hole in a faulty tin. Invisible holes resulting from faulty can manufacture or sealing are not uncommon. The presence of non-sporing bacteria as well as of aerobic lactic acid organisms indicate the entrance of aerial contamination.

Springers are swelled cans which have been forced open by the pressure of the internally generated gases. Generally the trouble is due to under treatment, but occasionally a leaky can will admit of aerial contamination from outside and subsequently seal up. Some springers contain no living organisms; the acids present may attack the tin lining and generate hydrogen, or fruit seeds or stones may, if the seed life has not been killed, develop in embryo and produce carbon dioxide.

Flat sours are cans which contain foods turned sour and bitter. The bacteria bringing about this result are spore-bearers, non-gas-generating and anaerobic, living on the carbohydrates present. They are rather slow in developing, and detection is not easy.

Preservation by Cold.—Although micro-organisms are extensively resistant to cold, various methods of refrigeration are largely employed for preservative purposes. In the experiments, which have proved that some bacteria are not killed by very low temperatures, the time of exposure has been, with one exception, comparatively brief. Thus Pictet and Young cooled *B. anthracis*, *B. subtilis*, and a few other species progressively down to −130° C., the entire duration of the test being about forty hours, after which growth was recovered on thawing. On the other hand, with *B. subtilis* spore-formation has not been observed below 6° C., and in *B. anthracis* not below 16° C. Coleman exposed meat for only six hours to −63° C.; when kept in a warm room under cover it then putrefied "in a few days." Macfadyen and Rowland subjected *P. vulgaris*, *B. coli communis*, and a number of other bacteria to −252° C. for six hours without killing them, and subsequently they submitted several pathogenic species to the temperature of liquid air for six months without impairing their vitality. It may be generally stated that protracted cooling inhibits development, with eventual destruction, and prevents organisms exercising their proteolytic power. Moulds as a class do not grow below 2·5° C., and their optimum temperature is much higher. Sedgwick and Winslow showed, in 1902, that of typhoid bacilli in ice or cold water over 40 per cent. will perish in three hours, and 98 per cent. and upward in two weeks. Sparks[1] records a 65 per cent. reduc-

[1] *Water*, September, 1908, 259.

tion in the *B. coli* count of a polluted ice maintained at −2° C. for two days, 95 per cent. in one week, 99·3 per cent. in two weeks, 99·99 per cent. in seven weeks, and sterility in twelve weeks. *B. typhosus* was slightly less resistant, being completely eliminated in nine weeks. Large quantities of meat are imported into England, frozen at the temperature of from 15° to 20° F. by means of ammonia, carbon dioxide, or sulphur dioxide refrigerating machinery, or chilled at a temperature of about 29° F. The air must not be too dry, and the amount of humidity most favourable varies with the substance preserved. Dr. W. Hanna[1] gives the following percentage saturations as adequate: Cheese 85 per cent., eggs 80 per cent., meat (chilled and frozen) 70 to 80 per cent., poultry 60 per cent., dry fruit 50 per cent.

We have analyzed a piece of meat kept by this method for a period of eighteen years. The following is a table showing the comparative analyses of fresh English beef, Queensland cow frozen for a few months, and the beef frozen for eighteen years. The prolonged storage had not impaired digestibility or flavour, and the meat showed no signs of decomposition.

	English Beef.	*Queensland Cow.*	*Beef Frozen for Eighteen Years.*
Total extract	100	100	100
Mineral salts	15·3	15·4	13·6
Total nitrogen	12·7	13·0	11·9
Nitrogen in extractives ..	7·1	6·0	6·2
Nitrogen in proteins	5·6	7·0	5·7
Soluble proteins	43·2	48·0	44·5
Albumin	0·59	1·4	Trace
Albumoses	41·3	47·7	47·4
Extractives	34·0	33·0	55·2
Acidity c.c. $\frac{N}{10}$ acid per 100 grammes extract	1028·0	958·0	955·0

It will be noticed that the continued freezing has raised the extractive figure, although the extractive nitrogen remains the same, an indication that there has been a slow breaking up of these non-nitrogenous bodies, the carbohydrates and fats, into simple and more soluble bodies.

The fact that time has little effect on the flesh is shown by the familiar illustration that the flesh of mammoths which have remained frozen for thousands of years in the ice of Siberian rivers has been eaten by several travellers, and was used by natives as food. As it is almost impossible to entirely exclude putrefactive

[1] *Public Health*, March, 1914, 198.

organisms, we have to avoid their injurious action by (1) cleanliness, (2) cold, (3) dryness. The necessity of cleanliness is shown by the fact that some species of bacteria and moulds can develop on frozen meat, and although they do not otherwise change, it may cause an unpleasant odour or taste, or discolorations. *Proteus vulgaris* was found by Levy in incrustations on ice-chests.

Luxuriant growths of the common moulds, *Penicillium glaucum* and *candidum* and *mucor*, are seen on the carcasses which have suffered from faulty refrigeration in transit.

Dr. Klein has shown that brown spots on chilled beef, which had occasioned great loss by causing rejection by the meat inspectors in England, left the interior of the meat perfectly normal and sound. He isolated the fungus causing the infection, describing and figuring it in his report as a *Saccharomyces*. He found it to be non-pathogenic, and that it does not grow at blood-heat, but grows at ordinary temperatures and as low as $-2°$ C., and that at $-8°$ to $-9°$ C. there was no growth. Therefore we may notice that it would not develop on hard frozen meat. Also, as it does not grow under anaerobic conditions, it does not penetrate into the surface. In 1905 one of us found that the surface of a sample of chilled meat was infected with a black mould, *Cladosporium herbarum*, accompanied by the similar *Chlamydomucor*. This was also present in the calico cloth bags used as wrappers. It is therefore essential to sterilize these calico and stockinette envelopes and to instal disinfectant measures at the factories. Dryness is to be sought in the surroundings, as damp encourages the growths, whilst a moist coating on the meat itself is especially to be avoided. In order to attain dryness in the air and on the surfaces, boxes containing dry calcium chloride are now largely used without much expense, as the substance is recovered by simple evaporation and redrying. At intervals, when the chamber is cleansed, the surfaces should be sterilized by vapour or spray of formaldehyde or sulphurous acid, and then dried in a current of air. For long railway journeys it has been proposed to use liquid air for cooling the refrigerator cars; "the evaporation is so controlled that the oxygen passes into spaces in the car walls, while the nitrogen is delivered round the foods, thereby avoiding oxidation," and the current would differ from ordinary air in that organisms could only rarely and accidentally be present.

The effect of low temperatures on animal parasites is dealt with by Ostertag in his handbook on "Meat Inspection." Of the dangerous animal parasites it has been established that *Cysticerci* are destroyed by freezing. Gage showed that in measly pork kept fourteen days at 10° to 15° C. all the *Cysticerci* die, while Reis-

mann found that this result occurs in joints of beef and in hams after keeping four days at 8° to 10° C. The legal enactment in Denmark is that "for domestic use and for sale in special booths in pieces not larger than 2·500 kilogrammes, and under statement of its nature, it is permitted to sell meat of animals slightly infected with *Cysticerci*, after its dangerous properties have been removed under veterinary supervision, either (1) by thorough boiling; (2) by pickling twenty-one days in 25 per cent. brine; or (3) preservation for twenty-one days in suitable (officially improved) cold-storage rooms in which a temperature of 3° to at most 7° C. prevails and a moisture content of 70 to at most 75 per cent." This, it will be noticed, would be chilled meat. The regulations in Saxony and Baden are similar; in the latter it is prescribed that the cold storage must be for three weeks under police supervision, and that the temperature must not exceed 5° C.

With trichinæ, on the other hand, freezing is less effective, although, according to Bouley and Gibier, these parasites in hams containing them were killed by a cold of −15° to −20° C. Kuhn found that trichinous meat kept in a refrigerator for seven weeks was still infested with the living worms. The sale of raw trichinous pork is therefore totally prohibited in Germany, although in Saxony meat *slightly* affected is allowed to market under declaration after thorough cooking or pickling.

A method successfully used in the United States for preserving fish is to freeze them on trays in chambers kept at about −16° C. then to dip the trays into cold water, when each fish becomes encased in a thick coating of ice; they are then packed and despatched by refrigerator car. One of the chief dangers in all cases is exposure to higher temperatures during transit from vessel or car to the cold stores, and in the subsequent distribution. In this respect, freezing, as distinguished from merely chilling, has greater safety.

Although we have evidence that bacteria moulds and parasites do not affect frozen meat when preserved under proper sanitary conditions, there is some evidence that enzyme activity has not been wholly restricted. It is common knowledge that frozen meat on thawing frequently liberates a reddish liquid of amphoteric reaction. We have obtained 70 cubic centimetres from 2½ pounds of frozen beef, while J. Simons[1] has obtained as much as 15 per cent. by weight of this fluid. The same author has measured the rate of autolysis of fresh and thawed frozen meat, and concludes that autolysis is more active in the latter.

The following table shows the amount of bases which we have

[1] *Le Froid*, January 25, 1914.

obtained from alcoholic acetic acid extractives of different kinds of meat:

	Weight of Base in Grammes obtained per 250 Grammes.
Fresh meat	Negligible
Fresh meat hung five days still fairly fresh ..	0·0041
Siberian frozen fowl	0·0029
Siberian frozen fowl kept three days thawed	0·0038
Frozen meat eighteen years old	0·0118

It is evident that prolonged storage increases the amount of bases present, and must be taken as a sign of enzyme activity.

In a sample of ice-cream purchased from a street vendor we have found the following bacterial contents:

Total number of organisms per c.c.	540,000
Blood-heat organisms per c.c.	230,400
Rapidly liquefying per c.c.	10,000

Bacteria of the *B. coli* group were present in a very large number.

Chemical Preservatives used in Foods.

Boric or Boracic Acid, H_3BO_3 (or $HBO_2.H_2O$), occurs in inodorous, pearly, crystalline scales. The solubility in water and in alcohol of 90 per cent. is about the same, 1 in 30. It dissolves in 3 parts of boiling water, and in 4 of glycerine.[1] It has been proposed in an Italian patent to import it from Tuscany in the form of the native solution, but the cost of transport would thereby be increased.

It is a weak acid, almost tasteless in dilute solution, and has no corrosive action either on tissues or metals; this and its absence of odour, with a certain amount of preservative power and little effect on animals, have led to a large number of patents for the use of boric acid and borates for preventing the putrefaction of animal and vegetable substances. It is in no sense a disinfectant, and its antiseptic powers are low, although for many years it has held second place after salt and nitre as a preservative for meat and vegetables. The original discoverer, Gahn, sold in Europe two mixtures—(1) boric acid with 1 part alum, called "aseptine"; and (2) boric acid with 2 parts alum, called "double aseptine." It seems probable that he recognized in the alum a greater activity than in the boric acid. Provisions in part preserved by boric acid are generally within one or two months covered with a black crust, but the presence of alum prevents this action taking place.

[1] *Brit. Phar.*, 1898.

Lehmann found that fresh beef with 1 per cent. of boric acid and 50 per cent. salt pickle kept for several months at 80° F. Endemann stated[1] that boric acid acted as a preservative to fresh meat only, and that previously salted meat could not be preserved by it. Lehmann infers in these cases it is not the boric acid that acts as a preservative, but the substances produced by it—*i.e.*, the acid phosphates. He states that "other mineral acids give exactly the same results without boric, especially phosphoric and hydrochloric."[2]

In investigating the effect of ordinary culinary operations on boric-cured hams and bacon we have found that when they had been soaked originally for a short time in the solution, or had been packed in a boric powder, the latter had penetrated very little beyond the rind, and was completely eliminated by the usual "washings" to remove salt. We also obtained the following results with some bacons cured with salt, saltpetre, and borax:

PERCENTAGES OF PRESERVATIVES.

Description.	*Common Salt.*	*Salt-petre.*	*Borax.*			
			Raw.	*After Boiling.*	*After Grilling.*	*After Frying.*
Raw unsmoked	4·27	·0083	·210	·120	—	—
Raw smoked	3·34	·0086	·175	—	—	—
Raw smoked "for grilling and frying" ..	2·24	·0086	—	—	·094	·031
Smoked and cooked "as supplied to the trade"	2·38	·0065	—	·070	—	—
Raw undescribed ..	—	—	·084	—	—	—

Showing that a large quantity of the boric acid is removed in cooking.

The great reduction in frying is explained by volatilization. Foulerton and Rideal[3] investigated the digestibility of meat preserved with boric acid by means of pepsin, the amount of dissolved nitrogen in the filtrate after one hour's digestion with pepsin at 38° C. being as follows:

Control (No Preservative).	*Boric Mixture in Meat (75 per Cent. Boric Acid, 25 per Cent. Borax).*		
100	*Per Cent.* 0·05 97·22	*Per Cent.* 0·1 90·17	*Per Cent.* 0·3 73·93

[1] *Chem. News*, April 2, 1880.
[2] Lehmann, *Practical Hygiene*, 1893, 2, 247.
[3] *Lancet*, November, 1899.

It is evident that there is a reduction in digestibility of the meat when more than 0·1 per cent. acid is present.

Sodium sulphite in the proportion of 1 pound to 1,000 pounds of meat has been found to keep the meat fresh and to retain its bright colour. The red colour of salted meat, according to Haldane,[1] is due to NO-hæmoglobin. With SO_2 no such compound is formed, but a pronounced spectrum of oxyhæmoglobin is produced.[2]

Various forms of spraying, especially with formaldehyde, have been used from time to time. In hot climates it is stated that a spray of very dilute hypochlorite keeps meat and fish fresh for a considerable time.

Preservation of Fruit and Vegetables.—The general method of preparing "preserved fruit" in sugar solutions or in the natural juices after subjecting them to heat sterilization is so well known as not to require detailed description. Tinned fruit and vegetables are prepared in much the same manner as meats, while dried fruits are easily prepared. Fruit is also largely preserved by refrigeration. In long transport it is recorded that from 14 to 26 per cent of oranges and lemons were formerly rendered unwholesome by decay, but that now, by careful handling, by cooling the fruit through its whole substance immediately before shipment, and then shipping under refrigeration, all the fruit, within about 2 per cent., is sound on arrival. Large cargoes of bananas are brought in perfect condition from Jamaica in ships' holds kept at 4·5° to 7° C by air currents cooled by means of a refrigerating machine, brine coils, and pumps.

It is agreed that fruits for cold storage should be put into it at the earliest moment after picking, as the cold and dryness prevent fungi "fruit rots." The freezing-point of apples, according to Madison Cooper, is below −0·5° C., and they are sometimes stored without injury at −1° C., but sudden freezing or sudden thawing injures the stock. Professor Siebil notes that grapes will stand −3·5° C., while lemons will be spoilt if they go below −2° C. The citrus family of fruits are peculiarly susceptible to temperature. Taylor states that, after being kept in cold storage, fruits generally spoil very quickly on removal, as the moulds, etc., have been only restrained. It has been suggested that other succulent fruits besides grapes might stand freezing well on account of their elastic cells, and strawberries have been stated to be little affected by the cold. After cold storage the fruit has to be ripened for market by a dry heat never exceeding 21° C. This is attained at Covent

[1] *J. Hyg.*, 1901, **1**, No. 1.

[2] J. Harrington, *Infect. Diseases*, **1**, No. 2; Altschuler, *Arch. Hyg.*, **48**, 2, p. 114.

Garden by electric radiators which mature Malagra lemons in about five days, and also ripen bananas, and on the other hand keep tubers and bulbs so dry as to prevent them from sprouting. Spraying with formaldehyde has been occasionally adopted to improve the keeping properties and appearance of fruit. The Board of Agriculture[1] conducted experiments at Kew on the treatment of fruits with formaldehyde, and found that all kinds kept for ten to twenty-one days longer than when untreated; they gave the following directions:

Put 10 gallons of water (preferably rain-water) into a cask or a zinc bath; add 3 pints of formalin, mix thoroughly; then immerse as many apples, contained in a net or loosely woven sack, as the water will cover. The fruit, after remaining in the solution for ten minutes, the sack being partly lifted up two or three times to ensure every part of its contents coming into contact with the liquid, should be removed from the sack and placed on a layer of straw, hay, or some suitable substance to drain and dry. It is not necessary to immerse in water, after their removal from the formalin mixture, apples that are intended for storing. Plums, strawberries, and other soft fruits should be placed in a sieve or some such firm open structure for immersion in the solution.

The strength of the formalin solution is said to be little affected by use, so that the process of sterilizing batch after batch of fruit can be continued until the solution is practically used up.

The use of hydrocyanic acid has also been suggested.[2]

Boric acid is nearly always detectable in fruits, but is mainly of natural occurrence.[3] Allen and Tankard[4] give the following table, showing the proportion of boric acid contained in various fruits and ciders:

Material Examined.	*Boric Acid* (H_3BO_3) *found.*
1. Apple (Norfolk)	0·009 per cent.
2. Apple (Foxwhelp)	0·013 ,, ,,
3. Apple (Old Foxwhelp)	0·011 ,, ,,
4. Pear, No. 1	0·007 ,, ,,
5. Pear, No. 2	0·016 ,, ,,
6. Quince	0·016 ,, ,,
7. Pomegranate	0·005 ,, ,,
8. Grapes	0·004 ,, ,,
9. Norfolk cider	0·009 gramme per 100 c.c.
10. Hereford cider	0·017 ,, ,, ,,
11. Devonshire cider	0·004 ,, ,, ,,
12. Apple juice (Devon)	0·004 ,, ,, ,,

[1] *J. Board of Agriculture*, December, 1906.
[2] *J. Soc. Chem. Ind.*, 1901, 862. [3] Lippmann, *Chem. Zeit.*, 1902, **26**, 465.
[4] *Analyst*, 1904, 304.

It was discovered in Russia in 1904 that the fruit drinks sold were largely sweetened with saccharin, and in consequence a severe supervision was established over the sale of this drug. Saccharin (benzoyl sulphonimide) has a distinct preservative power. More frequently than these preservatives we find sulphites, benzoic acid, or salicylic acid. K. Lehmann[1] states that no unpleasant effects were observed after fourteen days' consumption of jam containing 0·125 per cent. of benzoic and 0·125 per cent. of 1:3 – methyl-benzoic acid.

Preservation of Milk, Cream, Butter, Margarines, and Cheese.

Milk.—A number of pathogenic organisms find milk a favourable place of growth, so that infection of different kinds can be carried by it, and several epidemics have been traced to this cause. Hence the recommendations that milk should be boiled, and the necessity for extreme cleanliness in dairies. Infectious disease occurring on the farm must, under heavy penalties, be instantly reported, and the supply of milk discontinued until the case has been removed and the buildings properly disinfected. Milk-cans should be washed and scalded as soon as possible after use, drained and dried in a place free from dust, and kept covered till wanted. Removing any stale smell by charcoal is not a safe proceeding, as the odour is a sign that the cleaning has not been thorough; in such a case the can should be thoroughly steamed, and then washed. Water from ponds or contaminated wells should never be used for washing vessels that are intended for milk, as this has originated many cases of zymotic disease, and the purity of the supply should be periodically tested. Strongly smelling disinfectants cannot be employed for dairies, since milk is so particularly absorbent of odours. Probably hydrogen peroxide would be the best agent for this purpose, if it were cheaper. It is to be regretted that jets of steam are not more extensively used for cleaning milk vessels; it would be easy to fit up an apparatus for this treatment at railway-stations, where the cans could be systematically cleansed before going to the farms.

Thorner[2] has estimated the acidity requisite to coagulate milk on warming as corresponding to 0·207 per cent. of lactic acid, but we have found the coagulating point somewhat higher than this, as the coagulation is not very marked even when the acidity is 0·23 per cent., and we believe that when the acidity exceeds 0·25 per cent. of lactic acid the milk would be considered sour and unfit for sale.

[1] *Chem. Zeit.*, 1916, **40**, 725.

[2] *Lancet*, January 27, 1900.

The methods of milk preservation may be divided into the following groups:

1. *Sterilization by Heat.*—Milk can be kept for an indefinite time by heating it under pressure to 120° C., closing it whilst hot with sterilized stoppers, and storing it in a cool place. If exposed in a warm situation after this, the casein is apt to undergo some molecular change, by which it clots into granules, or even sets almost solid, but no putrefaction ensues. According to Wroblewski, sterilization of milk causes the conversion of a little of the milk sugar into caramel, the formation of a trace of lactic acid, the coagulation of albumin, and a slight alteration in the casein, but does not lessen the digestibility. Duclaux kept milk for five years in a vessel from which he had previously exhausted the air and heated the contents to 120° C.

2. *Pasteurization* is a partial sterilization at a temperature high enough to kill pathogenic organisms and to prevent change for a moderate time, without seriously affecting the physical qualities of the milk. The International Congress of Hygiene, 1903, declared that milk of which the origin and conditions of production were unknown should be considered as dangerous for public supply, and must be submitted to heat before consumption. When properly conducted, such heating removed any pathogenic properties without injuring sensibly the food value. Three methods were distinguished:

(*a*) In simple ebullition, as practised domestically, milk is raised to 95°-98° C. for a short time, and then kept above 80° C. for fifteen to seventeen minutes; this destroys *B. tuberculosis*, the most resistant of the ordinary pathogenic forms occurring in milk, provided the pellicle which forms on the surface of the fluid be removed, as this protects the tubercular organisms. The milk should be allowed to cool in the vessel in which it is heated.

(*b*) In domestic pasteurization by apparatus of the Soxhlet type, bottles containing the milk are placed in water, which is heated to boiling and then cooled, the operation lasting about forty-five minutes. The bottles are closed by spring stoppers with rubber rings, so as to allow the escape of vapour while heating, and to close the vessel hermetically on cooling. On inverting the bottle and giving it a smart tap, a sharp click should be observed, indicating that a partial vacuum has been formed.

(*c*) Industrial pasteurization on the large scale at 85°-90° C. According to Henseval and Mullie, in Denmark cream is heated to 85°, but in Belgium only to 70° or 75°; pasteurization improves it for keeping and for making butter. As milk is a somewhat viscous liquid, and does not conduct heat freely, it is kept in

circulation through coils or plates, and the regenerative principle is frequently adopted.

The Congress agreed that the methods (*b*) and (*c*) assured the destruction of tubercle bacilli, but did not sterilize the milk, which must be consumed within the following twenty-four to forty-eight hours. The favourable influence of agitation during the process was also recognized.

In any system of milk sterilization a certain variation of temperature is liable to occur, and it is therefore important to leave a margin above the theoretical minimum of "sterilization," especially where the process is intended as a safeguard against disease.

3. *Preservation by Freezing.*—North Germany and Denmark have shipped much frozen milk in blocks, "milk ice," mostly to England. Machinery is used to agitate the milk during freezing to keep the substance uniform. An American consular report from Chemnitz deals with the advantages of delivering frozen milk, since it preserves its original properties unchanged for weeks. Frozen specimens kept over a month in a refrigerating-room showed on thawing no alteration in taste, while the number of bacteria was much reduced. The cream remained equally diffused through the solid mass. The freezing-point of milk is about $-0{\cdot}5°$ C. Milk which has been frozen should be well shaken up in thawing. Supplemented by precautions of cleanliness and sterility of vessels, it is a great advantage for milk to be refrigerated immediately after milking, as this inhibits bacteria, which develop rapidly in the warm milk.

4. *Preservation and Sterilization by Ultra-Violet Light.*—Experiments conducted by Bates at Liverpool and others have found that ultra-violet light will sterilize milk if the latter is exposed in a sufficiently thin film to the action of the rays. Bloxan[1] makes use of freezing to form thin plates of milk, which are then exposed to the action of the rays. It has been suggested that the vitamins are affected by the process. Henri and Helbronner also make use of preliminary cooling or freezing.[2]

Freund[3] gives some account of experiments conducted on the ozonization of milk, a process which has been the subject of numerous patents.[4] Although the treated milk kept well, it acquired an offensive taste and turned brownish. On standing, a flocculent precipitate is formed.

Shelmerdine[5] subjects the milk to the action of an electric

[1] *J. Soc. Chem. Ind.*, 1911, 1027.
[2] Fr. pat., 442,807 of 1911; Fr. pat., 442,924 of 1911.
[3] *J. Soc. Chem. Ind.*, 1911, 1082. [4] *E.g.*, Fr. pat., 458,569 of 1913 of A. Magits.
[5] Eng. pat., 17,554 of 1911.

current, and specifies the subjection of each 20 c.c. of milk to a current of 1·5 to 6·5 amperes at 200 volts per 508 square inches of area of the electrodes.

J. M. Beattie[1] claims to have effected the destruction of tubercle and *B. coli* in milk by means of a rapidly alternating current, the odour and colour of the milk being unaffected by the treatment.

Fischer and Gruenert[2] investigated the influence of the preservative on the keeping qualities of butter. They came to the conclusion, as a result of their experiments, that salt was the best preservative when present to the extent of 30 per cent. By its presence the decomposition of the fat and casein was nearly inhibited for three months, but in the case of other preservatives, such as benzoic, salicylic, or boric acid, even when present to the extent of 1 per cent., this result was not effected.

A German Commission appointed in 1911 condemned the use of benzoates in food for the following reasons: Slightly putrefactive meat could be deodorized by means of this preservative, giving an appearance of freshness. Good margarine will keep for several months without preservatives, whilst, if preservatives are employed, the manufacturers tend to neglect cleanliness, especially with margarine and protein foods.

Condensed Milk.—The process was invented by De Leinac, in 1852, and modified later by Borden of New York, who introduced vacuum pans for concentrating the milk without burning. In 1866 the Anglo-Swiss Company started Borden's process on a large scale. The milk is brought in every morning by farmers, who are kept under very careful supervision as to cleanliness of surroundings and absence of disease. It is tested, mixed, and heated in a bath, with the addition of pure white sugar, then run into the vacuum pans (closed copper vessels from which the air and steam are exhausted), and evaporated rapidly at a low heat for two or three hours till it is of the consistence of honey. It has been kept practically unchanged for upwards of twenty years. Great cleanliness is, of course, necessary in the process, and the tins must be sterilized by a jet of steam. In New Zealand[3] the tins are first cleansed with lime-water, then with cold water, before steam sterilization. If there be any imperfection in the process, or if the tin be not properly sealed, the milk becomes solid and cheesy. If too highly concentrated, the milk-sugar crystallizes and the preparation becomes gritty.

Condensed milk is perfectly wholesome, but the balance of its

[1] *Lancet*, April, 1914, 969.
[2] *Zeit. Unters. Nahr. Genussm.*, 1911, **22**, 553.
[3] *Chamber of Commerce*, November, 1911.

food value is disturbed by the enormous proportion of sugar, about 50 per cent. For this reason it is unsuitable for infants. The directions on the tin as to dilutions are frequently misleading—1 in 5 or 6 for adults, and 1 in 12 for infants—as the concentration is only 1 to 3 or $3\frac{1}{2}$. Brands such as the "Viking," containing no added sugar, have been introduced.

Butter.—The production of sterilized butter has not been entirely successful, owing to the fact that the proper sterilization of the cream is prevented by the necessary changing of the receptacles during the manufacture. The cream is in consequence brought in contact with numerous surfaces, and is necessarily subjected for a considerable time to the action of the air. The demand for sweet cream butter is not great, and the flavour of the commercial product is due to a "ripening" of the cream caused by certain bacteria, which in the larger dairies are now scientifically selected and controlled. The lactic bacteria, by producing acid, check the development of other organisms which may produce injurious fermentative changes. In Europe, the conclusion has been very general that butter produced from pasteurized cream, with the use of special bacterial cultures as starters of the ripening, is superior to that made from unpasteurized cream.[1] We have seen that this opinion was endorsed at the Brussels Congress of Hygiene, 1903. In America, however, according to Conn,[2] the tests do not seem to have been so favourable to the pasteurized cream, as it does not produce so high a flavour.[3]

E. E. Ritsert[4] points out that, notwithstanding the occurrence of most diverse micro-organisms in rancid fats, both aerobic and anaerobic germs die when added to the fresh undecomposed fat, from which it is inferred that the change is not initiated by them. He also found that under the influence of sunlight, which killed the germs, the rancidity was produced more rapidly. Experiments were therefore made with sterilized lard—(1) protected from access of air, but exposed to sunlight, to diffused daylight, and kept in the dark; (2) with access of air, exposed to the sunlight, and kept in the dark; (3) in atmospheres of moist and dry oxygen, carbonic acid, nitrogen, and hydrogen. As a general result it may be stated that conditions favourable to the production of rancidity proved to be the action of light during contact with air, the change being induced the more rapidly the more intense the light. Thus it was

[1] Lunde, *Centr. Agric.*, 1892, 554; Steiner, *Milchzeitung*, 1901, 401; Marcas and Henseval, *Rev. Gén. de Lait*, 1902, 387.

[2] "Bacteria in Milk and its Products," Rebman, 1903.

[3] *Bull.* **45**, *Pennsylv. Agric. Exp. Sta.*, 1898.

[4] *Pharm. Zeit.*, September 13, 1890, 579.

found that sterilized lard, either moist or dry, when kept from contact with air in sealed tubes, remained free from rancidity for two months, even though exposed to sunlight and warmth. Oxygen, both dry and moist, was absorbed freely in the light, the fat becoming strongly rancid in one month; but none was absorbed in the dark, the fat remaining quite fresh. Nitrogen and hydrogen were not absorbed in any case, and the fat remained unchanged. Carbonic acid was absorbed in the light, and to a less extent in the dark, but the lard only acquired a tallow-like taste, and no odour.

Since butter as ordinarily made entangles about 10 per cent. of water, containing some of the butter-milk, partially preserved by salt, no external application of an antiseptic can be depended on.

Cheese, as is well known, soon undergoes putrefactive changes, without apparently rendering it unwholesome. Antiseptic, or, better, aseptic, wrappers of close canvas, soaked in boric acid, and boroglyceride (p. 49) are here of value, and unobjectionable, as the rind is not eaten. They may prevent the access of the organism producing "tyrotoxicon" (p. 39), which is the cause of poisonous cheese. Milk which has been heated forms a less solid clot with rennet, and Dr. Tjaden stated at the Brussels Congress that in his experience, after treatment at 85° C., there was no difficulty in ulterior applications, except that the fabrication of hard cheese with it had not been at present satisfactory. Klein and Kirsten[1] showed that milk which had been heated for fifteen minutes at 75° C. scarcely loses any of its capacity of being converted into cheese, but that an addition of calcium chloride shortens the time required by the rennet to coagulate the milk. The quantity recommended is 1 in 5,000. After the milk has been heated to 85° C., twice the amount, and after 100° C. two and a half times the quantity, will be required to restore the coagulability by rennet. The salt is innocuous.

The United States Department of Agriculture[2] recommend the immersion of cheese in paraffin wax to prevent the growth of moulds and loss of weight on drying. The procedure advised is to dip the cheese for from one to ten seconds in a bath of paraffin wax heated to 220° F. (190° F. is too low).

The "patent" preservatives which are occasionally used for the preservation of milk, cream, various fats, vegetables, and the like are both numerous and complex in character. As the art of sophistication of foodstuffs develops, the dexterity in evading the various pure food laws of the different countries becomes more pronounced and the position of the public analyst becomes more

[1] *Chem. Zeit. Rep.*, **23,** [vi.], 51.

[2] *Bureau of Animal Ind.*, Circular No. 181, November 1, 1911.

difficult. As an example may be cited the milk preservation system, consisting of an aqueous solution of sodium nitrite and formaldehyde (according to Monier-Williams, Food Report to the Local Government Board, 17, 1912, containing 9·85 and 0·30 per cent. respectively). Owing to the interaction of the nitrite with the tryptophane resulting from the hydrolysis of the milk casein, the usual Hehner's test for formaldehyde, which is based upon the formaldehyde-tryptophane condensation, fails, and it is necessary to eliminate the nitrite by means of urea before testing by Hehner's method.

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CHAPTER IV

THE STERILIZATION OF WATER

THE methods adopted for purifying water from micro-organisms may be roughly divided into two classes:

1. Those in which the elimination of the bacteria from the water is sought, and

2. Those in which the actual destruction of the organisms is accomplished.

The gradual elimination of a great number of bacteria may be brought about by storage, while in some cases sterile water may be obtained by filtration.

Effect of Storage.—The knowledge of the improvement that could be obtained by storing water can be traced back to early Egyptian times, whilst in Jerusalem and also in India we have the remains of tanks and cisterns that were famous in their day. Modern reservoirs are of large capacity. The Island Barn and Chingford reservoirs of the London Metropolitan Water Board hold respectively 1,000 and 3,000 million gallons, whilst the Kensico reservoir of New York City has a capacity of no less than 40,000 million gallons. Reduction in the bacterial population of stored water takes place by the following methods:

1. **Sedimentation.**—The effect of sedimentation can be enhanced by adding insoluble substances which, although not bactericidal themselves, drag down with them the bacteria in the water; their action may be classified into three distinct groups:

(*a*) *Plants and Plant Products.*—These may be mucilaginous like the quince, elm bark, or gum tragacanth, or they may act by virtue of the vegetable acids which they contain, forming insoluble precipitates with the earthy salts in the waters. The clearing nut of India, which is the fruit of a tree, *Strychnos potatorum* (Linn.),[1] has a high reputation and extensive use among the natives. Others, again, are astringent and tanninoid, among which the cinchona or Peruvian bark employed from antiquity by the South American Indians is the best known. A reference to similar practice is found in Exodus xv.

[1] See Trimen's "Flora of Ceylon," 1895, p. 176; "Useful Plants of India," 1873, p. 408.

(*b*) *Inert Chemicals and Powders.*—These were first systematically investigated by P. Frankland,[1] who conducted comparative experiments on spongy iron, powdered wood, charcoal, coke, chalk, china clay, lime (as in the Clark softening process), and other substances. The general conclusions are that the removal of bacteria is only partial, and subject to great irregularities caused by convection currents and the varying viscosity of the water. The organisms frequently rise from the inert precipitated matter, and recontaminate the water; this is especially the case where the precipitant contains a pabulum for the organisms such as the phosphates of animal charcoal.

(*c*) *Chemical Coagulants.*—The most usual coagulant is a soluble aluminium salt which reacts with the carbonates of calcium, magnesium, and ammonium present in the water, forming insoluble gelatinous hydrated alumina, which combines with colouring and other matters, and carries them down together with the organisms. As minerals, natural aluminium sulphate and alums are widely distributed, and their use for water purifying is a very ancient discovery. The Egyptians, from the earliest times, filtered their water through porous earthenware containing alum, whilst the Japanese and Chinese are also said to have used this process. Pliny[2] mentions "salsugo terræ," "agua alumina," and Vitruvius speaks of "aluminosi fontes." Alumino-ferric is used in large quantities for purifying water and sewage at the present time. Iron hydroxides and sodium phosphates have also a limited application.

2. By the action of sunlight on the surface of the stored water. This will be referred to later.

3. By ingestion of the organisms in higher forms of life, such as protozoa,[3] crustacea,[4] and infusoria.[5] Strohmeyer has observed that a healthy growth of algæ sterilized the surrounding water in the course of one day.

4. By exhaustion of their food supply and poisoning themselves with their own excretory products. The pathogenic organisms thrive best at blood heat, and are specially susceptible to these adhesive influences, together with the effect of low temperatures. The work of Russell and Fuller[6] and Houston[7] has demonstrated the gradual impairing of the vitality of these susceptible organisms and the disappearance of one characteristic reaction after another,

[1] "Micro-Organisms in Water," p. 193. [2] *Hist. Nat.*, lib. xxxv., cap. 15.
[3] Hautemuller, *Arch. Hyg.*, 1908, **54,** 89.
[4] Horhammer, *Arch. Hyg.*, 1911, **73,** 183.
[5] Stokvis and Swellengrebel, *J. Hyg.*, 1911, **11,** 481.
[6] *Trans. Amer. Public Health Assoc.*, 1905, **31.**
[7] *Annual Reports London Metropolitan Water Board.*

together with their virulence, by prolonged storage. This subject, including the important engineering and chemical problems involved, is more fully dealt with in books on water supply.

Methods of Filtration.

Sand Filtration.—Sand filters were first regarded simply as strainers for turbid water, and the fineness and cleanness of the sand as the most important point. Analyses later proving that the soluble constituents were considerably affected, an explanation was sought in surface action. Afterwards, from the fact that nitrates and carbonic acid were formed, a chemical theory of simple oxidation arose, involving a free supply of air.

Three discoveries, however, threw a new light on the process.

1. The size of the finer mineral particles is only about $\frac{1}{100000}$ inch (0·25μ), and that of most bacteria $\frac{1}{25000}$ inch, or larger (μ to 5μ), but both are smaller than the interstices between the grains of even fine sand; consequently it follows (*a*) that the clearing is not accounted for by simple straining, (*b*) that the organisms would be retained first.

2. Piefke in Berlin, about 1886, found that sterilized sand effected hardly any purification, and did not retain microbes. It had previously been noticed that sand filters did not become efficient for some days after relaying.

3. When the oxygen or air and the water were sterilized, little or no oxidation of organic matter occurred.

It was proved, therefore, that for the proper mechanical and chemical effects the action of organisms is essential. It must be remembered that some organisms have long flagella, while a large number, such as diatoms and bacteria, are normally surrounded by a gelatinous envelope which greatly increases their size, and enables them to adhere to surfaces, so that in a short time the sand in a new filter becomes covered with a living slimy layer which entangles suspended matters and effects the main part of the purification. This is called "schmutzdecke," and sometimes the "schlammdecke," or mud-covering, and until it forms the filtration is inefficient.

In the under layers of sand the nitrifying organisms, which work best in the dark, act as they do in soils, causing oxidation, and producing nitrates by the aid of the dissolved oxygen. Green algæ in their growth evolve oxygen, and so increase the amount in solution, while bacteria as a rule diminish it. Although the chief removal of organisms occurs in the "schmutzdecke," the lower layers of sand are not inactive, as Reinsch has shown at Altona.

For an example, he gives the average number of organisms per c.c. as: Raw water, 36,000; just under the schmutzdecke, 1,800; at bottom of sand (35 inches), 44.

The proportion of micro-organisms removed by the sand filters of water companies shows ordinarily a variation between 95 and 98·5 per cent., but should be well up to the latter figure. Koch laid down as a limit that water containing more than 100 organisms per c.c. must not be allowed to pass into consumption. That when carefully used these filters afford a remarkable protection against pathogenic species was proved by experience in the cholera epidemic of 1892 at Hamburg and Altona,[1] when in Altona the water was filtered carefully, in Hamburg not. Although the original water supplied to Altona was worse than that of Hamburg, the deaths in Altona were 221, in Hamburg 1,250, per 100,000. At the end of 1892 an outbreak occurred in Altona owing to a filter-bed breaking down, a proof that the slightest imperfection in the manipulation is a constant menace during any epidemic.

"Mechanical filters," of which there are various types (see Water Supply), are much used, especially in America, for purification on the large scale. The water is driven through a much smaller bed of sand or crushed quartz at about forty times the rapidity. Coagulation by sulphate of alumina, followed by lime, is generally adopted as a preliminary to form an artificial "schmutzdecke," or top film. Used in this way, they are capable of removing 96 to 99·5 per cent. of the organisms. With or without coagulants, they are specially suitable, in cases where the supply has to be drawn from turbid sources, for preparing the water for the ordinary slow sand filtration, as they are much more easily cleaned and renewed than large filter-beds.

Sterilizing Filters.—Sand and mechanical filters in good condition, and under favourable circumstances, occasionally yield a sterile effluent. But such a result cannot be depended on, and to secure it a much finer medium must be employed. At this date it is hardly necessary to refer to the large variety of filters formerly trusted, which have been proved by Plagge, Sims Woodhead, Guinochet, Johnston, and others, to be quite inefficient in preventing the passage of bacteria, though they may render the water bright in appearance. These filters were really worse than useless, as they formed a cultivation bed for organisms of all kinds, including pathogenic forms, and actually sometimes increased their numbers.

The only filter that has stood all tests is the Pasteur-Chamber-

[1] Koch, *Zeitsch. Hyg.*, **14**, 393; **15**, 89.

land. This so-called " candle filter " originated, as is well known, from Pasteur's laboratory experiments in preparing germ-free broth cultures for bacteriological investigations, when Chamberland introduced the practical application to drinking-water of the tubes that Pasteur had found efficient for excluding bacteria. The same remark applies to these as in connection with sand filters, that the removal is not accounted for entirely by a mere straining by the material, as the bodies of some of the organisms are smaller than the pores, though the gelatinous envelope of the bacteria and their entanglement, joined with the much greater fineness and evenness of the medium, and the consequent slowness of filtration, make the removal complete. But there must be also some molecular attraction dependent on the material of the tube and its manufacture, as a large number of fine-grained substances, to the naked eye apparently identical in texture, have been tried and found to be unreliable.[1] Even with the Pasteur filter it is stated that " it requires the highest skill in pottery to produce a uniform result as to sterilizing capacity, and some 30 per cent. of the finished tubes are rejected on test." Candle filters are manufactured by the Sanitats Porzellan Fabrik, at Charlottenberg, and in this country several English-made candle filters have appeared. At present, however, there is not sufficient evidence to warrant the belief that any of them give the protection against water-borne disease which is afforded by Pasteur filtration, and the assumption that they function similarly is a very dangerous one for the general public, who are unable to distinguish between the forms.

The methods of purification based on the destruction of organisms are divisible into physical and chemical processes of sterilization.

Physical Methods of Sterilization.

I. *Sterilization by Heat.*—Boiling is, of course, an efficient means on a small scale, but the expense is prohibitive when large quantities of water have to be regularly dealt with. In India the Larymore boiler has been largely used and found efficient, but the taste of the boiled water is often objected to, as the liquid not only is flat and free from dissolved gases, but has frequently a burnt flavour from overheated organic matter. A successful heat sterilizer must, therefore, be so designed as not only to yield a water which is bacterially pure, but to ensure the preservation of the natural flavour and gases of the water, and, further, some means of regenerating the heat required for effecting the sterilization must be

[1] Hesse, *Zeitsch. Hyg.*, 1911, **70**, 311; and Bullock, Craw, and Anderson, *J. Hyg.*, 1906, 1908, 1909; Hofstädter, *Arch. Hyg.*, 1905, **53**, 205.

included. One of the earliest methods for carrying out this object consisted in heating the water to a temperature of about 115° C. in a closed vessel (when the natural gases are not evolved, nor are the salts deposited to any considerable extent), and using the outgoing water for warming that entering the boiler by means of interchanging coils. In such a system the heated water is not exposed to the air, and is therefore kept free from any subsequent contamination. At Brest, in 1892, apparatus on these lines by Rouart and Geneste-Herscher and Co. were officially tested. Later Professor Vaillard, of the Pasteur Institute in Paris, and Mons. Desmaroux devised similar plant, so arranged that all the water passed through a superheater in which it was subjected to a minimum temperature of 113° C. for about five minutes. Connected with the superheater was a temperature exchanger made of a double series of spiral compartments, which cooled the sterilized water to within a few degrees of the supply. This apparatus has been used at the Sanatorium de St. Trojan in Paris. When made on a large scale, the economy in fuel is greater, and at Tsaritzine, on the Volga, a large installation is heated from a common source, and there produces enough sterilized water for a population of 10,000.

A difficulty in all such apparatus, however, is met with in the deposition of salts from hard waters in the temperature exchanger, and as, for perfect cooling, the tubes or compartments must necessarily be small, there is danger of such tubes blocking with the deposit, unless facilities for frequently cleansing are provided. More recently the heat sterilization of water has been effected in plant in which the water is not heated under pressure, but is brought to the boil, and at once passes over a weir into a temperature exchanger. Since the water only boils for a few seconds, it retains most of its original gas and taste, and the apparatus can be so constructed that it is impossible for any water which has not been boiled to pass into the cooler. The Forbes apparatus is designed on these lines.[1] A constant level in the tank placed above the exchanger is ensured by a float-actuated valve which maintains the water-level in the boiler slightly below a cup placed therein. The valve-box therefore regulates the flow of the water, irrespective of the pressure on the surface, in a similar manner to the bird fountain or aerostatic feed apparatus used when a constant level is required with a small volume of water. The sterilizer operates at a rate which will be dependent upon the size and intensity of the flame of the burner, as the water will boil over the cup at different rates. It is obvious that, although the speed in a given apparatus depends entirely upon the rate of boiling or the heat applied, the tempera-

[1] U.S. patent, December 13, 1898.

ture of the sterilized water will correspondingly vary if the same cooler be always used. It was said to be practicable to build a sterilizer in any size, even to the extent of sterilizing the water supply of a city or town, at a cost of from 13s. 9d. to 14s. per million gallons, including interest on the plant, fuel, and labour. In such apparatus in America, 1 pound of coal has sterilized from 2,000 to 5,000 pounds of water. The Forbes sterilizer claimed as follows:

(1) A source of water supply having a level maintained below that required for causing the water to pass entirely through the apparatus.

(2) The application of heat to a part of the water in the apparatus at the point reached by gravity (due to the maintained level in the source of supply) until ebullition is produced, thereby causing the water to rise and pass through the remainder of the apparatus; and

(3) The transference of the heat from the hot water passing from, to the cold water passing to, the point where the heat is applied.

In this country the Lawrence sterilizer has been in use for some time at Guy's Hospital and elsewhere, and accomplishes the object somewhat differently from the Forbes apparatus. It has a vertical boiler in which are placed depositing trays of iron above the water-line, and a series of plates, termed "locators," in the boiling water. The inflow passing downwards is met by the steam produced below, and is thus progressively heated until it attains the highest temperature, and the most violent ebullition, in the lowest compartment. The gases in solution are expelled, and the carbonates of lime and magnesia are almost entirely deposited as a friable scale upon the trays and locators, which are removed from time to time for cleaning or replacement, while the small amount of sludge collecting at the bottom can be blown out without trouble. The softened liquid then passes upwards through an outer division of the cylinder to an interchanger, where it gives up its heat to the raw inflowing water, and finally issues at a temperature depending upon the rate of boiling, so that the heat is in this way almost wholly recovered. Very little attention is required, and trouble with reagents is avoided. When used for softening boiler-feed water, it is found best to cool only to 17° C. above the inflow to obviate the loss by radiation involved in storing or transferring hot water. In common with the Forbes pattern, the rate of flow is regulated by the heat applied, but it is clear that without special provision unsterilized water can pass through into the heat chamber, and so contaminate the supply. By inserting in the boiler a metal plate fitted to a carefully adjusted valve, the steam produced in the boiler can be

made to regulate the flow of the water, so that to a certain extent the apparatus can be made as automatic as the Forbes plant.

Results obtained in working different forms of heat sterilizers in our own laboratory show that, even with very varying rates of flow, sterile water can with care be usually ensured. At the same time, when working rapidly, the amount of dissolved gas in the treated water is much reduced, but the fault can be remedied, if required, by storing in carefully cleaned vessels protected by cotton-wool.

The chief objection to heat sterilizers at present is the blocking up of the interchanger when used with dirty or hard waters, and in army service the difficulty of providing fuel. Further, heat sterilizers of non-pressure types clearly do not ensure the destruction of spores, and therefore can only be used as a precaution against cholera and typhoid, and other non-spore-bearing pathogenic organisms. With candle filters (p. 65) it is clear that theoretically the transport problem is reduced to a minimum, as there is no expenditure of any material during the period of use, so that the weight required is simply determined by the actual filter itself and necessary accessories. On the other hand, for small units and individual troopers, when away from their base, the weight of even a small pocket filter is considerable, and the advantage then lies in some form of chemical sterilization.

II. *Sterilization by Light.*—The beneficial effects of sunlight on water were noticed at a very early date. As early as 1640 Dr. Hart cautioned his readers against the use of well-water "to which the sun hath no reflection." While the growth of green algæ can be prevented by excluding light from water during storage, yet the beneficial effect of light in destroying the germs of disease is in this way hindered or lost. The algæ may become troublesome, but are not dangerous like the pathogenic bacteria, and as the former undoubtedly cause a disappearance of some of the organic matter present, when not superabundant or of objectionable species, conferring odours or tastes, they are actually useful.

The germicidal power of sunlight is strongest beyond the visible spectrum in the ultra-violet, while ordinary daylight and most forms of artificial illumination, so far from retarding growths, will often assist them.

Downes and Blunt[1] were the first to investigate systematically the sterilizing action of light on contaminated water. They found direct sunlight speedily fatal to most bacteria, and even in a little longer time to spores, while diffused light is harmful in a less degree.

[1] *Proc. Roy. Soc.*, 1877, **26**, 488.

Dieudonné[1] showed that the germicidal power of the light increased as it progressed from the red to the ultra-violet.

Westbrook, at Marburg in 1900, showed that the action was not simply a physical one, but depended greatly on the function of the chemical rays in promoting oxidation; therefore free access of air is necessary. Observers have found that the inhibitive property of direct sunlight may penetrate in clear water to 6 or 8 feet, but with any turbidity it is soon arrested. Buchner's[2] results with *Vibrio cholerœ*, *B. typhi*, and *B. pyocyaneus*, were that light is germicidal down to 1·6 metres (5 feet), but that its antagonistic effect on some bacteria in clear water did not become imperceptible till a depth of 3 metres (9·8 feet) was reached. Whipple[3] remarks that disinfection by sunlight is not a factor at depths greater than a few feet, although in the Tropics the effect may be more marked and even become of importance.[4]

The earliest scientific study of the biological effects of ultra-violet light was by Finsen and his pupils, who applied the bactericidal effect of the rays, produced artificially, to the curing of lupus and other fungoid diseases. The germicidal power of light in general, and of ultra-violet light in particular, having been proved, the next point was, as always, economical generation and use.

Ordinary gas burners, incandescent mantles, or glowing filaments are very poor in such radiations, but, on the other hand, incandescent vapours are frequently rich in this actinic light, especially those of iron, aluminium, and mercury. Early experiments were carried out with electrodes of iron, or iron with aluminium cores, for the production of an electric arc between the ends. The water was allowed to run in a thin film exposed to the rays, but the time of exposure to the light was generally not sufficient and difficulties occurred in the removal of the oxides of iron or aluminium formed. At Neuilly-sur-Marne a lamp of this type has sterilized a cubic metre of water with a current consumption of only 20 watts.

Leo Arons[5] was the first to make successful use of glowing mercury as a source of light. In 1895 M. Chas. Lambert submitted to the Paris Service des Eaux the description of a process for "subjecting water to an intense illumination, while opposing no obstacle to the ultra-violet rays of the spectrum," and later M. de Mare patented "the use of quartz lamps with mercury vapour for sterilizing potable liquids such as water."

[1] *Arb. Kais. Gesund.*, 1894, 405. [2] *Arch. Hyg.*, 1893, **17**, 179.
[3] Internat. Cong. App. Chem., N.Y., 1912.
[4] Clemesha, "Bacteriology of Surface Waters in the Tropics," 1912.
[5] *Wied. Ann.*, 1892, **47**, 767.

In 1909 Drs. Courmont and Nogier communicated to the Academy their research on the subject, which was followed by many others, proving that the pathogenic and other organisms were destroyed by short exposure, not connected with ozone formation, as has been supposed; but the water had to be specially freed from suspended matter, since particles screened the microbes from the irradiation. It is because ordinary glass, though transparent, absorbs a great part of the rays that the lamps are constructed of fused silica. To utilize all the available light, the lamps are frequently entirely immersed in the water to be sterilized, and in many cases they are protected by a thin transparent envelope, which, of course, involves a small air space and some absorption of the rays. With immersed lamps two difficulties occur: in the first place, after a while the lamp becomes covered with a scale of deposited earthy carbonates and iron, blocking out the rays; secondly, the temperature is considerably lowered by the immersion, and the light emission for a given watt consumption seriously reduced. Consequently the lamp is often placed directly above the water, although this involves a sacrifice of energy. Dr. Recklinghausen remarks: "In such a system, and in spite of reflectors, only perhaps 30 or 40 per cent. of the light emitted entered the water and obtained its effect."

The use of baffle plates makes the water pass several times under the influence of the rays, thus lengthening the period of exposure. The action is very little affected by the temperature of the water; even ice, if transparent, can be sterilized in about the same time as water.

As has already been mentioned, the action is not dependent on the production of ozone, and is not dependent on the amount of dissolved oxygen in the water; only minute traces of hydrogen peroxide are formed after several hours, whereas the sterilization takes only a short exposure.

Various classes of organisms are not all equally sensitive to the rays, just as they are not equally sensitive to heat or to chemical agents, *B. subtilis* and tetanus being the most resistant of those tested.

The following table, from tests carried out in the Sorbonne University, illustrates the effective range of the rays in an ordinary water infected with *B. coli*, but free from colour and suspended matter:

Distance from Lamp.	*Number of Seconds required to Sterilize with a 220 Volt Lamp.*
10 centimetres	1
20 ,,	4
40 ,,	15
60 ,,	30

It will be noted from these figures that the time of sterilization does not follow the "law of the inverse square of the distance" with any great degree of accuracy. This rather surprising result has been confirmed quite recently by some careful experiments by R. Scharff at Massachusetts, who came to the conclusion that no such generalization was to be found between distance and sterilizing power.

The system of Henri Heilbronner and Recklinghausen has been installed in many towns in France, the largest installation being at Amiens, dealing with nearly 4,000,000 gallons per day. Small installations are in use in various hospitals and at a public drinking fountain in Paris. A transportable plant has been adopted in the French Army.[1]

III. *Chemical sterilization* is mainly to be regarded as an emergency method. The considerable total expense for even the cheapest chemical, apart from the labour and trouble involved, must necessarily render the operations costly. Under special circumstances, however, this method may become useful and even necessary.

Oxidizing agents have generally been favoured on the ground that oxygen is the natural purifier, but we have seen that oxidation is only a part, and not the most essential one, of natural purification. Their great disadvantage is that they are largely consumed by easily oxidizable substances, which may be physiologically harmless, before an excess can be established to act on bacteria; hence the water must be prepared beforehand by removal of most of the organic matter. The variations in the amount recorded as necessary by different observers are due in great part to this cause.

It is obvious that for drinking-water only such reagents are available as do not affect its wholesomeness or palatability. In water supplies, however, from which the greater part of the organic matter has been removed by some preliminary process, the quantity of some oxidising agents required is so exceedingly small that it would have no injurious effect on the consumer. Among these substances the manganates and permanganates have long been popular. Potassium permanganate was employed on a large scale by Lereboullet for the drinking-water of the soldiers in the Franco-German War of 1870; at that time it was not a question of destroying the organisms, but solely the organic matter present. In India it has been widely used for purifying wells and tanks, these being regularly "pinked" by officials as a defence against cholera, Hankin considering it to be a specific for cholera bacilli;[2] recent reports on the efficiency of the practice have, however, been un-

[1] *La Science et Vie*, December, 1913. [2] *Brit. Med. J.*, March 16, 1895.

favourable. Its action on bacteria has been examined by numerous observers. Koch[1] states that it is effective only in concentrated solutions. Calvert[2] found 1 in 125 necessary to prevent growth in bouillon for six days. Miquel states that 3·5 grammes were required to sterilize 1 litre of beef-tea, or 1 in 268. Demarquay, from surgical experience, considered that 1 in 1,000 "disinfected very well, but its action was rapidly exhausted, and it did not prevent the secretions from retaining their virulence." Vallin was of similar opinion,[3] also Blyth[4] and Klein.[5] Dr. A. H. Burgess found that 1 in 40 was required to destroy *B. coli communis* in one hour.[6]

Lepeyrère, at the Paris International Congress of Hygiene in 1900, suggested the use of a mixture of potassium permanganate, sodium aluminate, and sodium and calcium carbonates for the purification of water in campaigns. After standing a few minutes, the water was passed through "purified peat fibre" mixed with manganese dioxide. The process was examined by Dr. A. Warner[7] with water infected with *B. typhosus*; even when filtering slowly it did not get rid of the pathogenic bacteria.

Permanganate, together with lime, salts of iron, and carbonic acid, has been successfully applied in the Linden process. It was adopted by the town of Ghent before the war to purify for drinking purposes the water of the River Scheldt, which is particularly foul and polluted.

Ozone.

Ozone has the exceptional advantage of being easily obtained everywhere from atmospheric oxygen, and recent progress in ozone generators and electric supply leads to the belief that this gas may be economically produced. In several directions it has been used for public supplies on a large scale, and it promises to be further extended as a "finisher" in the sterilization of water. The chief difference between the action of ozone, O_3, and of atmospheric or ordinary oxygen, O_2, is that the latter will not act on most varieties of organic matter without the help of organisms—either direct, in their processes of life, or indirect, through a special class of enzymes, called oxydases, that some of them produce. In the sterilizing function of ozone only one-third of the oxygen actually contained in it ranks as "available" oxygen. The gas attacks metals, india-rubber, gutta-percha, and wood, and is thereby itself destroyed; hence apparatus for its production, storage,

[1] *Mittheil. Kais. Gesundh.*, 1881.
[2] *Brit. Med. J.*, March 16, 1895.
[3] *Désinfectants*, 1882.
[4] *Proc. Roy. Soc.*, 1886.
[5] Stevenson and Murphy's "Hygiene," 1893, p. 61.
[6] *Lancet*, June, 1900.
[7] *Public Health*, July, 1901, 704.

or conveyance, must be constructed of stoneware or glass, or, less advantageously, of protected metal. The air to be ozonized is first freed from dust by cotton-wool strainers, then dried, to avoid the formation of nitric acid, and passed through a cooled space traversed by a silent electrical discharge. Sparks should be avoided, as heat reconverts ozone into ordinary oxygen. To obtain a strength of 7 per cent. (the highest mentioned) was found by M. Chassy to cost in electric energy ninety times as much as ½ per cent., so that if economy be considered, it is best only feebly to enrich the oxygen, while accelerating the circulation of gas. Ozonizers are of a number of forms.

Baron Tindal, about 1896, proposed to the municipality of Paris to sterilize, by means of ozone, 5,000 cubic metres (1,100,000 gallons) of crude Seine water daily. His first experiments were made at Oudshoorn, Holland, in 1893. The system was installed experimentally in Paris, Brussels, and Ostend, and was proved by the reports of Dr. Van Ermengem and others to sterilize at a reasonable rate canal and other waters which had been previously filtered.

In 1898 Siemens and Halske erected an experimental plant at Martinikenfelde, near Berlin, and it was found necessary to first remove coarser impurities by a quick filter. The original water from the River Spree showed 100,000 to 600,000 organisms per c.c.; the effluent was sometimes sterile, and never contained more than 2 to 9 organisms per c.c. That the water is not always sterilized may be due to the fact that the ozonization is less than the amount of 4 grammes per cubic metre which Van Ermengem found to be effective.

Marmier and Abraham's apparatus, installed at Lille in 1898, has a plate ozonizer with cooled electrodes, working with 40,000 volts, and the water is sterilized as above in a masonry tower. The Commission who approved of the apparatus and its results reported that only a few spores of highly resistant and harmless *B. subtilis* were left, and that these disappeared on about twelve hours' storage, the water remaining sterile in the air for four days, though showing no trace of ozone a few minutes after issuing from the apparatus. No antiseptic compound was formed, as water bacteria were not inhibited when added to the liquid after treatment. The report concluded that of the few organisms which escape destruction in the tower, nearly all succumb after some minutes in the reservoirs. The only other alterations in the water were a decrease in the organic matter and an improvement in physical character.

Froelich, about 1890, proved that ozone destroyed micro-

organisms, and that its action was most effective in presence of moisture. He showed[1] that ozonization sterilizes water, oxidizes nitrites and sulphuretted hydrogen, and throws down iron as ferric hydroxide, and made the important suggestion that ozone should follow filtration. About the same time Kowalowski and Krukowitsch in Russia, and Christmas in Paris, investigated its bactericidal power. Ohlmuller, in 1892,[2] found that water from the River Spree was sterilized in ten minutes by 86·6 milligrammes of ozone per litre; sewage was not sterilized in an hour by 156·3 milligrammes; but distilled water to which bacteria in great numbers had been added was sterilized most easily, anthrax, typhoid, and cholera bacilli being killed in two to ten minutes, proving that where water was not too contaminated with organic impurities, ozone destroyed completely these pathogenic bacteria. Ransome and Foulerton, in 1903,[3] even succeeded in killing bacteria in milk.

Ozone is now rather extensively used in Europe for sterilizing partly purified water. In 1908 one of us was called upon to examine the De Frisé system at the Paris waterworks at St. Maur, and found very successful results. The River Marne water, after ordinary sedimentation and filtration through gravel and sand, was still unfit for a supply, but by afterwards ozonizing it gave a well-aerated brilliant liquid of natural bluish tint, and quite inodorous, containing per c.c. only one or two innocuous organisms of the *B. subtilis* type. The *B. coli* test became invariably negative, although altogether 1,580 c.c. were examined, with a maximum of 200 c.c. at one test. It was found that 57 kilowatt hours per million imperial gallons were required for the sterilizing operation, and 76 kilowatt hours for pumping. These figures would be reduced to 47·5 and 63·4 kilowatt hours respectively per million United States gallons. The De Frise apparatus used Siemens-Halske ozonizers with a simple and efficient ozonizing tower, and a circuit by which ozone escaping after action was returned and used again, thereby effecting an important economy. The Paris municipality decided in July, 1910, that the part of the city drinking supply derived from the Marne (about 20,000,000 gallons daily) should, after coarse filtration, be sterilized by ozone, half by the De Frise and half by the combined Otto process. The latter employs "emulsers," which are injectors effecting a mixture of ozonized air with the water, the action being completed in "columns of self-contact." Ozone sterilization has been installed in about thirty French towns, in Rumania for the Danube, at Petrograd for the Neva, at two

[1] *Electrotechn. Zeit.*, 1891, **26.**

[2] *Arbeit. Kais. Gesund.*, **8**, 229.

[3] *Proc. Roy. Soc.*, February 14, **78**.

waterworks in Holland (the pioneer), Belgium, Germany, Italy, Spain, Brazil, and Egypt, and experiments have been undertaken at Darjeeling in India.

Other processes differing in mechanical details are the Vosmaer, tried at Philadelphia, and the Howard-Bridge, at Lindsay, Ontario, Canada.

One of the largest plants is that at Petrograd, Russia, for 11,000,000 gallons per day. The water is first treated with sulphate of alumina, then passes on to thirty-eight sand filters at a rate of 1,000 gallons per square metre of filtering surface per hour, and finally enters the five sterilizing towers along with ozonized air. There are 128 Siemens-Halske water-cooled ozonizers. The air is freed from moisture by refrigeration, and is ozonized to the degree of 2·5 grammes per cubic metre. The total cost from the raw river to the finished water was recorded in 1911 as 0·86d. to 0·97d. per 1,000 gallons. At St. Maur, Paris, M. Colmet Daage estimated that the cost, under the most favourable circumstances, was 0·31d. per 1,000 gallons, excluding interest, amortization, and repairs. At Nice, where cheap water power is available, the average annual cost is given as 0·164d. per 1,000 gallons, and at Rimiez, where there is, besides, no pumping, it was only 0·125d. A portable ozone purifier has been adopted by the Spanish Government for the water supply of armies in the field.

The preference for ozone as a water-sterilizing agent has been hindered by several difficulties. One is the question of expense. In this regard the manufacture has been considerably cheapened. Another is that it has to be applied in the gaseous form diluted with air, so that a large quantity of inert gas must be pumped, and with this admixture the ozone does not very readily dissolve. The latter fact has been overcome by using towers and saturaters, as mentioned above. Moreover, the conversion of oxygen into ozone is a reversible action, requiring a number of precautions as to detail. In spite of the numerous researches, the best conditions are not yet fully agreed on; therefore, we have not reached finality in the economy of ozone production. It is stated that "the best results ever obtained with a silent discharge apparatus gave 36·7 grammes of ozone per kilowatt hour, the theoretical yield being over a kilogramme." A certain amount of the loss is due to the formation of ultra-violet light in the machine. When an ozonizer is acting properly, the interelectrodic space has an almost uniform violet illumination without any sparking. Regener[1] showed that the ultra-violet light limits the concentration of ozone. (See Ozone.)

Siemens and Halske have several devices for preventing corro-

[1] *Ann. Physik.*, 1906, **9**, 1033.

sion of the metallic parts of the apparatus. British patent 17,787 of 1910 reverses the usual procedure by drawing ozonized air through the water instead of forcing it through from below, so that the main work shall be done, and the ozone almost entirely used up, before entering the pumps. This appears expensive mechanically. Their French (international) patent, 431,402 of 1910, introduces small quantities of water into the pumps at the same time that the gas is admitted.

The Peroxides.

Hydrogen Peroxide has not found any extended application as a water-sterilizing agent, although at first sight, owing to the fact that on decomposition water is the only resulting product, it would appear to be as ideal a reagent as ozone.

The balance of recent researches, especially those of Reichet,[1] has proved, however, that a concentration of 1 in 1,000 is necessary, and its cost and instability, the impurities of the commercial article, and the difficulties of transport of large quantities of a liquid, interfere with its use for sterilizing water.

Sodium Peroxide is a powerful oxidizing agent which generates H_2O_2 when dissolved, and, being a solid, is free from the last-named objection; either when used alone or in conjunction with the usual softening agents, such as lime or soda, it has advantages in that it sterilizes as well as softens. As by combination with softening so much of the organic matter is removed, the action of the hydrogen peroxide on the bacteria is better ensured. With the same object, where the organic matter is high, partial softening by ordinary methods can precede the addition of sodium peroxide. This process has the further advantage that the final effect is only a slight addition to the natural sodium salts, and that acid moorland waters are naturalized and bleached, and their plumbo-solvency removed. Appended are two examples of satisfactory results that have been obtained in our laboratory:

A. London tap-water, containing an average of 30 organisms per c.c.; permanent hardness, 3·71 parts per 100,000. To separate quantities were added (1) 3 parts per 100,000 caustic soda, (2) 3 parts per 100,000 of sodium peroxide.

B. Somewhat impure water, containing 93 organisms per c.c.; permanent hardness about 4 parts. (1) Three parts per 100,000 of caustic soda, (2) 1·5 caustic and 1·5 sodium peroxide.

Blanks were mounted in each case, and all the waters after the first shaking were allowed to settle, in series A at about 10° C., in series B at 18°. The number of organisms per c.c. were as follows:

[1] *Zeitsch. Hyg.*, 1908, **61**, 49.

	A.			B.		
Hours.	*Blank.*	(1.)	(2.)	*Blank.*	(1.)	(2.)
1	31	28	11	115	94	62
3½	27	18	·1	103	100	34
24	19	16	0	173	117	2

(1) Shows the result of softening alone; (2) that of softening with the aid of sodium peroxide. The multiplication of organisms in B (1) at the higher temperature is in accordance with what we have previously noticed in simple softening.

Calcium Peroxide, patent 17,460 of 1900, is sold under the name of bicalzit. Hetsch finds it to be more effective than hydrogen peroxide, typhoid organisms being killed by ½ part per thousand. Freyringe and Roche in 1905 advocated its use for drinking-water, recommending the addition of small quantities of sodium bicarbonate, with subsequent filtration through manganese dioxide to remove the calcium carbonate formed, and any traces of hydrogen peroxide not decomposed in the water. They state that two or three hours is necessary to ensure sterility.

Magnesium Peroxide is sold for sterilizing mineral waters. A commercial preparation is stated to contain about 33 per cent. of the pure peroxide, the rest being magnesium carbonate. Croner[1] obtained sterilization generally, but not always, with 0·7 to 1 gramme MgO_2 per litre. Dr. Proskauer and others[2] advise the employment of MgO_2.

Lime.—As early as 1885 P. Frankland[3] observed a removal, and to a certain extent a killing, or at least inhibiting, of organisms in waters softened with lime.

The fault in this respect of a mere softening with a minimum dose of lime is that the action is only a partial removal of the organisms, and that only some of them are killed. It has already been pointed out that when sedimented for some days the mechanically carried down or inhibited bacteria rise again and develop in immense numbers in even the upper layers.

Kruger[4] confirmed the above-mentioned after-distribution and multiplication in a number of waters. In a typical instance he added slaked lime equivalent to 14 grains per gallon of CaO, by which the water was rendered strongly alkaline. The average

[1] *Zeitsch. Hyg.*, 1908, **58,** 487.

[2] *Kong. Mittheil. Leb. Hyg.*, 1911, **1,** 390; Young and Sherwood, *J. Ind. Eng. Chem.*, 1911, **3,** 495.

[3] *Proc. Roy. Soc.*, 1885.

[4] *Zeitsch. Hyg.*, 1889.

number of organisms per c.c. was, in the unlimed water: first day 5,142, third day 21,344, twenty-third day 15,714; in the limed water: first day 662, third day 824, twenty-third day 1,580. In the first case the reduction in the longer time is probably due to the well-known effect of storage. In the treated water the multiplication has continued, though the numbers are much less; therefore the excess lime, as Frankland remarks, has acted as a bactericide. Dr. Burlureaux of Paris is also quoted as having shown that bacteria are actually destroyed in the softening with lime. Liborius[1] and Pfuhl[2] came to the conclusion that 1 gramme of CaO per litre was an effective germicide for typhoid organisms. Grether,[3] Dunbar and Zurn,[4] on the other hand, could not obtain sterility with this and even larger amounts.

Use of Excess Lime.—Dr. Houston[5] has taken the method up, and states: "I have found that quicklime (about 75 per cent. CaO) added to raw Thames water in the proportion of 1 part of quicklime to 5,000 parts of water (0·02 per cent.) kills *B. coli* in five to twenty-four hours." In his Eighth Report, 1912, he records further experiments on "excess lime" as a water sterilizer, and summarizes strongly in its favour, saying: "Fifteen pounds of quicklime, costing 1½d., would be added to 7,500 gallons of raw unstored Thames water. This would kill within twenty-four hours the *B. coli*, and inferentially, but certainly, the microbes also of epidemic water-borne disease—*e.g.*, the typhoid bacillus. The water would also be improved considerably as judged by chemical and physical standards. The excess of free lime (about 0·007 per cent. = 4·9 grains per gallon of CaO = a hardness of 8·8° Clark) would then have to be neutralized with 2,500 gallons[6] of adequately stored water, which, according to all my experiments, would not contain any of the microbes of epidemic water-borne diseases. Rapid filtration alone would then be required to remove the precipitate of inert carbonate of lime." According to the data given, the initial average hardness of 15° Clark is reduced in the final mixture to about 5·3°, but, of course, the sulphates are left, so that there would appear to be no danger of the water being rendered lead solvent, like soft waters generally, though this point is not mentioned. But "the disadvantages of the excess lime method grafted on to an existing purification are many and serious," mainly because "the mere cost of lime would probably be about double that of the present sand filtration." The expense, however,

[1] *Zeitsch. Hyg.*, 1887, 15 [2] *Ibid.*, 1889, 507. [3] *Arch. Hyg.*, 1886, 189.
[4] *Vierteljahr. Off. Med.*, 1898, **16**, Sup., p. 138.
[5] *Seventh Research Report to the Metropolitan Water Board.*
[6] 2,500 in 7,500—that is, one-third of its value.

has been much lower in practice, and if it secures public safety, it is to be demanded.

Dr. Houston's experimental colicide success with 1 part of quicklime added to 5,000 parts of water amounts to 20 parts per 100,000, or 14 grains per gallon, equal to 1·2 ton of this quicklime per million gallons. The proportion of free lime neutralized and rendered inert by the carbonic acid of the water would vary from time to time, and the quantity required to give the effective bactericidal excess would have to be regularly tested, also the volume of stored water required to neutralize the excess lime. He found also that in crude London sewage (Barking outfall) the *B. coli* were killed by a dose of 1 part of quicklime (about 75 per cent. CaO) in 2,000 parts of sewage.

The Halogens.

Chlorine, bromine, and iodine are amongst the most powerful of the germicides. Their action on the organic matter in the water is complex, partial oxidation and chlorination taking place simultaneously; loose additive or adsorption compounds are also formed, especially in the case of iodine. The $-NH_2$ group present in protein-containing substances is especially reactive with chlorine, forming unstable chloramines, $-NHCl$, which in general possess germicidal powers frequently exceeding that of chlorine itself.

In consequence of the combined action they (1) deodorize the gases of putrefaction—sulphuretted hydrogen, phosphoretted hydrogen, ammonia, and compound ammonias; (2) lessen, by bleaching, the colour of water; (3) decompose ptomaines and other organic matters; (4) form antiseptic substances inimical to bacteria, but in small quantities innocuous to higher life; (5) precipitate the albuminoids, therefore attack the bodies of organisms themselves. In many of these actions light is necessary, and heat is also favourable. As with nearly all chemical sterilizers, unless the water first undergoes a partial purification, the great part of the reagent is wasted in attacking comparatively inert matters. Krönig and Paul in 1897 found that the disinfecting power of the series Cl, Br, I, decreased in the ratio of increasing atomic weights, 35·4, 80, 127, but that it varied with the kind of organism and the conditions.

Of the halogens actually employed for water sterilizations, chlorine is the only one used on an extensive scale. Bromine and iodine are only employed in emergencies or for special purposes, their cost being prohibitive for industrial operations.

Chlorine sterilization of public water supplies is now common practice, and this germicide is applied to the water in three forms: as bleaching powder, sodium hypochlorite, and as chlorine gas.

Bleaching powder, or chloride of lime, when freshly prepared, approximates in composition to the formula $Ca<^{OCl}_{Cl}$, containing some 33 per cent. of available chlorine—*i.e.*, chlorine that is active in oxidation and in germicidal capacity. On storage, especially in hot, damp climates, it deteriorates rapidly; market samples are sometimes as low as 20 per cent. available chlorine.

Sterilization of the water to be treated is usually accomplished by the addition of the bleaching powder dissolved in a minor volume of water through some suitable proportionating device such as a V notch with float attachment or Venturi type injector, or by means of a small pump with variable lift geared to the main water pump.

The necessary quantity to be added to effect sterilization is governed by a variety of factors, discussed in detail in the literature devoted to water purification. Polluted waters naturally require a larger chlorine consumption than relatively pure waters, since the consumption of chlorine by the non-living organic matter in the water is by no means a negligible factor. Waters having a chlorine consumption of more than 4 or 5 parts per million of chlorine or 12 to 15 parts of bleaching powder may usually be considered as sufficiently polluted to warrant some purification process prior to sterilization. A second factor of importance is the nature of the organic matter present in the water. It would appear from some experiments conducted by one of the authors on the Somme River water during the war that by the interaction of chlorine with organic matter of animal origin, although a high "chlorine consumed figure" may be obtained, yet sterilization is easily effected, whilst the same dosage of chlorine for a water having an identical "chlorine consumed figure" is far less efficacious in sterilization when the organic matter is of purely vegetable origin. This is doubtless associated with the formation of germicidal chloramines with the protein matter or their hydrolysis products in the former case. The importance of the time of contact as a factor cannot be over-emphasized. As an example, the following figures of Phelps, quoted by Barton,[1] are instructive:

Available Chlorine added in Parts per Million.	*Bacteria per Cubic Centimetre after Time of Contact in Hours.*			
	0	0·5	1	2
3	1,000,000	500	270	230
2	1,000,000	4,600	2,100	3,400

[1] *La Chloration*, Paris, 1918.

It will be noticed in this case that with the smaller concentration of chlorine there is a distinct aftergrowth, whilst with the higher concentration the germicidal activity is not lost even after two hours of contact; in neither case is sterilization effected. It is therefore necessary, if small quantities of chlorine are employed, to ensure an adequate time of contact, as long as can be conveniently arranged. An alternative and frequently employed method is to add a relatively large excess of chlorine with a relatively short time of contact, such as twenty minutes to half an hour, and subsequently resume the excess of the reagent by some suitable dechlor, such as sodium bisulphite, ferrous chloride, or gaseous sulphur dioxide. The dosage for natural waters may, as has already been indicated, vary within wide limits according to the conditions of operation; thus, at Niagara Falls 0·06 part per million of available chlorine has been found efficacious, 0·5 part per million being, however, by no means infrequent in America.

Other hypochlorites, such as magnesium hypochlorite, "Hermite Fluid," sodium hypochlorite as "chloros," containing 10 per cent. of available chlorine, or Eau de Labarraque, containing 2·5 per cent. of available chlorine, and more rarely the original Eau de Javel potassium hypochlorite, have been employed for water sterilization. Electrolytic hypochlorite prepared by the electrolysis of brine solution has found a small application for the treatment of water. In general, however, these substances are usually employed for special purposes, such as sanitary or medical work (see Chapter VI.) rather than for routine water sterilization.

The mechanism of the action of these hypochlorites in water purification is by no means clear.

We have already alluded to the interaction of hypochlorites with amino compounds to produce chloramines of marked germicidal activity.

Albuminous substances are, however, rapidly coagulated by chlorine, and may be precipitated from solutions.

In addition, it has been noted that the germicidal activity of hypochlorites in a water containing dissolved carbon dioxide is greater than in an alkaline water of similar nature; likewise the germicidal action of a definite hypochlorite concentration is lowered on exposure to bright sunlight. It appears reasonable to suppose that hypochlorous acid ($K_{17} = 3{\cdot}7 \times 10^{-8}$) is the active germicide, rather than its salts. The acid is some ten times weaker than carbonic acid ($K_{17} = 3{\cdot}0 \times 10^{-7}$), and would thus be liberated from its salts in a carbon dioxide containing water. Hypochlorous acid possesses a different absorption spectrum to that of its salts, is more unstable, readily decomposing with the liberation of oxygen,

and presumably has a different chemical structure, with which is probably associated a higher germicidal activity.

Hypochlorite treatment is frequently employed in conjunction with other chemicals, usually precipitants, such as ferric chloride in Duyk's ferrochlor process,[1] or with aluminium sulphate as at Cheltenham in England, and with the Merrimac water in the United States. A few experiments have likewise been conducted with hypochlorite permanganate mixtures; the manganese hydroxide formed by reduction is, however, not so readily removed from the water as ferric hydroxide, and far less easily than alumina.

For medical work (see p. 201) Dakin's and similar solutions, consisting of a solution of sodium hypochlorite with a suitable buffer salt, are now extensively employed.

The Chloramines.—Chloramine, NH_2Cl, prepared by the interaction of sodium hypochlorite and ammonia in the presence of some colloidal material such as glue,[2] was found by one of the authors[3] to possess a high germicidal coefficient (see p. 195), and is apparently produced in small quantities in waters when submitted to chlorination. The idea of preparing chloramine from bleaching powder and ammonia without the addition of a colloid has been developed by Race in Canada for the purification of water on a large scale with a considerable amount of success. Chloramine is not formed by the direct interaction of ammonia, water, and chlorine gas.

Chloramine solutions are relatively unstable, and a search for more stable substituted chloramines which should possess the necessary stability for purposes of transport, but at the same time retain their high germicidal powers, led Dakin to investigate the simpler chloramines of the type—



prepared by Chattaway, Blanksma, Orton, Jones, Revett, and others.[4]

Chlorine.—The use of chlorine gas as a sterilizing agent has now assumed large proportions, and may be said to be the standard method of water treatment. Although the method was developing

[1] *Bull. Soc. Belg. de Géol. et d'Hydrol.*, 1909, **22**, 98.

[2] See Raschig, *Chem. Zeit.*, 1907, **31**, 926.

[3] *J. Roy. San. Inst.*, 1920, **31**, 2.

[4] *Proc. K. Akad. Wetensch.*, Amsterdam, 1902, **51**, 178; *Proc. Roy. Soc.*, 1902, **71**, 156; *Chem. Soc. Trans.*, 1909, **95**, 1456; *Zeitsch. Physikal. Chem.*, 1913, **82**, 201.

rapidly before the war, a renewed impetus has been given by the ready accessibility of liquid chlorine of a high degree of purity in steel cylinders manufactured for poison-gas purposes. In addition, chlorine, being a by-product of the ever-increasing electrolytic alkali industry, may be purchased at very low cost, manufacturers being generally in difficulty as to its disposal. Chlorine cylinders are readily transported by rail or water, and the pressures at normal temperatures, 54 pounds per square inch at 32° F. to 216 pounds at 122° F., are not too high to cause difficulties in operation.

In 1903 Nesfield[1] suggested liquid chlorine stored in lead-lined iron cylinders for water sterilization, and this was later on developed by C. R. Darnell of the U.S. Army,[2] and a modified plant on these lines was used by the Allies in the war. The water to be treated is raised from a sump and pumped along a main. Geared with the centrifuge pump is a small accessory pump, which serves to maintain a suitable pressure in a small water reservoir, the pressure being proportional to the speed of rotation, and consequently to the delivery of water in the main. The fluid pressure in this reservoir actuates a valve mechanism controlling the chlorine delivery from a cylinder through a supply pipe direct to the water in the main. The official tests carried out in the United States with this simple apparatus were highly satisfactory. In 1914 Leavitt and Jackson[3] developed a different type of dosing apparatus, in which the chlorine cylinder was set on the yard-arm of a balance. A sliding weight actuated by a suitable mechanism to adjust its velocity of travel along the yard-arm according to the water flow maintained the balance in equipoise; any deviation from the mean position caused a corresponding increase or decrease in the aperture of the release valve of the chlorine cylinders.

The Electro-Bleaching Gas Company's apparatus, which had at one time no inconsiderable industrial application, was non-automatic in character, and made use of the principle of dosage by means of a minor volume of water. The apparatus consisted of two specially designed reducing valves, the first to reduce a variable gas pressure down to a constant value of *ca.* 15 pounds per square inch, and the second a fine adjustment regulating valve admitting the chlorine through an ingeniously designed type of Venturi flow meter into the base of a vulcanite absorption tower. As contact substance coke or similar material could be employed, and absorption by means of water was effected on the counter-current principle

The Wallace and Tieman Company of New York, in which the preceding company is now incorporated, have developed numerous

[1] *Public Health*, July, 1903. [2] U.S. patent, 10,007,647 of 1912.
[3] U.S. patent, 1,087,908 and 1,088,232 of 1914.

ingenious dosing apparatus, based both upon the minor volume of water principle and on direct application. In the smallest type of apparatus the rate of chlorine flow is measured by the number of chlorine gas bubbles issuing per minute from a standard orifice into a small volume of water, which then flows into the main delivery. For slightly larger types an ingeniously constructed pulsing type of meter is utilized to measure the rate of supply into the minor volume of water. For large apparatus a Venturi type of flow meter is employed, and the gas is admitted direct into the water main or conduit through a silver tube terminating in an alundum diffuser.

In England the Paterson Engineering Company have installed several chlorine dosing apparatus, utilizing the principle of the minor volume of water as a vehicle for conveying the chlorine gas into the water system, whilst the flow rate of the chlorine gas is measured by means of a siphon meter, either direct reading or integrating in its action.

Chlorine Peroxide.—ClO_2 is one of the most energetic of sterilizers, and was first used for waters by Bergé.[1] It is prepared by the action of sulphuric acid on potassium chlorate, the resulting gas being passed into water:

$$3KClO_3 + 2H_2SO_4 = KClO_4 + 2KHSO_4 + 2ClO_2 + H_2O.$$

This is easily and safely effected by an apparatus described by M. Howatson.[2]

Although the solution is very fatal to bacteria, it is far milder in odour than chlorine or hypochlorous acid, and seems innocuous to animals.

For the same reasons as with previous chemical reagents, to work economically it is necessary to subject the water to a preliminary treatment, which in the Howatson-Bergé process, as operated at Brussels and Ostend, consisted of softening and mechanical filtration. At the latter place the potassium chlorate used in the preparation is 2 grammes per cubic metre of water, which would give theoretically 0·74 gramme of ClO_2, or 0·74 part per 100,000. Van Ermengem, in 1898, found that the canal-water, with 890 to 23,000 organisms per c.c., after the treatment in fourteen cases was sterile, and in five contained one or two colonies of the resistant and harmless *B. subtilis* or *B. ramosus*. At Lectoure, in Southern France, the town supply, drawn from the River Gers, and seriously polluted with sewage, has been for many years purified by this process. Dr. Ogier reported that the river-

[1] An account of his experiments is given in *Ann. Trav. Publ. Belg.*, 1898, 369.

[2] Also see English patent 4,917 of 1898.

water contains 21,000 organisms per c.c. before and only 7 or 8 after the treatment with peroxide. In our own experiments it was found that 2 parts of chlorine peroxide per 100,000 did not kill *B. typhosus* in a vigorous pure culture in two hours, but that 5 parts killed it in half an hour. These results are comparable with Dr. Ogier's, but obtained under somewhat different conditions. The slight excess of ClO_2 rapidly disappears from the water.

Bromine has been frequently proposed for sterilizing water, the objections being the dangerous properties of liquid bromine, and the taste and physiological action of the bromide produced. In 1897 several practical suggestions were made. Altmann patented a solution of bromine in potassium bromide, using 4 parts Br per 100,000 of water acting for five minutes, and removing the excess by ammonia. The solution has the inconvenience of bromine, and is more bulky; the use of a potassium salt has also disadvantages.

Schumberg, of the German Army, recommended free bromine, 6 parts per 100,000, for sterilizing water in expeditions, on shipboard, and in cases of suspicion, stating that sterility was obtained in five minutes. He removed the excess by a tablet of sodium sulphite and mannite, the latter probably to conceal the taste; later sodium thiosulphate and bicarbonate were employed. The method was tried in the Sudan campaign of 1898, but the difficulties of transport of liquid bromine in glass bulbs militated against its use. In the same year Braithwaite proposed to avoid this by adopting a solid mixture of a bromide and bromate, followed by acid sulphate of soda, to liberate the bromine, but the method does not seem to have been tried on a large scale. The quantity he recommended was sufficient to give 1 grain of bromine per quart, or 5·7 parts per 100,000, practically the same as Schumberg used. In our own experiments we have found that 2 parts of Br per 100,000 kills *B. typhosus* in less than half an hour. Schüder[1] has come to the conclusion that Schumberg's process fails almost completely in the quantities suggested by him, and therefore agrees with the opinion expressed by L. Parkes and S. Rideal in a paper at the Epidemiological Society in January, 1901.[2] The fact, moreover, that there must necessarily remain in the water a residue of bromides, which are known to have a marked physiological effect, cannot be considered either natural or safe, and should preclude the recommendation of bromine for sterilization of water for drinking. A similar remark applies to iodine (which was used for the same purpose by Allain at Marseilles), to iodine trichloride and cuprous chloride, and to many other compounds that have at various times

[1] *Zeitsch. Hyg.*, **37**, 306.

[2] See also a paper by Dr. H. Frazer, *Pub. Health*, September, 1902, 721.

been proposed. Our own experiments with iodine trichloride showed that with 2 parts per 100,000 *B. typhosus* was alive after twenty hours, but that 5 parts killed it in half an hour.

Fluorine Compounds.—The soluble ones are strongly antagonistic to moulds, and in a less degree to bacteria. The former character has led to their being added to brewery waters. Sodium silico-fluoride (isotachyol) has been found to be a powerful germicide, while Dr. Frank recommends the silico-fluoride of aluminium.[1] They are stated to have no injurious action on health.[2]

Sterilization by Acids.

Kitasato's results with *B. typhosus* in nutrient media have been summarized by Horrocks in the following table:

	Per Cent. of Reagent.		
	Growth.	*Growth Restrained.*	*No Growth.*
Acids—			
Sulphuric acid	0·049	0·065	0·08
Hydrochloric acid	0·1	0·158	0·2
Nitric acid	0·1	0·157	0·2
Sulphurous acid	0·09	0·2	0·28
Phosphoric acid	0·15	0·224	0·3
Acetic acid	0·2	0·255	0·3
Carbolic acid	0·2	0·258	0·3
Formic acid	0·22	0·278	0·34
Oxalic acid	0·23	0·285	0·366
Lactic acid	0·27	0·36	0·4
Tartaric acid / Citric acid / Malic acid	0·338	0·384	·0·476
Tannic acid	1·3	—	1·66
Boric acid	1·5	2·0	2·7
Alkalies—			
Caustic lime	0·0725	0·0805	0·0966
Caustic potash / Caustic soda	0·1	0·14	0·18
Ammonia	0·148	0·2	0·3
Lithium carbonate	0·514	0·6	0·666
Potassium carbonate	0·566	0·74	0·81
Barium hydrate	0·65	0·83	1·00
Ammonium carbonate	0·72	0·845	1·00
Sodium carbonate	2·00	2·2	2·47
Salts—			
Potassium iodide	6·66	8·0	9·23
Potassium bromide	8·0	9·23	10·37
Potassium chloride	9·1	10·6	10·2

In these experiments broth and gelatine media were carefully neutralized before adding the substances, then inoculated with *B. typhosus* and kept at room temperature, subcultures being taken at 4 or 5 and at 10 to 15 hours.

[1] *Wasser u. Abwasser*, December, 1910.

[2] Peiret, *Public Health*, October, 1908.

Very different results are obtained, however, when water free from organic matter is employed instead of nutrient media. Thus, 0·096 per cent. of caustic lime to kill typhoid in strong broth is reduced to 0·0074 per cent., or less than one-tenth, when the broth is diluted with fifteen times its volume of distilled water. Similarly, in bouillon containing less than 1 per cent. of peptone, *cholera vibrios* are killed by 0·01 per cent. hydrochloric acid in half an hour, but require four times this quantity in the presence of 2 per cent. of peptone. It would therefore appear that chemical reagents, whether they possess oxidizing properties or not, are more efficient as sterilizers when the water to be treated is comparatively free from organic matter.

Our own results with some of these substances in impure water, inoculated with varying amounts of typhoid and kept at room temperature, are:

Reagent.	*Per Cent.*	*Time (Hours).*	*Results.*
Sulphuric acid	·025	20	Killed
,, ,, ...	·030	(*a*) ½	Alive
		(*b*) 1	Alive
		(*c*) 20	Killed
,, ,, ...	·035	½	Killed
Sulphurous acid	·030	20	Killed (alive at 1 hour)
Caustic soda	·050	½	Alive

The organic acids, like tartaric, citric, and acetic, also possess this property; and in 1893 the use of tartaric acid for purifying water, in conjunction with a filter, was patented, and its use has been suggested in Italy for sterilizing salads before consumption. Dr. Christmas, in 1892, showed that citric acid, although fatal to the cholera bacillus when used in the proportion of 8 parts in 10,000, did not destroy the bacillus of typhoid in a less strength than 1 in 1,000. It may be that lemon juice and vinegar, as dietetic adjuncts in salads and uncooked shell-fish, have further been extremely useful in minimizing the dangers of typhoid derived from such sources.

Metallic Salts.

Several metallic salts have been used in emergencies, but their cost generally makes continued use prohibitive. Silver salts in solution are bactericidal. Waters containing chlorides precipitate them as silver chloride, a part of which remains suspended and retains activity. In our laboratory *B. coli* was killed in twenty-four hours by a 0·1 per cent. solution, but the same strength failed to

kill *S. pyg. aureus* in the presence of only a small quantity of chloride and organic matter.

Paterno and Cingolani found 1 in 400,000 of silver fluoride (tachyol) fatal to non-sporing bacteria in half an hour. Hetsch, with 1 in 500,000 of silver fluoride, destroyed cholera germs, but not those of dysentery or typhoid; with 1 in 200,000 he killed cholera in ten minutes, typhoid and dysentery in twenty minutes. Traetta Mosca extended this work, and found silver sulphate, chlorate, and perchlorate all "strong and effective for sterilizing water." Copper has long been known to possess bactericidal, and especially algicidal, powers. In 1893 Khronke[1] showed that 1 in 20,000 of cuprous chloride, together with some ferrous sulphate, sterilized water in six hours, after which time 1 part of lime in 100,000 was added to precipitate the copper oxide. This was removed by sedimentation followed by sand filtration.

In 1904 one of us suggested the use of copper vessels for the automatic sterilization of water by simple contact. Kraemer,[2] in 1906, found that the period of contact required by copper with the surrounding water to produce sterility was from two to four hours.

Metallic and colloidal copper kill coli and typhoid in water after four hours. Kraemer recommended $3\frac{1}{2}$ square inches of copper strips immersed in each quart of water five to eight hours for household purification.

In 1904 and 1905 Moore and Kellerman at Washington showed that copper sulphate was, in the strength of 1 in 10,000, a good algicide and a fair bactericide, sterility being obtained after three hours.

Clark and Gage[3] found copper sulphate rather uncertain in its action, sometimes as much as 3 in 1,000 being required to ensure sterility. The general conclusion is that copper sulphate in the strengths 1 in 100,000 to 1 in 50,000 is an efficient algicide, but only of doubtful value as a germicide.

The methods just outlined have been applied in special cases to the treatment of swimming-bath water, fish-ponds, polluted sea-water in oyster-beds, and to sewages. It is well known that oysters are a common vehicle of typhoid,[4] and it is now customary to effect the cleansing of oysters with sterile sea-water. Not much progress is to be recorded in the treatment of sewage with germicides, although several minor plants are in operation utilizing chlorine

[1] *J. Gasbeleucht*, **36**, 513; also Rideal's "Water Supplies," 1914, 178.

[2] Kramer, *Amer. J. Pharm.*, **78**, 140.

[3] Clark and Gage, *J. Infect. Dis.*, 1906, Supp. 2, 75.

[4] See graphical representation by P. Vincey, *Bull. Soc. d'Encour.*, 1913, **277**.

(0 to 10 parts per million) or sulphur dioxide gas as sterilizing agent. It is found, however, that the general methods of bacterial hydrolysis, or the activated sludge system followed by adequate aeration and dilution of the effluent, is the most economical system of disposal, and that partial or complete sterilization is only to be employed when circumstances indicate clearly the essential need of some such operation.

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CHAPTER V

PUBLIC DISINFECTION

The Disinfection of Rooms and Public Vehicles.—It has already been indicated that methods involving sterilization of the air or rooms are usually designed to carry the disinfectant to the walls, ceilings, and floors, on which most of the micro-organisms are found deposited; consequently more rapid and efficacious disinfection in rooms is accomplished by means of the disinfectant spray. Formaldehyde solution is frequently used, the strengths adopted being from 0·5 to 2·5 per cent. There is great risk of imperfect spraying except with a good apparatus in the hands of an experienced operator, crevices and parts of the room or furniture being frequently missed by the spray. When the walls and rooms are exceptionally dirty, or when very special disinfection is needed, as in plague, both a spray and a vaporous disinfectant should be used.

Fresh air, light, and frequent cleansing are the essentials to be aimed at in thickly-populated districts. In washing floors a strong carbolic soap, or, better, a cresylic preparation, is very useful. Curtains and bedding must be occasionally brushed and shaken in the open air. When sweeping floors and carpets, tea-leaves or damp sawdust should be used to prevent the diffusion of germs in the dust, since micro-organisms remain suspended in the air of a room for a relatively short period, provided that the air is damp and quiet.

As a substitute, antiseptic absorbents may be used; one on the market, "Floorfix," was found to consist of damp sawdust weighed with a little sand and containing moist sugar and formaldehyde (about 1½ per cent.). Recently the practice of oiling the floors with slow-drying oils, with or without the addition of disinfectants, has been somewhat extensively adopted with, it is stated, excellent results. Oil paints, or well-varnished papers, are preferable for walls, as they can be easily washed. A very important point, especially in connection with hospitals, is that walls should consist of impervious material not affording a lodging-place for the growth of disease bacteria. Several exhibits with this object were shown at the Building Trades Exhibition, 1903. Flock papers have

become obsolete, from their forming such a favourable nidus for the growth of organisms. Ordinary papers are sometimes cleaned with bread-crumb to avoid dust, but the removal of bacteria is incomplete.

Hygienic Wall-Papers prepared with various disinfectants incorporated in the pulp have been suggested. Mercuric chloride has even been proposed to be introduced, but its use should not be permitted on account of the danger of its being evolved in the dust. Resorcinol, 1 in 2,000, is patented by Sinclair and Brown for this purpose. It has been proposed to incorporate salicylic acid with the plaster coating of walls; it is non-volatile and inodorous, but it is very doubtful if it would be efficacious. It always communicates a pinkish colour, owing to the presence of iron salts. Kosinsky, of Warsaw, invented a portable apparatus for heating air to any required temperature, and forcing it at the rate of about 1,000 cubic feet a minute through radiating tubes against walls and other surfaces for drying and disinfection. It is also intended for large disinfecting chambers, in which the rapidity with which the air passes combines with the high temperature (stated in the report to be 660° F., but this is obviously an error) in bringing about the desired result. It is also suitable for warming buildings, and for removing vapour and moisture from crowded rooms—*e.g.*, in a theatre, after the exit of the audience, to prevent the condensation and settlement of injurious moisture and dust. An official commission at Warsaw proved that a private house, the building of which was commenced in May, 1882, with the capacity in ground floor and first story of 7,000 cubic feet, was completely dried in fourteen days, and severe sanitary inspection proved the building to be completely sterilized.

In India, according to the report of the Plague Commission, the disinfection of houses that had contained cases has been universally carried out. The disease sometimes recurred in the same building, in one instance thirty-four days afterwards, but may have been due to a fresh infection. Mercuric chloride was generally used, and in Poona was pronounced efficient if operated by British soldiers, while in Baroda there was frequent recurrence in houses thus disinfected under the supervision of the health officer himself. Mr. Hankin showed that the cow-dung which is so large an ingredient of the floors of native houses contained much alkali and other substances which precipitate the mercury, and that the remedy was to be found in strongly acidifying the solution. Peroxide of hydrogen was also said to have been successful. The digging out and burning of the floors was dangerous to the workmen. Unroofing and exposure to sun and air was of service in the dry districts of Sind and the

Punjab, but was not always practicable. All operations involving disturbance should have been accompanied by liberal spraying.

Roger[1] found 1 in 50 carbolic acid and 1 in 500 mercuric chloride (acidulated with hydrochloric acid) the best disinfectants for mud floors in India during plague. He found that 1 in 750 phenol and 1 in 20,000 $HgCl_2$ are effective in destroying plague bacilli in test-tubes in fifteen minutes. He preferred the carbolic acid for practical work, as it has been seen that the effectiveness of the mercuric salt is reduced in much greater proportion than the carbolic acid; floor disinfection, of course, does not minimize the danger from rats. A memorandum with elaborate instructions as to cleaning and disinfecting school buildings was issued by the Scottish Education Department in 1907. Among other recommendations, they stated that every schoolroom should be cleansed by moist cleaning and disinfection at least once a year. Some rooms, particularly infant rooms, may require such thorough cleaning several times a year. Offices should be sprayed with disinfectants as often as is necessary to keep them free from offensive odours.

In spraying walls, it is best to start from a bottom corner of the room, working along horizontally, and gradually extending upwards, in order that the wetting of walls may proceed evenly and without splashing; this will ensure walls drying without patches or stains.

Furniture and Woodwork can be washed and scrubbed, or, in special cases, should be washed with 1 in 1,000 mercuric chloride (in a few instances this may cause discoloration), or with 1 per cent. formaldehyde (2½ per cent. formalin), taking care of the hands. Upholstered furniture, when infected, requires very careful and thorough treatment; it should be avoided in bedrooms. Beeswax and turpentine are better than the common furniture polishes, as the surface is to some extent disinfected and rendered non-absorbent. All cracks and crevices should be carefully filled up with putty to prevent the lodgment of vermin or germs.

Sinks, if made of stoneware, can easily be cleaned. Here *Condy's fluid* (permanganate) is serviceable, but strong soda is ordinarily better. For toilet utensils sodium hypochlorite (chlorinated soda) in 5 per cent. solution should be occasionally used, also for milk cans and pails. In the case of metal baths it should not be used too strong, as it removes paint. Bedsteads, in addition to scrubbing with soap and water, can be afterwards washed with chloride of lime and water, 10 per cent., and left in the air till the odour has almost disappeared. Paraffin oil is sometimes used, but its odour is very persistent. Polished floors are to be recommended in preference to porous floors and carpets.

[1] *J. Hyg.*, 1902, 138.

Sick-Rooms cannot be disinfected in presence of human beings. All placing of saucers with chloride of lime, permanganate, etc., under the bed or about the room is simply illusory, but the practice of hanging up damp sheets certainly assists in the deposition of micro-organisms from the air, thus minimizing the chance of infection. Similarly, fumigation by medicated lamps or candles, burning pastilles, or brown paper, is useless. Sufficient of the disinfectant to kill the micro-organisms of the air would make the air unfit to breathe. The following precautions, however, will be of service:

1. *Isolation.*—If possible, the other inmates of the house should live on a different floor. Where this, on account of poverty or other cause, is unattainable, contact should be carefully avoided.

2. *Clothing.*—The attendants should wear cotton and linen, not woollen, garments. This is now compulsory in hospitals and most institutions. The greatest personal cleanliness should, of course, be observed. The following is a way of removing soiled clothing from the room: At the bottom of a large air-tight tin trunk, such as is used for travelling to India, is placed a piece of felt or blanket, or three or four thicknesses of flannel. This is sprinkled with crystals of carbolic acid and covered with a linen cloth. The crystals will soon deliquesce and soak into the stuff. The lid should never be left open. The soiled clothing is put in, and when full it is left for an hour for the phenol vapour to penetrate, and then carried out into a yard, where it is filled with boiling water containing soda, and washed as soon as possible. The washing must never be done, nor the clothes hung out to dry, on the same day as the ordinary house washing, nor should they be ironed or starched in the same room or with the same utensils. This dry method of removal of clothing is probably better than the usual one of plunging into a disinfectant solution (phenol or mercuric chloride), as it is easier, and the weight of the water and constant carriage are avoided.

3. *Excreta*, vomit and sputa, according to earlier directions, should be received into about a pint of mercuric chloride solution, 1 per mille, with 10 per mille of common salt and 1 per mille of hydrochloric acid coloured with indigo to avoid mistakes, a large quantity of such a solution being kept ready (see Ch. VI.). Dr. Fischer recommended aniline water for disinfecting tuberculous sputa (Ch. VI.). "Five per cent. phenol did the same in twenty-five hours; mercuric chloride, 1 in 500, failed. Dry heat of 100° C. sometimes fails, though it acted after sixty minutes. Boiling ten minutes or steam for fifteen minutes succeeded."[1] Disinfected excreta must not be thrown away before the agent has had time

[1] *Mittheil. Kais. Gesundh.*, 1884.

to penetrate. If disease begins in houses where the sick person cannot be properly accommodated and tended, medical advice should be taken as to the propriety of removing the patient to an isolation hospital. "Where dangerous conditions of residence cannot be properly remedied, the inmates, while unattacked by disease, should remove to some safer lodging."

4. *Light and air* should be freely admitted. Vallin strongly recommends the use of water spray in the room, as he says that the water entangles the bacteria and dust, and the dissolved oxygen in the water destroys them. He also approves the use in the water of a small quantity of resol (dimethyl-resorcin), a body proposed by M. Pabst, as agreeable and non-corrosive. A 1 per cent. solution of peroxide of hydrogen might also be employed for the same purpose. The sick person should be protected by a screen from this process, from draughts, and from too much light.[1] It is well known what benefit is derived in some lung diseases from the common bronchitis kettle. Dr. W. Ferguson has suggested its use as a fumigator in pneumonia and diphtheria by the following simple modification: "Take an ordinary bronchitis kettle, remove the first joint, and replace it by a common tin funnel loosely filled with tow. Pour on the tow 1 drachm of pure phenol, and at intervals more. The steam carries off the phenol."[2] But whatever utility these practices may have *medicinally*, we must again emphasize that they cannot be considered as *disinfection*. Curtains, hangings, carpets, and all unnecessary furniture should be removed.

After-Disinfection.—Phenol, chlorine, and sulphurous acid have each had their advocates.

(*a*) *Phenol.*—Pouring strong carbolic acid on a hot shovel is dangerous to the operator. Calvert manufactures a perforated iron cylinder delivering a mixture of 2 parts phenol and 1 part water on to a red-hot iron heater; the whole is compact and can be carried by a hook. There is also Savory and Moore's vaporizer, in which phenol falls on a hot plate, and many others. But phenol vapour is not reliable as a disinfectant (Miquel and others[3]), and the smell remains persistent. The following is the substance of directions given at various times by the Local Government Board and other authorities for disinfection by chlorine or sulphurous acid. These agents, however, have now been largely displaced by formaldehyde (see p. 16).

(*b*) *Sulphurous Acid.*—After the removal of such articles as are best disinfected by heat, and the closure of windows and crevices, the gas in ample quantity should be evolved, the doors being

[1] *Désinfectants*, p. 407.

[2] *Lancet*, 1880, ii., 757.

[3] See also *Pharm. J.*, [iii.]. **2**, 545.

closed for six hours or more. The amount of gas required for the disinfection of a moderately-sized room can be obtained by burning 1½ pounds of roll brimstone in a pipkin over a small fire placed in the middle of a room, with an old tray or the like to protect the flooring. These processes should be effected by skilled persons acting under the directions of the Medical Officer of Health. All wall-paper should be stripped from the walls and burned, and the same room ought to have its ceilings and walls thoroughly washed and lime-whited.[1] Boake's liquid sulphurous acid, bottle or tins, are much more convenient (see p. 23).

(*c*) *Chlorine.*—Three pounds of good chloride of lime and 3 pounds commercial hydrochloric acid should be used for every 1,000 cubic feet. This quantity is divided into several parts and placed in deep stoneware vessels as high as possible (since chlorine gas is heavier than air), and the acid allowed to drop in gradually by a funnel with narrow tube. The room should then be closed for twenty-four hours. The operation presents many difficulties in practice, requires the removal of metals or the protection of fixtures with vaseline, sometimes involves much damage, and the subsequent opening of the room is very dangerous even when breathing through a towel soaked in ½ to 1 per cent. ammonia solution. Finally, it is not always successful, and has been virtually abandoned.

In the above fumigation with chlorine there is an important omission. Inasmuch as the dry gas will not disinfect, it is necessary to generate steam by a boiler or large kettle over a good fire for some time before commencing, so as to make the whole room and the air thoroughly damp but not too wet.

(*d*) *Non-volatile disinfectants* can be applied by mechanical means. Thus bleaching powder can be used as a wash, and the walls, floor, and ceiling coated by means of a brush. Mercuric chloride solution and formalin, or, in fact, any liquid disinfectant, can be sprayed into the room. Many forms of sprayers have been devised. The importance of a fine division of liquid depends on the fact that it enables the work to be done with the minimum useful amount of disinfectant, saving the expense and inconvenience of waste liquid. The parts containing the disinfectant can be lined with ebonite, so that the sprayers may be used with any liquid disinfectant without any risk. The cost will vary slightly with the disinfectant used. Taking perchloride of mercury, 1 in 1,000 solution, it is found that an ounce of salt disinfects more than 3,000 square feet of surface.

Dr. Leslie Mackenzie pointed out the advantage of spraying out

[1] *Circular of Med. Off. of Health, Local Government Board.*

hospital wards at intervals, and found that in a scarlet fever ward various minor affections disappeared after formalin spray had been used while the ward was temporarily emptied for a few days. The "Mackenzie Spray," sold by the Thresh Company, is a pump with air-chamber capable of maintaining a steady jet for ten minutes.[1] The "Invicta" sprayer is a portable tank into which air is driven until a pressure of 15 pounds is recorded on the pressure gauge, then the disinfecting liquid is forced in with the same pump until 45 pounds pressure is reached. The quantity of liquid is about $1\frac{1}{2}$ gallons; the spray will last about twenty minutes, and is controlled by a stopcock. The exit is by a tube with ball valve coming from the lower part. It has been improved and adopted by Dr. Robertson, M.O.H. for Leith,[2] and he reports that it is very successful.

The State Board of Maine in 1900 issued a special circular of directions for disinfection of rooms, furniture, etc., used by consumptives, in view of the difficulty of killing *B. tuberculosis*. Details are given of the employment of steam or boiling for fabrics and of formaldehyde gas and spray for rooms and upholstered furniture. Fifty c.c. of formalin poured upon a cloth in the lower part of a disinfecting chamber of 1,089 cubic inches capacity disinfected books that were standing on end in twenty-four hours, but not those lying flat.

Letters.—At some asylums all letters are disinfected with dry steam before sending out. Rosenau at Havana treated the mails by clipping off a corner of the envelopes and dropping in a little formalin from a fine jet, then keeping them overnight in a sack or tight box sprinkled with the disinfectant.

Clothes, bedding, mattresses must be removed at once in a closed van to a disinfecting station to be treated with superheated steam. Dry hot air is now only used in special cases (books, leather, and some other materials), and apparatus solely for this purpose is not often made. Occasionally, however, a baker's oven may serve, if not for the destruction of the spores of splenic fever, for killing the non-sporiferous bacteria of cholera, typhus, and diphtheria, and especially for animal vermin (Klein). The bodies of persons who have died of infectious diseases should be at once wrapped in a cloth soaked in 1 per cent. solution of mercuric chloride prior to burial or cremation.[3] Adolf and Heider find that hot solutions of disinfectants are much more active than cold.[4] In Belgium, infected clothes are boiled in a solution of zinc chloride, or with a mixture

[1] *Brit. Med. J.*, 1901, 898.
[2] *Public Health*, May, 1903.
[3] See also *Medical World*, December 17, 1898.
[4] *Arch. Hyg.*, **15**, 55.

of 240 grammes zinc sulphate and 120 grammes salt dissolved in a pail of water. Commercial zinc salts cannot be used, as the presence of iron salts causes them to produce stains on linen. At Aberdeen the Medical Officer of Health reports[1] that house, bedding, and clothing are dealt with, and other details are treated, with exceptional care. The infected rooms are fumigated with sulphur, washed with water containing formalin—a sufficient quantity of which is supplied gratuitously for each case by the sanitary department—and the clothing and bedding are removed for steam disinfection at the disinfecting station.

Hospitals obviously need special precautions, and are generally provided with their own steam disinfecting plant, and in many cases with cremators for the destruction of infectious stools, bandages, and valueless articles. The polished wood floors are cleansed regularly with 1 in 20 carbolic acid or an equivalent of another disinfectant, and the walls, fittings, and utensils[2] are attended to in the ways we have indicated.

Clothes, bedding, woollen, and other articles are most reliably disinfected by steam at a temperature not exceeding 225° F.

Articles consisting of a porous or felt-like structure are, owing to the presence of the air imprisoned in the meshes, bad conductors of heat, as is shown by the following experiments of Whitelegge.

A roll of blanket was kept in a hot-air oven between the temperatures of 245° and 255° F. for eight hours. After this period the temperature at various depths of the roll was obtained and recorded as follows:

Under 2 layers	230° F.
,, 4 ,, ...	221° F.
,, 6 ,, ...	215° F.
,, 12 ,, ...	196° F.

When, however, such materials are exposed to a current of saturated steam, some of the steam condenses in the process of warming up the object; the laminæ or spaces left by the steam on condensation provide a means for fresh steam to penetrate and condense in the deeper layers; penetration can in this way take place through the twelve layers in from ten to fifteen minutes. It is evident that current steam offers considerable advantages over a dry heat, unsaturated steam, or a mixture of steam and air. This principle is the basis of modern steam disinfectors. Steam disinfectors are generally of one of two types—low-pressure or high-pressure disinfectors.

[1] *Public Health*, July, 1903, 584.

[2] See an article by Dr. Louis Parkes, *ibid.*, June, 1903, 540.

Although steam at low pressure penetrates bulky articles more slowly than steam at high pressure, and a somewhat longer time of contact is required to ensure proper disinfection, yet the greater simplicity and lighter construction of the low-pressure types offer advantages which are not present in the somewhat more efficient type.

When a steam disinfector is installed in a school, hospital, workhouse or similar building, the following points should be attended to:

1. The same attendants should always work the machine. When a new attendant is put in charge, care should be taken to instruct him how to work the machine properly.

2. A recording thermometer or thermograph has a great advantage over the usual thermometer fitted, since it offers definite proof of negligence on the part of the employé or unsatisfactory working of the machine.

3. When the machine is situated in the building itself, care should be taken to ensure that only the proper attendant has access to the entrance and exit doors of the disinfector.

4. The attendants collecting the infected clothes should pass their overalls through the machine before removing the disinfected articles, and should also wash their hands with some disinfectant solution.

5. The room in which the entrance door of the disinfector is situated should be frequently sprayed with disinfectant solution.

The **public laundry** is occasionally, although rarely, responsible for the spreading of infectious diseases, either indirectly from infected clothes sent to the laundry or direct from one of the operators in the laundry. Sir Thomas Oliver[1] finds that in some cases the number of laundresses subject to pulmonary tuberculosis was in the proportion of 1 to 11. Although disinfection may be accomplished in the process of boiling for certain materials, others, such as silk and woollen goods, cannot be boiled, whilst in any case the after-process of "doing up" and sorting all increase the risk of infection. Oliver advised that all bundles of clothing, as soon as they are opened at the laundry, should be immersed in some disinfectant of controlled strength, and this suggestion was approved of by the *Laundry Journal* (February 10, 1910).

In the post offices of the French Government, dry sweeping and sprinkling with water are forbidden, while rooms with tiled floors are flushed with water every day. Parquet floorings, it is ordered, are to be wiped over daily with hot turpentine, sprinkled with damp sand, and swept. Once a week the floors are sprinkled with a disinfectant. It is further advised that tables, desks, and telephone

[1] "Diseases of Occupation."

apparatus should be wiped with cloths dipped in a similar disinfectant. Systematic disinfection is also required in museums, churches, and public libraries. In these it is a frequent practice, as at the Chicago Public Library, to use an ozonizer in conjunction with the ventilating system; we have, however, previously pointed out that the risks of aerial-borne infection are very small, and that ozone, although very effective for removing odours and generally for "freshing up" the air, would, in the concentrations necessary for sterilization of the objects with which it came in contact, act on the mucous membrane and cause sore throats. In libraries, the chief source of infection, as shown by M. Cazal and Chatrin, is to be found in the handling of books previously exposed to the proximity and contact of an infected person. Stringent enforcement of regulations in England under the Public Health Act of 1875 has done much to minimize this evil, especially with respect to circulating books in infectious houses. It might be mentioned that the moistening of the finger with saliva for the purpose of turning over the leaves in a thin-leaved book is a particularly pernicious practice. There is no good method of disinfecting books without affecting the bindings.

Stables, pigsties, and cowsheds require to be regularly cleaned, and to be periodically disinfected, like rooms, with removal of the animals, to prevent disease occurring. It is of little use to be perpetually deodorizing with powders. Dryness, ventilation, and cleanliness are better safeguards.

For cattle-markets and fairs a cresol disinfectant is probably the best. A description of the chief ones is given in Ch. XII.

Slaughter-houses are particularly difficult to disinfect on account of the large amount of albuminoid matters present. It has already been noted that it is almost impossible to sterilize blood in the cold. Mercuric chloride and phenol are unsatisfactory because of their action on albumin; chlorine and sulphurous acid are rarely to be recommended; wood charcoal only serves to deodorize, and does not disinfect. Copper sulphate is one of the most useful agents in these places, but cleanliness and rapid removal of offal are the first considerations. Cunliffe and Barlow subject the refuse to heat and destructive distillation. Slaughter-houses for infected or suspected animals are usually situated near seaports, and require special methods of isolation and extra precautionary measures.

In the Diseases of Animals (Disinfection) Order of 1906 the mode of disinfection to be adopted in the case of glanders or farcy and foot and mouth disease was prescribed as follows:

The place or thing, or the part thereof required to be disinfected, shall be thoroughly coated or washed with:

(*a*) A 1 per cent. (minimum) solution of chloride of lime containing not less than 30 per cent. of available chlorine; or (*b*) a 5 per cent. (minimum) solution of carbolic acid (containing not less than 95 per cent. of actual carbolic acid), followed by a thorough sprinkling with limewash; or (*c*) a disinfectant equal in disinfective efficiency to the above-mentioned solution of carbolic acid, followed by a thorough sprinkling with limewash; and these alternative modes of disinfection were authorized generally for other orders in which disinfection with limewash or a solution of carbolic acid and limewash is prescribed.

Vehicles.—In cases of supposed infection, Sanitary Inspectors are authorized to disinfect without charge, and give a certificate. Cushions and removable fittings are sterilized in a steam oven. Formerly all exposed woodwork was washed with carbolic soap, and carbolated oil was smeared over metal-work with the view of disinfecting it and also protecting it from chlorine, which was then evolved inside by one of the methods given on p. 97, and the vehicle was shut and left so for an hour. Sulphurous acid or formalin is now used, and a longer time is allowed.

A systematic disinfection of railway carriages under a uniform system is urgently needed. At the International Congress of Hygiene, Brussels, 1903, it was resolved that: (1) Fittings should be arranged to facilitate cleaning and disinfection, with the suppression of loose textile materials, and easy removability of cushions and furniture. (2) Cleaning of surfaces by damp cloths and removal of dust by a vacuum apparatus were recommended. (3) Disinfection must be regular and frequent, apart from any incidence of exceptional disease, and must include (*a*) complete disinfection of removable furniture; (*b*) washing of surfaces and spraying with antiseptics, or efficient fumigation with formaldehyde or other effective agent; high-pressure steam at 110°, or dilute hypochlorites, were effective, but were liable to cause damage. (4) Special conveyances are required for the sick and for dead bodies; the latter should be in sealed coffins, and for long distances should be embalmed. (5) An International Commission should be appointed to fix, by methodical experiments, standard methods and regulations to be adopted.

With reference to cattle and luggage waggons the Congress resolved that the former ought to be disinfected after each journey, and the latter after they had carried putrescible or suspected substances, with in each case a previous thorough cleaning. See the valuable reports of Redard, Csatary, and Adolph Freund of the practice on French, Hungarian, and Austrian railways. The latter showed that after the most careful cleaning with very hot water there remained an organic film which required repeated irrigation

with an active disinfectant. He prefers hypochlorites in dilute solution, and uses simple spraying apparatus.

The C.P.R. cars are subjected to systematic disinfection on the lines recommended by the Brussels Congress. The car is stripped of everything movable, then swept and brushed out, finishing with vacuum cleaning. The car is then washed both inside and outside, and once a fortnight fumigated with formalin.

Previously to the installation of the vacuum process compressed air was used for cleaning; this method is most unhygienic. The adequate washing and disinfection of pillows, sheets, and blankets on sleepers is still a matter of difficulty, and the present position, relying on inspection as to visible dirt, is far from satisfactory.

The disinfection of ships is in many respects similar to that adopted for houses and public rooms; the passengers and crew, with all their personal belongings and effects, are landed, while a disinfectant boat is run alongside or the vessel is brought alongside the pier on which the necessary fitments are situated. In the case where a complete sterilization of the whole ship is necessary, all movable fixings, including bedding linen, are removed and disinfected by steam (see p. 99). Saloons and cabins may be sprayed down with formaldehyde solution, while the steerage and men's quarters are washed with mercuric chloride or, better, a tar acid disinfectant solution. Accessible surfaces which are in constant use must first be washed with soda solution to remove grease. Bright metal-work is seriously affected by mercuric chloride and by sulphur fumes, and should therefore be washed with formaldehyde or tar acid disinfectant. The hold is usually sterilized by pumping in sulphur dioxide through supply pipes or burning roll sulphur 3 to 5 pounds per 1,000 cubic feet in iron pans in the hold itself. This is followed by drawing fresh air through.

The New York Sanitary Officers have been making experiments with strongly ozonized air for this purpose.

Special attention must be paid to rats, mosquitoes, and other disease carriers frequenting ship-holds.

The laying of dust on roads is receiving much more attention than formerly. This is all the more important as the traffic on the roads increases, although the conversion of horse traction into mechanical is a change for the better as far as the question of contamination is concerned.

The increased use of kyanized wood paving, asphalt, tar macadam, and similar materials on roads, tends to make the dust both less and less contaminated than on the older type of water-bound surface. The daily flushing of manholes, traps, and gullies, especially in hot weather, with some disinfectant solution is a valuable precaution.

Permanganates and hypochlorites are frequently employed for this purpose. Although they are very effective smell removers, and are doubtless used for that purpose, yet, owing to their instability in the presence of organic matter, effective sterilization of the road surface or the manholes never is obtained by the ordinary practice of municipal authorities. This is well shown in the following experiment:

Two spaces, each 27 square feet on the asphalt in Victoria Street, London, outside our laboratory, were watered—(*a*) with 2 gallons of water; (*b*) with 2 gallons of water containing 1: 5,000 potassium permanganate. The runnings from each were ladled into bottles and submitted to analysis, with the following results:

	Colonies per Cubic Centimetre.
Gelatine plates at 22° C.	(*a*) 1,930,000 (*b*) 85,000
Agar plates at 37·5° C.	(*a*) 0·001 c.c. gave numerous colonies, and the plates were crowded in twenty hours. (*b*) 0·10 c.c. ditto.
Carbolized gelatine plates at 22° C.	(*a*) 122,200 (*b*) 4,830

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CHAPTER VI

PERSONAL AND INTERNAL DISINFECTION

THE " last line of defence " includes the precautions taken by the private individual. These may be considered to include cleanliness of the person and purification of the clothing, the importance of cleanliness of the home having already been dealt with.

In the transference of disease by direct contagion in those cases where it is evident that milk or water is not the intermediary, it is usual to look for some article that has been exposed or may have been exposed to direct contamination.

Dr. Park of the New York Board of Health and Professor Hildish of Yale have found that the small paper money notes current in the U.S. and Canada frequently contain pathogenic bacteria. Dr. Basquet of Bordeau proved that tram, railway, and omnibus tickets frequently serve as carriers of disease; metallic coins are also not free from this defect. C. E. Winslow[1] has shown that internal bacteria are frequently transferred to the exterior of the body, and thus a direct route of infection is provided. Under such circumstances typhoid fever and similar diseases may, for all practical purposes, become a contagious disease. This point was first suggested by Sedgwick and Winslow,[2] and subsequently deduced by Notter[3] on investigating the casualties from enteric fever among the British troops in South Africa. For this reason disinfection of the skin is frequently advocated.

In fever cases it is now generally customary to sterilize the hands by washing in a 1 per mille solution of mercuric chloride with a little salt and hydrochloric acid (p. 95), and rinsing them with plain water before washing with soap. In cases of very great danger the clothes are afterwards disinfected by steam. Although many other antiseptics have been proposed for the hands, mercuric chloride seems still to be one of the best; it should not be diluted beyond 1 in 1,000. The same solution should also be used by nurses and attendants when leaving the room; a convenient way of preparing it is to dissolve one " soloid " in a pint of water, taking care to stir

[1] *J. Med. Research*, 1903, **10**, 3.
[2] *Trans. Amer. Public Health*, 1902, **28**, 288.
[3] Report 1903, App. iii., 131.

well till all has dissolved. Infectious matter is particularly liable to remain under the nails.

The disinfection of the hands and instruments in surgery has been the subject of numerous investigations. Reinecke and others prefer alcohol, which, however, is hurtful to the hands. Dr. R. E. Weir[1] pronounced chlorine to be less injurious and equally efficient. He places "a large pinch" of bleaching powder in the palm of the hand, then a crystal of washing soda "about 1 inch wide," and a little water, rubs the resulting cream (sodium hypochlorite and calcium carbonate) for three to five minutes over the hands and arms, and washes off in sterile water.

Professor Mukulicz finds from a series of tests that it is impossible to render the hands perfectly aseptic. He first disinfects his hands as far as possible with alcohol and mercuric chloride, and then draws on a pair of cotton or linen gloves previously sterilized by boiling.

Regarding the value of alcohol as a disinfectant for the hands, Salzwedel and Elsner[2] maintain that alcohol is of use in preparing the hands for operations, not merely because of its hardening effect on the epidermis, but also as an active antiseptic; they consider it intermediate between carbolic acid and corrosive sublimate. The hands, after washing with soap and water, should be well soaked in 80 per cent. acidulated spirit before operating.

E. C. Hansen[3] states that epidermal bacteria, especially in cases of suppurating eczema, are, when moist, killed in one minute by absolute alcohol, and in most cases by 50 to 60 per cent. alcohol.

This statement is also supported by G. N. Brockhart[4] and by A. Fabludowski,[5] who finds that the value is considerably increased by the addition of tannic acid, and that the hands can be sterilized by two minutes' immersion in the liquid.

Glycerol, when heated to 120°, is, according to the *British Journal of Dental Surgery*, 1916, most effective for rendering instruments, and especially rubber tubing, sterile. The rubber is said to be rendered extremely elastic and supple by this treatment.

Thoroughly drying the cut and painting with a solution of Stockholm tar or Burgundy pitch in alcohol, ether, or acetone, is among the other treatments suggested.

Sterilizing the skin with iodine has been investigated in some detail by Groslich,[6] Routier,[7] Porter,[8] Stretton[9] and others with

[1] *N.Y. Med Record*, April 3, 1897, 469.
[2] *Berlin. Clin. Woch.*, June 4, 1900. [3] *Zeitsch. ges. Branc.*, 1908, **31**, 50.
[4] *Monatsh. prakt. Demat.*, 1911, **52**, 1. [5] *Deutsch. Med. Wochenschr.*, 1911, 405.
[6] A. Grossich, *Zentr. Chirurg.*, 1908, No. 4; *Prescriber*, 1909, 42.
[7] Routier, *Semaine Médicale*, January 6, 1909.
[8] F. W. J. Porter, *Brit. Med. J.*, February 6, 1909.
[9] J. Lionel Stretton, *ibid.*, August 14, 1909; *Prescriber*, 1909, 165.

favourable reports. Waterhouse,[1] using a 2 per cent. solution in rectified spirit, and Bogden[2] a 1 per cent. solution in benzene, have recorded its similarity in connection with surgical operations. Lance recommends it as an application for the bites of animals and insects, and Brewitt[3] advises a solution of iodine in benzene and paraffin for subjects with sensitive skins. Turner and Catto[4] use a mixture of iodine tincture and methyl alcohol with good results. Heussner's solution of iodine in benzene has been used with success by Levy and Hörrmann,[5] and by the various medical units in the European War. The coloration of the skin caused by such tinctures is their chief disadvantage, but such can be removed by a solution of sodium thiosulphate.

None of these give absolute immunity, so that, in case of accidental puncture during a *post-mortem* or operation, or in handling contagious matter, such as dead meat, skins, or evacuations, it is probably safest to wash immediately with mercuric chloride, dry, and at once cauterize, and thus combine the two precautionary measures. When, unfortunately, the abrasion has not been noticed at the time, this treatment should still be resorted to. Afterwards, hypodermic injections of an antiseptic have been recommended, and cinnamic acid, styrol, phenyl-propionic acid, β-naphthol, and betol are used for this purpose; phenol, or any other reagent which coagulates the blood, is, of course, inapplicable. For ordinary bites and scratches similar treatment may be adopted; the part should be afterwards protected by antiseptic gauze or wadding. Burns and scalds are liable to septic poisoning if the epidermis is broken, so that they also should be protected, but not cauterized. Wasp-stings and insect-bites have caused death. The best remedies are liquor plumbi subacetatis or Goulard's extract, and the old-fashioned hartshorn and oil.

Zinc peroxide, "Ectogan," is said to be often useful in the treatment of ulcers.

Disinfectant Soaps and Ointments.

In spite of increased knowledge of disinfectants, little attention seems to have been paid by soap manufacturers to this subject, so that soaps which were introduced many years ago still find favour with the public, although their efficacy as germicides is very small. This has arisen partly from the fact that it is seldom that disinfec-

[1] H. F. Waterhouse, *Lancet*, April 16, 1910.
[2] A. Bogden, *Zentr. Chirurg.*, January 15, 1910.
[3] Brewitt, *Münch Med. Wochenschr.*, February 8, 1910.
[4] Turner and Catto, *Lancet*, March 18, 1911.
[5] *Münch. Med. Wochenschr.*, 1911, 1130.

tant soaps are properly tested as to their germicidal action upon specific organisms under conditions which approximate to their use in practice, and partly owing to the fact that there are many disinfectants which have valuable properties as such, but which are totally unfitted for use in conjunction with soaps.

The conditions which obtain when a disinfectant soap is used are very different from those of ordinary disinfecting. As a rule, the time of contact is much shorter, and the volume of water or vehicle much less. As the time of contact is short, so it is necessary that the percentage of active ingredient should be high. As the volume of water used per unit weight of disinfectant soap is usually much less than is recommended when a liquid disinfectant is employed, this will assure a higher percentage strength of the active ingredient if it is present in the soap in anything like reasonable proportions. On the other hand, it is important to note that, unless the disinfectant employed is readily soluble in water, actual contact of the infected parts with the disinfectant cannot be attained in the limited time given to washing. In coal-tar soaps and those containing oils which are not very soluble in water, although the disinfectant is emulsified by the soap, the actual laving of every part of the infected area by the active ingredient for the necessary time to effect the death of the micro-organism is by no means certain. Organisms differ very markedly in their resistant power. Many of them form spores which are especially difficult to kill, so that even when a soap contains an approved disinfectant, the latter must be present in quantity above that required for the fatal dose for the most resisting spores.

It is of extreme importance to the soap manufacturer that he should not only carefully select his disinfectant and ascertain its purity and efficiency, but should also devote especial care in admixing this ingredient in the right proportion, the exact amount of the medicament being stated on the wrapper of each piece.

The disinfectant power of warm 2 per cent. soda solutions is considerable, even without the presence of any fatty acids, and they can be used with advantage for scrubbing floors, mantelpieces, and furniture. At 60° C. a contact of five minutes ensures the death of most organisms.[1]

The stock or basis of a medical soap or ointment is by no means unimportant. It is necessary that the medium in itself should produce no disturbing action; therefore in many of the best-known brands great care is devoted to the attainment of chemical neutrality—*i.e.*, that the fatty acids and alkali shall be combined in molecular proportions, since free fatty acids are said to induce in-

[1] Simon, *Zeitsch. Hyg.*, 1903, 349; also Kurpjuweit, *loc. cit.*, 369.

flammation, while any large excess of alkali is known to be irritant. Raw materials are carefully selected as neutral, uncoloured, and almost inodorous glycerides. It is probable, however, that such expensive precautions have been too far insisted on, as even a chemically neutral compound of a fatty acid with an alkali is decomposed in contact with water, a portion of the potash or soda being set free. F. Krafft and A. Stern,[1] in confirmation of Chevreul's early work, have found that soap in a large quantity of hot water gives a precipitate of the sodium salts of palmitic and stearic acids, while sodium oleate, not being so readily decomposed, remains in solution along with free alkali. An olein basis would therefore seem preferable to the employment of a harder fat. At the same time, since for disinfectant soaps the chief condition is that the agent should be rapidly disengaged *in sufficient quantity* in contact with the surfaces, a softer and more easily dissolving soap is directly indicated.

The alkali of commercial soap is, of course, soda, but *potash or soft soap* figures in several Pharmacopœias as "Sapo kalinus," "viridis," or "mollis." It is generally made with linseed oil (B.P olive oil), has a pale brownish-green colour, and is reckoned to be specially beneficial in some skin diseases. It would be useful to determine whether an admixture of a potash soap with the ordinary soda soap would produce a basis giving greater activity when used in such proportion as not to give too great softness to the product. E. W. Lucas has already shown[2] that a mixture of 1 part potash soap to 5 of soda soap solidifies, and can be advantageously employed as a basis for liniments. The solubility of drugs in a potash soap does not appear to have been investigated. The chief objection to commercial soft soap is that, not having been "salted out" or separated, as soda soaps are, it retains, besides a large and very variable amount of water, all the glycerine of the original fat, and in addition the saline impurities of the alkali used, some of which may interfere with the action of the medicaments. To meet this objection, Müller and Graube[3] have prepared a "pure soft soap," which they term "Savonal," by saponifying olive oil in the cold with alcoholic potash (which contains almost exclusively potassium hydroxide, most of the impurities being insoluble), and neutralizing the resulting solution by careful addition of fatty acids obtained from a portion of the alcoholic soap by precipitation with hydrochloric acid. The alcohol is then distilled off in a water-bath, when "Savonal" in an unctuous condition is left. It will be noticed that the glycerine is still left in. A really pure soap, if necessary,

[1] *Ber.*, **27**, 1747.
[2] B.P. Conference, 1894.
[3] *Pharm. Zeit.*, 1897, 546; *Nouveaux Remèdes*, **13**, 437.

could be quantitatively prepared by saturating alcoholic potash with the washed fatty acids, also dissolved in alcohol. By testing measured portions, using phenolphthalein as an indicator, the relative amounts of the two solutions could be obtained. Heat is avoided as much as possible, on account of the production of odour or colour. A liquid is prepared by adding "a few percentages of glycerine" and enough distilled water to make up the specific gravity 1·050 to 1·055; this is used as a medium for many drugs. Among the strengths given are: Phenol, naphthol or resorcin, 5 per cent.; salo 15 to 10; cresol, 0·25 to 2; chrysarobin, 10; iodine, 1 to 2, with 10 per cent. of potassium iodide.[1]

Many of these antiseptics will not dissolve to a clear liquid in the aqueous soap. If the alcohol were not all distilled off he solubility would be often increased, the product approximating to many of the official Linimenta.

Wunscheim states that phenol, orthocresol, lysol and creolin have less disinfecting power in glycerine soap solutions than in aqueous soap solutions of the same strength.[2]

Unna and others are of opinion that medicaments are more easily absorbed if the soap is "superfatted," or contains an excess of the fatty menstruum; but however preferable for toilet purposes as more emollient to the skin, these soaps seem not to be so suitable as vehicles for many drugs as those containing a moderate excess of alkali. The presence of free oils or fats is distinctly inimical to antiseptic action. Koch was the first to point out that carbolic acid dissolved in olive oil, or "carbolized oil," possessed no antiseptic properties. Lenti[3] concluded from his observations that fatty substances are unsuitable vehicles for disinfectants, as they impeded the germicidal action of mercuric chloride, phenol, and several other bodies.

J. Bosisto states that an ointment containing simply the volatile oil of eucalyptus is inferior to the fresh leaves as used in Australia.[4] E. Sage[5] says that neither vaseline nor lard is a suitable solvent for a preparation of cocaine, and that the idea of the superiority of such a preparation to one containing the hydrochloride, dissolved in a little water and rubbed up with fat, is fallacious. Dr. Breslauer's experiments with mercuric chloride, boric acid, silver nitrate, etc., admixed with oil, vaseline, lanoline, and other excipients, prove that while the lanoline gave the best results, the presence of the free oil or fat in all cases strongly militated against the germicide, various bacilli surviving in oil far longer than in aqueous solutions.

[1] *Year Book Pharm.*, 1900, 209.
[2] *Chem. Zentr.*, 1901, i., 408.
[3] *Union Pharmaceutique*, **35**, 58.
[4] *Pharm. J.*, [iv.], **2**, 224.
[5] *Ibid.*, **3**, 28.

It would seem, therefore, that the presence of water was necessary to the antiseptic and even to the full medicinal action of ointments (which would explain the above result with wool fat or lanoline, containing as it does about 25 per cent. of diffused water), and that it would be preferable to mix in a mortar an aqueous solution of the drug with the fatty basis shortly before being used, as these moist ointments in many cases do not keep well. A. St. Onge[1] gives a table of the proportions of water, alcohol, and glycerine, which he found miscible with various fats.

Dr. Baldas[2] found no pathogenic organisms in crude oils of commerce, but proved that if they were introduced, they could remain in the oil and retain their virulence for two months unless the oil were heated. He remarks that this should lead to great care with regard to the oils used in medicine and surgery.

Vicario noticed, in 1891, that fixed oils frequently contained germs. Cutting oils employed for lubrication in lathe work are often badly contaminated, leading to sickness of the operatives. From these and other observations it has been recognized that oils and fats used in ointments and soaps must be sterilized by heat; usually this is done in course of manufacture.

It must be remembered that soaps themselves have considerable antiseptic power. The early experiments of Max Jolles[3] have shown that in the case of typhoid bacilli the disinfecting action is more marked at 4° to 8° C. than at ordinary or higher temperatures, therefore that with cold water soaps would be more active than with hot. When rags infected with the germs were treated with a soap solution the effect was very marked, even a 1 per cent. solution being injurious to the germs in fifteen minutes, and a 6 per cent. solution resulting in their entire destruction. A 3 per cent. solution was fatal in one hour, and in 1 per cent. no germs remained capable of development after two hours' immersion. *B. coli communis* was less easily destroyed; at low temperatures a 2 per cent. solution was fatal in six hours. According to Harz and Von Miller, a solution of 1 in 1,500 or 1 in 2,000 of soapy water is fatal to all injurious plant parasites.

There is no doubt that prolonged contact with soap renders surfaces practically sterile, but, under common circumstances, ordinary soap fails to be effective.

Reithoffer[4] refers to the different behaviour of various germs to soap solutions. Thus anthrax bacilli are easily killed in weak solutions (?), but typhoid and cholera germs are far more resistant.

[1] *Zeitsch. oesterr. Apoth. Verein*, **34**, 712; *Year Book of Pharmacy*, 1897, p. 219.
[2] *Giorn. Real. Soc. Ital. Ig.*, February, 1901.
[3] *Zeitsch. Hyg.*, 1895, 130.
[4] *Arch. Hyg.*, **27**, H. 4.

He notes that in Behring's opinion the disinfectant power of a soap is dependent on its alkalinity. Experimenting with common soft soap, with scented almond soap, and with a patent potash soap, Reithoffer found that they all had a high degree of disinfecting power against typhoid bacilli, *B. coli*, and the cholera organisms, but their action is very feeble against pus cocci. *Staphylococcus pyogenes aureus* will remain unchanged for an hour or more in 18 to 20 per cent. soap solution, whilst a 10 per cent. solution of the same soap will kill typhoid bacilli in one minute. Experiments with carbolic and lysol soaps showed that although the power as tested on cocci was slightly higher than the simple soap, yet it was much weaker than was a solution of the disinfectant without the soap. From these observations it may be concluded that in surgical practice the use of a disinfectant soap is inefficient, the better plan being to wash first with soap, and afterwards to apply an antiseptic lotion.

Beyer[1] has shown that in the case of hospital clothing with various surgical stains, soaking the garments in solutions of various soaps for one or two days failed in every instance to kill cholera, typhoid, and pyogenic organisms. He attained success with lime-water in from twenty-four to forty-eight hours, but woollen goods were spoiled. In this case, if the soap had been supplemented by a good antiseptic, more favourable results might have been attained.

Reichenbach,[2] investigating the germicidal power of the alkali salts of the fatty acids, found that the palmitates had the strongest bacterial action. The potassium salts of the saturated fatty acids are comparatively strong bactericides, but the unsaturated acids, with the exception of elaidic acid, are not.

With reference to medicinal agents used in soaps, acids and free halogens are obviously incompatible, the former being neutralized by the alkali, or precipitating the fatty acid, the latter combining at once with the fat. A hypochlorite of K or Na is compatible to a certain extent, but the disinfectant action is much less than that of free chlorine. The oxygen compounds of bromine and iodine do not seem to have been studied in this respect. A vast number of organic bromo- and iodo-compounds have been introduced; some of them seem to be useful, but most are irritating; the majority have very unpleasant odours.

Fluorides and silico-fluorides are strongly antiseptic and non-poisonous (p. 86), and were patented under the name of "Salufer." They might be used in conjunction with soap, as Thompson states

[1] *Fortschritt der Medicin*, No. 1, 1897.

[2] *Zeitsch. Hyg. Infekt. Krank.*, 1908, 296.

that a solution of sodium silico-fluoride is not irritating, and " is stronger than 1 per 1,000 solution of $HgCl_2$," and it is obviously compatible with soap.

Sulphur.—Sulphur and alkaline sulphides blend well with soap, and have long been known as useful in skin diseases. Sulphur, even in the form of " milk of sulphur," is very slow in its action, on account of its insolubility. The alkaline sulphides are caustic, having been used from Roman times as depilatories; and recently ichthyol and sphagnol have been suggested as convenient means for administering sulphur in soaps. Most of these gradually evolve H_2S, and therefore yield an unpleasant odour, hence are not popular, although this gas is a prominent feature of their antiseptic action.

Boric acid in soaps would be converted into sodium borate, and would have little efficiency. It is added to destroy alkalinity.

Metallic Salts.—These can only be introduced into soap in very small quantities, as nearly all, except the salts of Na and K, are precipitated in an insoluble form, and on washing disappear from the water in the curd, which can have little effect or value.

Various oleates, or solutions of metallic oxides in oleic acid, more or less well defined as compounds, have been introduced into the Pharmacopœias. They mix well with unguents, and are said to be more readily absorbed and less irritating than older remedies. Hence it has been proposed to incorporate them with soaps. But since the efficiency of soap depends upon its solubility in water, the curdy precipitate, as mentioned above, is probably inert; since also most oleates of metals are insoluble in water, the question arose as to how far an oxide or an oleate could be made soluble for use in ordinary washing. As an example, some zinc oleate, B.P., was dissolved in a minimum quantity of soda; to the hot clear solution 10 grammes of yellow soap were added and incorporated. When cold, the soap separated from the mother liquor, which was strongly alkaline, and contained practically all the zinc. This process not working, zinc hydrate was prepared and boiled with soda to form a sodium zincate as neutral as possible. Yellow soap was then dissolved in the filtered solution, boiled down, and allowed to set. It formed a soap of good washing qualities, not unduly alkaline. On using with water in the ordinary way, the zinc was found to be in solution, showing that there was no separation of insoluble zinc oleate. It would therefore seem that metallic oxides dissolved in soda or potash might give better results than the oleates.[1]

In most arsenical soaps the amount of arsenic present is almost

[1] See *J. Soc. Chem. Ind.*, 1901, 498.

infinitesimal, and quite insufficient for antiseptic or disinfectant properties, although the small quantity with constant use might have some effect on the skin.

The powerfully antiseptic action of mercury salts suggested their employment in medicated soaps. It was difficult, however, to prevent the production of the insoluble mercuric oleate, which has little or no germicidal action, and also prevents the formation of a good lather; while any surfaces on which a mercurial preparation is used are liable to become blackened by H_2S, and organic matter is apt to reduce and throw the mercury out of action. One form of mercurial soap contains mercuric chloride, ammonia-mercuric chloride, together with β-naphthol, eucalyptol, and methyl salicylate. The salts are incorporated with a neutral soap in a dry state in the process of milling, and are therefore possibly present unchanged. It is claimed that they are active at the moment of decomposition, as in washing, though afterwards converted into oleate.

The double iodide of K and Hg has even stronger germicidal powers than $HgCl_2$. In certain proportions it is easily incorporated in the soap stock, and one of us has found that when dissolved in warm water there is no separation of any insoluble mercury compound. The strength recommended is 1 to 3 of HgI_2 and 1 to 3 of KI in 100 of soap. It is said to be effective in a proportion of 1 part of HgI_2 to 4,000 of water. A soap of this kind, which is on the market, has been found by analysis of some samples to have the following composition in the three grades sold:

Nominal Strength.	*KI.*	HgI_2.	*Biniodide,* $KIIgI_2$.
3 per cent.	2·25	2·39	3·4
1 ,, ...	0·94	0·63	0·9
½ ,, ...	0·45	0·26	0·37

More potassium iodide is therefore present than is sufficient to form the double salt. Potassio-mercuric iodide has the advantage of being compatible with strong alkalies, as is shown in the preparation of the Nessler test; moreover, it does not precipitate albumin, and is not easily reduced. Organo-metallic compounds containing mercury are frequently strongly germicidal, and have been incorporated in various soaps. Schrauth[1] has stated that only those organic mercury compounds are suitable where the mercury is

[1] *J. Soc. Chem. Ind.*, 1911, 382.

combined directly to the carbon atom. He found the most suitable to be the alkali salts of hydroxi-mercury, carboxylic acids, and certain halogen hydroxi-mercury benzoates Schrauth and Schoeller[1] have confirmed the view that some mercury organic compounds have strong germicidal action, and that the disinfecting power is by no means proportional to the ionization of the mercury salt, as was formerly supposed. They find that by the influence of substituting for a hydroxi group united to the mercury by iodine, or cyanogen, the power is decreased, while a mercury atom united with both of its valencies to the benzene nucleus has no germicidal power. Obviously, mercurial soaps should not be used popularly or indiscriminately. We can conclude that with regard to metallic soaps, as it is known that a metal in the form of oleate is readily absorbed by the skin, if an internal effect is wished for, an oleate soap will succeed; but if a local antiseptic or disinfectant action be required, oleates or other insoluble salts are practically useless, and means must be taken to obtain a mixture like the mercuric iodide soap or the zinc soap mentioned above, which yields the metal in a soluble form to water. The latter use of soap is obviously the natural one, the former more properly belonging to an ointment or liniment.

In a series of bacterial tests in our laboratory comparison was made with a curd soap containing 32·5 per cent. of water and 60·8 per cent. of fatty anhydrides, using for the experiments a 2 per cent. sterilized solution. Inoculation with active bouillon cultures gave results which may be summarized in the tables, + indicating growth and − sterility:

I.—Bacillus Coli Communis in Vigorous Growth.

Time.	*Curd Soap.*	*A Scented Curd Soap.*	*Carbolic 10 per Cent.*	*New Disinfectants.*		HgI_2 *3 per Cent.*	*Formalin 0·4 per Cent.*
				A.	*B.*		
5 minutes ..	..	..	..	..	..	−	+
15 ,, ..	..	..	..	..	..	−	+
25 ,, ..	..	..	..	..	..	−	+
30 ,, ..	+	+	+	+	+	−	−
1 hour ..	+	+	+	+	+	−	−
1½ hours ..	+	+	+	+	+	..	..
2½ ,, ..	+	+	−	+	+	..	..
3½ ,, ..	+	+	−	+	Much attenuated	..	..
4 ,, ..	−	−	−	−	−	−	−

[1] *J. Soc. Chem. Ind.*, 1910, 1328.

II.—STAPHYLOCOCCUS PYOGENES AUREUS.

Time.	*Curd Soap.*	*Scented Curd.*	*Carbolic 10 per Cent.*	*New Disinfectants.*		HgI_2 *3 per Cent.*	*Formalin 0·4 per Cent.*
				A.	*B.*		
10 minutes ..	+	+	–	+	+	–	+
20 ,, ..	+	+	–	+	Attenuated	–	+
30 ,, ..	+	–	–	–	–	–	–
Between 1 and 4 hours	–	–	–	–	–	–	–

The relative amounts of disinfectants present in the solutions of the same strength (2 per cent.) would be:

Carbolic acid 0·2 per cent., or 1 in 500 of phenol.
A 0·05 per cent., or 1 in 1,665 of disinfectant.
B 0·03 per cent., or 1 in 3,332 of disinfectant.
HgI_2 0·05 per cent., or 1 in 2,000 of HgI_2.
Formalin 0·008 per cent., or 1 in 12,500 of formaldehyde.

It will be seen that in these experiments the formaldehyde was used in unduly small quantity, but the results are good. Paraformaldehyde and lime-water added to a soap just before solidification is the basis of a patent.[1]

Carbolic and Cresylic Soaps.—An ordinarily stated commercial strength of these soaps is 10 per cent., but it is frequently much less. The odour of all forms is very pronounced, and often constitutes an objection Several varieties are advertised as "of delicate odour" and "not unpleasant in any boudoir," etc.; but, although the homologues of cresol have a higher disinfectant power than phenol, they will still, if in effective proportion, manifest their distinctive odour, so that a soap of the tar order, however disguised with eucalyptus, gaultheria, or other scents—which in themselves, however, have little disinfectant value—cannot be free from a more or less tarry odour. A large number of "toilet" soaps are advertised in conjunction with the names of various disinfectants, and contain such an infinitesimal quantity of the various reagents as to be quite useless in a germicidal sense; they are, in fact, objectionable, as conveying the feeling of a fallacious immunity.[2] "Carbo-sapol" contains 50 per cent. of Calvert's No. 5 carbolic acid, 25 per cent yellow soap, and 25 per cent. soft black soap.

[1] *J. Soc. Chem. Ind.*, 1908, 138.

[2] The percentage of phenoloids should always be stated on the packages of these soaps.

Professor Mikulicz, of Breslau, uses a spirit soft soap for disinfection of the hands. This owes its efficacy mainly to the alcohol, as the alkalinity of the soft soap in solution is not high. A liquid ethereal antiseptic soap for this purpose is now manufactured in America, and is also employed as a parasitic dressing.

Essential Oils.—The disinfectant power of the essential oils has been much over-rated, and to be at all effective they require to be used in such quantities as are liable to cause serious irritation to the skin, many of them having a blistering action as powerful as turpentine or mustard. When desired as perfumes, the amount added should be minute, an over-strength having caused many soaps, otherwise well manufactured, to lose favour. When such ingredients are added to the crutching-pan, it is always desirable to neutralize the free alkali at this stage by the ammonium-salt process, or to postpone the addition of the oils until after the operation of fitting. Such has been the reaction against perfumes that prominent brands are advertised as "unscented," and others as "delicately scented."

Volatile disinfectants, such as phenol, camphor, thymol, etc., suffer considerable loss if introduced in crutching in the ordinary manner or added during remelting, so that the quantity present becomes uncertain; it seems, in fact, desirable that all such medicinal soaps should be milled or plotted, as the machines are very convenient for regulating the amount of disinfectant added.

The cakes should evidently be packed in tinfoil (except in the case of mercury soaps, when oiled paper or thin gutta-percha should be used), and should be kept in a cool place. It has been proposed to coat the surface of the tablet with a film of gelatine or wax.

In a series of comparative experiments made in 1896, using 2 per cent. solutions and broth cultures at 37° C. of two representative organisms with the usual precautions, one of us found that oil of cloves when present in a soap had little antiseptic action.

Organism.	*Time required to Kill the Organism.*					
	Curd Soap.	*Carbolic Soap, 3 Pounds per Cwt.*	*Clove Oil Soap, 3 Pounds per Cwt.*	*Clove Oil Soap, 7·5 Pounds per Cwt.*	*Biniodide Soap, 0·5 per Cent.*	*Biniodide Soap, 1·0 per Cent.*
B. coli communis	Between 2 and 4 hours	Between 2 and 4 hours	Alive after 6 hours	Between 2 and 4 hours	Less than 15 minutes.	Less than 15 minutes.
S. pyogenes aureus	Organism alive after 6 hours				Between 15 and 20 minutes	Under 15 minutes

The carbolic and two clove-oil soaps have therefore an antiseptic action equal to, but not exceeding, ordinary curd soap. In the case of *S. pyogenes aureus*, the limit of time required to produce disinfection was not reached, but as both the strength and the time much exceeded those which obtain in practice, it was not considered necessary to prolong the experiments. The time had also much exceeded that required by the biniodide.

A comparison of the amount of antiseptic present in the case of the carbolic and mercurial soaps would point to the *a priori* probability of the above results, since—

The 2 per cent. solution of carbolic soap contained 0·052 per cent. phenol.
The 2 per cent. solution of mercurial soaps contained 0·01 and 0·02 per cent. of mercuric iodide respectively.

Solutions of 1 in 10,000 and 1 in 5,000 of mercuric iodide are known to possess decided antiseptic properties, but a solution of 1 in 2,000 of carbolic acid is practically useless.

Another series of experiments with *B. coli communis* and 2 per cent. solutions gave:

Curd soap	Sterile between 1 and 3 hours.
Zinc hydrate soap (*ante*, p. 114) ..	Alive after 3 hours.
Carbolic soap	Sterile between ¼ and 1 hour.
Coal-tar soap	,, ,, ,, ,,
Sanitas soap	Alive after 3 hours.
Terebene soap	,, ,, ,,

The variation in these results is influenced by the amount of water present. Thus, taking a dry curd soap, such as was used in the above experiments, in proportion corresponding to soaps containing 33 and 66 per cent. of water, the following results were obtained:

	3 *per Cent. Dry Soap.*	3 *per Cent. of Soap containing* 33 *per Cent. of Water.*	3 *per Cent. of Soap containing* 66 *per Cent. of Water.*
Time required to kill *B. coli communis*	Attenuated after 1 hour	Less than 3 hours	3 hours

Soaps containing active oxygen are made with perborates and percarbonates.[1]

Ointments.—With the exception of vaseline, which in itself is certainly somewhat antiseptic, and to a certain extent the pre-

[1] Wolpenstein, *J. Soc. Chem. Ind.*, 1908, 1028.

parations of glycerine such as "glycerinum saponatum," the bases of ointments are only antiseptic in the sense that they exclude air and moulds and bacteria from the surface covered. Otherwise their virtues are simply emollient, or depend on the drug, such as mercury or zinc, which is incorporated with them.

Sulpholeate of sodium has been sugested for dissolving antiseptic drugs and yielding them to the skin.[1]

Lanoline and cold cream contain water, and thus differ from other ointment bases. If, therefore, antiseptics are incorporated with them they dissolve in the water, and so come in contact with the surface of the wound and kill the organisms present. When oil, vaseline, etc., are used, as they contain no water, the antiseptic remains in the ointment, and only a fraction reaches the surface of the patient, hence the uselessness of carbolized oil as shown by Koch and Breslauer. The property of formaldehyde to form condensation products with fat and oils has led to its use for the preparation of antiseptic oils. *Lanoform*, for example, is wool fat heated with formaldehyde.

Mouth Washes and Tooth Powders.—These are too numerous to be fully discussed. They are chiefly empirical mixtures which owe their reputation to custom or advertisement. Some people use only water with a little soap in it to clean the teeth, but it is of advantage to assist the friction with a powder, and also to use an antiseptic which will penetrate the crevices which cannot be reached by the brush. Wood-charcoal powder is excellent, but rather disagreeable. The best is said to be areca nut; it should not be used constantly, as it is apt to scratch and wear away the enamel. Prepared chalk is the best foundation for tooth powders, as it neutralizes any acid, and, being softer than the enamel, it polishes but does not scratch. Powdered myrrh, Peruvian bark, quinine, and other ingredients are frequently added. Honey, borax, various scents, such as orris and rose, are among other substances which are commonly found in dentifrices. As a mouth wash, where there is decay and the breath is offensive, one of the best applications is chlorinated soda diluted to about 1 per cent., and used occasionally. It is not very pleasant, but it removes all odour. Saccharin, sodium bicarbonate, oil of peppermint, benzoic and boric acids, tannin, tincture of iodine (dangerous), and tincture of myrrh are also occasionally met with.

Cleansing Personal Utensils.—The regular washing and cleansing of private articles such as brushes, combs, and razors should always be insisted upon. Barbers should pass their instruments through some disinfectant such as 1 in 1,000 mercury sublimate or its equiva-

[1] *Therap. Gaz.*, 1891.

lent in phenoloid disinfectant. For regular clients special sets of instruments might be kept under hygienic conditions.

The cleansing of utensils used for eating and drinking requires careful attention, especially in public eating-houses and hospitals. O. Roepke[1] gives two authentic cases in which syphilis was transmitted by the use of a common drinking-glass in a beer-hall.

The use of the chained cup in connection with the public drinking fountain cannot be condemned in too strong a measure. The replacement by paper cups obtained from automatic machines or drinking directly from a vertical fountain of water are substitutes which deserve attention.

Munch advises disinfection of bath tubs (besides disinfection of the urine as systematically as of fæces) used by persons who have or have had typhoid fever recently. He suggests that micturition during the bath is of frequent occurrence in typhoid.

Disinfection of Clothes.—The disinfection of clothes and fabrics is usually accomplished by means of a steam disinfector (see *ante*). If this is not available, the clothes may be boiled with a germicidal solution of determined strength; this method, however, is generally more costly and more liable to injure clothes.

Disinfection of Cavities of the Body.—Several methods in use have been alluded to in the chemical section. The following is a summary of processes:

(*a*) *Washing out* by inflow and outflow tubes with lukewarm water, then with a weak solution of an antiseptic, which should not be one with a strongly poisonous action on the system. Phenol, resorcinol, and mercuric chloride have been absorbed with dangerous, and even fatal, effects. Iodine is very irritant. Iodol has been recommended, likewise betol and phenyl-propionic acid.[2] Salicylic acid is dangerous, irritant, and not effective. A solution of silver nitrate in distilled water has been tried with great success; the objection to it is that if weak (1 in 1,000) it is almost wholly precipitated by the chloride of sodium in the fluids of the body, and if stronger (1 in 200) it has on some occasions caused sloughing. Silver preparations free from these faults have been described, (p. 88). Sulphocarbolate of zinc, 1 in 1,000, has the advantage of being mildly astringent, and seems to be safe; a sulphocresylate would probably be still safer, and is a stronger antiseptic. *Aluminol* (p. 254) is a useful and powerful astringent. Glycerine is irritant to mucous membranes, but it is useful when it is necessary to keep surfaces moist. On boric solutions, see p. 49. A number of the

[1] *Deutsch. Med. Wochensch.*, 1905, **31.**

[2] Klein, in Stevenson and Murphy's "Hygiene," p. 261.

newer antiseptics are advocated for this special branch of antisepsis, but they await more extended and impartial surgical trials, as many of the earlier statements have not been verified by recent experiments.

(*b*) *Spraying.*—Any of the former may be used in the form of spray, the advantages being that stronger solutions may be used, that only the affected parts are treated, that the irritating and depressant action of large volumes of water are avoided, that a local refrigerant effect may with safety be produced, that much less of the medicament is required, and that the action can be watched, and the process repeated with facility and without shock. The various spray-producers nearly all act on the same principle; a current of air is blown by an india-rubber ball, with a second ball to render the blast steady, across the narrowed orifice of a vertical tube dipping into the liquid in the bottle. The strength and fineness of the spray are regulated by the relative size and position of the orifices, and the amount of liquid delivered is known by the graduations on the bottle. Chlorine water, with or without cocaine hydrochloride, has been employed, and boric sprays are frequently used for the throat. Solutions in ether were recommended by Philip Sterne as far back as 1767[1] as antiseptic spray. As sprays said to more easily penetrate parts covered with hair, mercuric chloride, chrysarobin, resorcinol, and formaldehyde have all their special uses.[2]

(*c*) *Gargles* of honey and borax, tannin, and alum have been used from time immemorial. This method is easily used by unskilled persons, but it is inferior to that of spray, as there is no certainty that the parts affected will be reached. It is evident that no drug which will be poisonous if swallowed can be employed.

(*d*) *Injections of Gases or Vapours.*—It is a familiar fact that if an abdominal cavity be wounded, septic poisoning and peritonitis is almost certain to supervene, and that washing out may be dangerous, owing to the intense irritation, and may even cause the above disastrous result. In these cases spraying is also interdicted. Life has frequently been saved by gaseous injections, and sulphur dioxide seems to be the best remedy to employ. This can be obtained by blowing a current of air through a tube containing some fragments of sulphur, and allowing the gas produced to enter the cavity. The part of the tube containing the sulphur is heated by a spirit lamp, taking care that the end of the tube is kept cool. Blowing air through a saturated solution of sulphurous acid or through a mixture of a sulphite with acid is inferior to the above, as the quantity delivered is uncertain. Liquefied sulphurous acid

[1] "Advice to the Consumptive." [2] *Pharm. J.*, **21**, 1040.

from a Boakes' bottle cannot be used for this purpose, as the cold produced is intense and would produce shock. Unfortunately sulphurous acid, by being absorbed into the system, is recorded to have produced fatal effects in one or two cases. Baxter experimented specially on its effect on the virus of peritonitis[1] with favourable results. Chlorine, bromine, and iodine vapours are irritant and dangerous. Many others, such as chloroform, ether, phenol, etc., are excluded by their narcotic action. Iodoform vapour has caused poisonous effects. Carbonic acid is very soothing, and rapidly subdues inflammation, but for this purpose the gas must be thoroughly washed. It is only a feeble antiseptic, but would be a better medium for other antiseptics, such as eucalyptol, than air.

(*e*) *Inhalations.*—Chloride of ammonium is beneficial in bronchitis and asthma. The simple breathing of the vapour of vinegar and hot water also gives relief. Koch proved that a number of essential oils when inhaled with steam are inhibitory to tubercle.[2]

Antiseptic Dressings usually include cotton-wool, wood-wool, or gauze, which act as germ excluders; they are kept moist with diluted soda chlorinata (p. 200), or with boric acid solution (p. 204); sometimes phenol, 2½ per cent., or mercuric chloride, 1 in 1,000, are used, but they are liable to produce ill effects on absorption. There is a great advantage in changing the agent every few days; even the most innocuous are liable to become irritating if continuously used. An alcoholic solution of coal tar has been much used for many years under the name of Wright's Liquor Carbonis Detergens. Diluted cresol and Sanitas fluid are useful in rotation with boric and with chlorinated lotions. Glycerine is objectionable. Zinc sulphocarbolate and sozal (the aluminium salt) are used as astringent and antiseptic lotions. Diaphtherin in 1 per cent. solution has been much used in Germany. Tichborne recommends[3] zinc sulphite as non-poisonous and not irritating.

Gauzes and Wools are described under iodoform, boric and salicylic acids, and zinc-mercuric cyanide. Hydronaphthol gauze has recently been much praised. Salicylic gauze is irritating. Thymol or eucalyptus gauze would seem to be the best and safest. Benzoated gauze, 5 per cent., has also been recommended.

M. Duquaire, of Lyons, has invented an ingenious antiseptic paper. The material is asbestos, with about 5 per cent. of ordinary paper pulp, worked into soft paper and soaked in a petroleum-benzene solution of beeswax. The solvent having been evaporated

[1] *Appendix to the Report of Med. Off. of the Privy Council*, 1875.
[2] Marshall Ward, *J. Soc. Chem. Ind.*, 1893, 943.
[3] *Brit. Med. J.*, 1890, 1064.

off in the open air, the tissue is ready for use. When required it is set on fire, and is so made aseptic, and may be employed at once for dressing wounds.[1]

Unfortunately many of the antiseptic wools and dressings met with commercially are of uncertain composition, and insufficient attention has hitherto been paid to the importance of storing these articles in such a way that the antiseptic present shall not be volatilized.

In France their sale, except by duly qualified pharmacists, is forbidden, but the question does not seem to have been discussed in England.

Surgical instruments must be rinsed in a disinfectant which does not corrode steel; the various cresol preparations are much used for this purpose. Those that turn turbid with water have the disadvantage that the instruments cannot be so well seen. A good preparation seems to be potassio-mercuric iodide, 1 in 4,000, or two of the soloids to a pint, for hands or instruments.

Antiseptic Hypodermic Injections.—Several of these have been much employed recently in France, particularly for phthisis; the basis is olive oil, and all the ingredients are carefully sterilized by heating to 120° C.

Picot uses guaiacol 5, iodoform 1, olive oil to 100; Morel-Lavallées' solution consists of eucalyptol 12, guaiacol 5, iodoform 4, olive oil to 100.

Also solutions in olive oil of creosote 1 in 15, and eucalyptol 2 to 4 in 10 have been suggested.[2]

A number of mercurial compounds are used specially in syphilitic affections. These are later enumerated and described.

Internal Disinfection.—In the alimentary canal, and sometimes in other parts of the body, there are always present large numbers of micro-organisms, and it is probable that the process of digestion itself may be assisted by certain microbes. Even pathogenic bacilli may enter in limited numbers without producing disease. They are not destroyed by the gastric juice, but rarely survive in the struggle for existence with the far more numerous non-disease-producing organisms. If they are present largely in food, water, or air, it is impossible to exclude them from the body, and difficult to kill them when they have entered.

The removal of bacteria may, however, be brought about in hastening their elimination by purgatives, or by entangling them and their products by inert substances like wood-charcoal, which is known to have proved most beneficial in indigestion and flatu-

[1] *Chem. and Drug.*, 1890, 39. [2] *Therap. Gaz.*, 1891.

lency—states which are probably due to, or at least intensified by, organisms promoting abnormal fermentations.

It had been hoped that oxidizing agents like chlorinated soda, peroxide of hydrogen, potassium permanganate, and even potassium chlorate, would be capable of attacking bacteria in the alimentary canal. But the last mentioned passes right through the system into the urine without change, while the others not only disturb digestion, but are rapidly used up by the easily oxidizable organic matters present—*i.e.*, they act on the food before affecting the far more stable bacteria. Much was expected from hydrogen peroxide, but results have been disappointing. Dilute chlorine water is said to have been given internally with great benefit in enteric fever, especially when the stools were offensive.[1]

Sulphuretted hydrogen water and sulphites were formerly given with the object of destroying organisms. They are unpleasant, disturb digestion, and do not seem to bring about the desired effect.

Internal Antisepsis.—Although it is difficult to kill the bacteria within the alimentary canal, it is quite feasible to hinder their growth by an inhibitory or antiseptic treatment, and so at the same time to lessen the auto-intoxication produced. If the contents of the stomach were undergoing fermentation by the action of yeast, etc., it would be quite possible to stop the process by means of phenol, creosote, or an essential oil, with a dose so small as not to injure the coats of the stomach. But the same dose would also stop or at least impede salivary, pancreatic, and gastric digestions. Therefore these powerful agents, though occasionally given in capsules, are not in general favour. It has been suggested that the use of condiments such as salt, vinegar, pepper, mustard, and spices is really an instinct founded on their antiseptic action, since many animals resemble man in this respect. The effect of mineral waters, too, depends in a large measure on the antiseptic action of carbonic acid, and not on the alkali, since soda-water generally does not contain soda in any efficient quantity.

It has been already pointed out that acids are antagonistic to most bacteria. Dilute sulphuric acid has been preferred in many diseases, especially cholera, on account of the additional advantage of its astringent action. Sulphuric lemonade, made by the addition of the acid, which should be perfectly pure, to sweetened and sterilized water in quantities sufficient to give a marked but pleasant acidulous flavour, may be employed freely, and according to all experience with much benefit. Excellent effects have been attributed to the habitual and free supply of a pleasant flavoured

[1] "Local Gov. Officer," 1907, 86.

sulphuric orangeade among the employés of the post office during several cholera seasons. It is cheap and innocuous, and is very likely to do much good. Although ordinary lemonade contains citric acid, it is more costly, and is inferior to sulphuric for this special purpose.

The Vienna mixture for choleraic diarrhœa consists of 15 drops of aromatic sulphuric acid (sulphuric acid 1 in 12, with rectified spirit, cinnamon, and ginger) to 1 ounce of sweetened water; to this is often added, under medical advice, 5 or 10 drops of ether and 5 drops of laudanum. The mixture has been much used and highly thought of in Austria, Germany, and France, and by the English Local Government Board.

For intestinal antisepsis neither phenol nor creosote can be employed, being too poisonous and irritating. Betol, however, has been successfully used, the β-naphthol produced by its decomposition being comparatively non-injurious. Resorcinol, guaiacol, thymol, and sodium benzoate are sometimes used as internal antiseptics, and in cases of colitis have proved their efficacy by deodorizing the bowel discharges. Sodium sulphocarbolate is also much used. The action of calomel in cases of duodenal indigestion seems to be bactericidal.

Quinine and its source, cinchona bark, probably owe a great deal of their power in fevers to their antiseptic action.

Several of the derivatives of guaiacol, such as benzosol, have been highly recommended. Pheno-salyl is a good preparation for washing out the bladder and urethra.[1] Urotropine as a prophylactic against typhoid fever owes its efficacy to the generation of formaldehyde.

Vaccination.—Vaccination and other preventive measures of inoculation are as yet foreign to the scope of the present work, but may properly be regarded as precautionary measures relating to personal disinfection.

There is little doubt that chemico-disinfection plays an important part in the general problem of disinfection in the blood-serum, as we shall note when dealing with the work of Ehrlich on chemical spirilla and trypanosomicides, but the other important factors, such as removal of bacteria by means of the phagocytes, are, however, not as yet directly translatable into phenomenological chemical language. The reactions in the blood-stream caused by the adventitious ingress of foreign organisms are relatively complex. One drop of blood contains approximately 5,000,000 red corpuscles and 2,000 white cells or phagocytes floating in the blood-plasma. On

[1] On intestinal antiseptics *v.* Burney Yeo, *Brit. Med. J.*, 1899, 1250; Vaughan Harley and Goodbody, *ibid.*, 1899, 1254.

the infiltration of the foreign organisms, bacterial or protozoal, both the phagocytes and the blood-plasma attack and digest them. It is estimated that one phagocyte can deal with from ten to twenty microbes before it is poisoned by the toxins secreted by its food. The ordinary process of physico-chemical actions is, however, more perceptible in the action of the blood-plasma. From the blood-plasma a series of substances termed antibodies (see Chapter XI.) have been isolated; these react in different manners with the micro-organism. Antibodies include antitoxins, which react specifically with the toxins of the micro-organisms; agglutin, which agglutinate or cause clumpings of the bacteria; substances which exert a direct solvent action on the germs, and appear to render them more easily absorbed by the phagocytes. Poisoning of the blood-stream may be caused by an accumulation of dead phagocytes and spent plasma, by the secretion of "aggressions" which paralyze the phagocytical activity, or by the accumulation of bacterial toxins; whilst preventive and curative measures constitute either the injection of dead germs so as to stimulate the production of antitoxins in the plasma, a procedure frequently followed in typhoid, or the injection of a serum containing the antitoxin, as in tetanus and diphtheria.

The Disinfection of Wounds.

The disinfection of wounds during the European conflict has presented difficulties much graver than in any previous period, and greatly differs from earlier experience. Most modern surgery has relied on *excluding* dangerous organisms and encouraging natural processes of repair, but such favourable circumstances could very seldom be reached.[1] It was found that all wounds in this war were already septic when ordinarily received, on account of the length of time before the patient is treated. The wounded often could not be picked up, sometimes for twenty-four or forty-eight hours, and the chances of rendering a wound aseptic are small after twenty-four hours, and *nil* after forty-eight. Wounds are rapidly infected with organisms. Many of these divide and double their numbers in twenty minutes, so that each organism could give rise to 15,000,000 in twelve hours. First aid cannot often be given, so that the pathogenic bacteria have a long time to develop, and these are of the dangerous kinds derived from manured fields and from

[1] M. Tuffier (*Paris Acad. de Médecine*), sent by the Minister of War to inspect treatment of wounded, recognized that the superiority of antiseptic over aseptic treatment was incontestable. "French first aid applies tincture of iodine to the wound; this, with bandaging, is often sufficient for healing simple wounds. Tetanus is frequent. For emphysematous gangrene they inject peroxide of hydrogen."

populous districts. Their earliest treatment is in the "clearing hospitals," mobile units placed as near as possible to the field ambulances. In actual practice this generally means an interval of twelve hours, with "as many as 500 to 1,000 patients received in twenty-four hours, their clothes all thick with mud."[1]

The stores of dressing and bandages required were greater than in any previous war. In the usual procedure the skin was painted with iodine, the wound washed with a carbolic antiseptic and dressed. Every man was injected with antitetanic serum, and in reference to the pressure it is mentioned that in one place "after using 30,000 doses of tetanus antitoxin they ran temporarily short." Besides this, other injections were in use, and the British Medical Association Research Committee's Section of Bacteriology, headed by Sir Almroth Wright and Captain Douglas,[2] furnished the Admiralty, War Office, and French and Belgian Armies with over 350,000 doses of antisepsis vaccine.

The soldier's greatest foe after battle is putrescence of wounds. An early record of this is that after Phalsbourg, in 1795, "wounds became so offensive as to cause nausea to those near, and to occasion the poor fellows to be deserted." Bullets themselves and other weapons of war are usually more or less aseptic, and do not infect the wound unless clothing or other matters obtain entrance with them. It is common experience that bullets pass through, leaving inconsiderable effects beyond slight local sepsis in some cases.

Professor Aschoff noted that German projectiles as a rule caused greater damage than French, as the former, when striking, break up and expose the leaden core.[3] Apart from mechanical injury, however, the serious infections are not metallic, but bacterial, and supervene after the wounded have lain on the ground.

In the earlier stages of the war suppurating wounds occurred in 60 per cent. of the wounded prisoners in Belgium, which was rashly taken to show that "the German field dressing was not a very efficient preventive against sepsis."[4] Tetanus was very rife, and antitetanic serum was extensively used. Later information proved that tetanic infection from the soil affected the armies of the Allies and Germany with equal severity. It was noticed that tincture of iodine used in these wounds rendered innocuous the specific organisms, or at any rate made their action take a mild form.

Bacteriological investigations showed that the prevalent causes

[1] Sir A. Bowlby, *Brit. Med. J.*, December 19, 1914.

[2] They have departments in London at the Mount Vernon Hospital, Hampstead, and at St. Mary's Hospital, Paddington, for bacteriological investigation of infected wounds.

[3] Feldärzliche Beilage, *Münch. Med. Wochenschr.*, No. 6.

[4] *Lancet*, September 12, 1914, 721.

of mortality were a group of spore-bearing *anaerobic* bacteria, of which over ten distinct varieties have been isolated; hence oxidizing agents were indicated as antagonistic to their mode of growth. Among generally used oxidizers has been—

Peroxide of Hydrogen, used extensively even before the war. At the beginning Captain Max. Page, R.A.M.S., found that emphysemataceous gangrene could be treated successfully by local incision and the application of hydrogen peroxide.[1] A Royal Naval report in October, 1914, stated that "wounds are grimed with dirt, oil, dust, and pieces of clothing. For suppurating wounds we found peroxide of hydrogen our sheet anchor in 10 or 20 per cent. solution." Colonel Makins, Surgeon to the Forces, says that in all cases peroxide of hydrogen has been applied locally to the wound. In French field hospitals, when wounds have been soiled by contact with earth or filthy straw, a protective inoculation of antitetanic serum was the regulation treatment; *it must be given at once to have any effect.* For gangrene, injections of hydrogen peroxide were used. "Unfortunately they are very painful, as for preservation the solution is always acid." This refers to a disadvantage of H_2O_2, its instability. To minimize the rate of decomposition during storage and transit it is customary to add a stabilizing agent such as tannic or phosphoric acid. The commercial description of 10 or 20 volumes means conventionally the number of volumes of oxygen gas that the solution gives off when treated with peroxide of manganese. "Perhydrol" is a solution of 100 volumes strength or containing 30 per cent. by weight of H_2O_2. But although increasing the strength diminishes the weight and bulk of transport, it is not generally advisable, as it increases the expense in greater proportion, and does not render the preparation more stable, therefore the 10 or 20 volume solution is the common supply. Some failures have undoubtedly been due to the reagent having become weaker by keeping, therefore substitutes have been introduced in the form of soluble solid metallic peroxides which can be easily carried and used in definite strength. The choice of the base was limited. Peroxides of sodium and potassium are caustic, those of barium and strontium are poisonous; magnesium peroxide has proved very useful, but it is expensive. A preparation called "perhydrit" or "hyperol" is mentioned as a compound of H_2O_2 and urea, with a trace of citric acid to render it stable. Sodium perborate is neutral, and is strongly advocated as an oxidizer in some French hospitals.

For emergency dressings *vioform* (hydroxyquinoline chloro-

[1] *Lancet*, August 8, 1914.

iodide, [$C_9H_6N(OH)ICl$]) gauze was employed by the Germans. Only 3 out of 400 showed suppuration in an ambulance train after this treatment. For anaerobic infection H_2O_2 was recommended, "especially in the solid form, which can be powdered on the wounds like iodoform; the perhydrit of Merck and the pergenol of Byk have proved convenient forms." Everywhere tetanus caused high mortality, and there is unanimity as to the benefit of antitetanic serum. Von Behring says that 20 c.c. was generally sufficient for preventive treatment, whereas after spasm has occurred at least 100 c.c. should be given intravenously. More potency is ascribed to *luminal*, a phenyl-veronal derivative (Bayer). "At the Hamburg Naval Hospital they had great success with combined antitoxin and salvarsan."

Salvarsan must not be exposed to the air, as oxidation and formation of As_2O_3 results, and thus requires greater care in administration than can be given in the field.

Hypochlorites have been tried in the European war as oxidizers against anaerobes, and would be good and cheap agents except for a quality converse to that of hydrogen peroxide solutions—that they are *alkaline*, and equally produce a certain amount of irritation. Dr. Chavasse, Inspector-General of the French Medical Service, recommended that "every wound and its surroundings should be painted once with 1 per cent. tincture of iodine. The tendency, especially among amateur nurses, to change dressings when they appear to be soiled should be strongly repressed (on account of injury through disturbance, and the danger of introducing fresh infection)." He also advocated moistening the dressings with dilute **chlorinated soda.** M. Hartmann stated at the Académie de Médecine that in his experience tincture of iodine was only useful when used at once; after twenty-four hours he applied hydrogen peroxide or strong solution of carbolic; **chlorinated soda** gave good results. Musgrave Woodman, of the British R.A.M.C., says that "iodine in this war has, in my experience, failed; strong antiseptics are clearly indicated." The moral of these apparently discrepant observations is that each of these applications can do good in a great number of cases, but fail when the infection has had a long time to develop.

A later report of the results obtained in thirty-nine cases of tetanus[1] gives the mortality as 71·8 per cent.; the treatment was 2 per cent. carbolic and antitetanic serum. Hartmann says that this serum saved in all cases at Besançon. In British field hospitals tetanus, both from bullets and shells, was treated by injections of

[1] *Brit. Med. J.*, January 2, 1915, 45.

carbolic, antitoxin, and magnesium sulphate, but "acute cases were almost always fatal whatever the treatment."[1]

Permanganate still keeps its position as a powerful and portable oxidizer definite in strength. Lieutenant-Colonel Rogers, from long experience in India, found permanganate of great value for sloughing and tetanus-infected wounds against tetanus and gas-forming anaerobes, and that potassium permanganate solution of 1 to 4 per cent. cleans and heals more rapidly than 10 per cent. peroxide of hydrogen.

The disadvantages accompanying the use of the majority of germicides of the "peroxide" type is that their penetrative action is very feeble, and that the oxygen liberation, when brought into contact with the blood-serum of the wound, is liable to be rather violent, causing both pain and fugacity in germicidal activity.

Whatever may be the nature and gravity of wounds, they all alike become almost incurable if accompanied by tetanus. Tetanus toxin appears to be the most poisonous substance at present known. Lambert computes its fatal dose to be 0·23 milligramme (0·0035 grain), whereas that of cobra venom is 4·38 milligrammes (Calmette), strychnine 30 to 100 milligrammes, and anhydrous prussic acid 54 milligrammes. Fortunately there are several agencies that can render it inert. It is destroyed by an exposure to 60° C. for twenty minutes, or to 65° C. for five minutes, and is attenuated by exposure to light and air at ordinary temperature. It is not harmed by 0·5 per cent. carbolic acid, but is destroyed by iodine trichloride, by peroxide of hydrogen, and by potassium permanganate. Its important constituent is called tetanospasmin.

Experiments have shown that if tetanus spores are thoroughly washed, so as completely to deprive them of their toxins, they can be injected with impunity into a susceptible animal, as the phagocytes can then destroy the toxin-free organisms. The destruction of the toxins by an oxidizer has a similar effect, and the action also extends to other organisms of the class. Injection of oxygen gas by Bayeux's instrument, which measures the amount and regulates the rate, was found effective in cases of septic fractures.[2]

Injections of magnesium sulphate are based on the investigations of Meltzer and Auer with animals, and its use on patients in this war has been found successful in banishing pain and inducing sleep. The dose is usually ½ gramme in 10 per cent. solution.

Another bacillary disease with about the same fatality as tetanus, and primarily caused by a gas-forming anaerobic organism, is *gangrenous cellulitis*, or *gas gangrene*, which has attacked about

[1] *Brit. Med. J.*, December 19, 1914, 1053.
[2] *Ibid.*, December 12, 1914, 1021.

½ per cent. of the recent wounds of all the armies. Much work on the cultivation of this anaerobic organism was done by Mr. Rowlands and Sir Almroth Wright. In the hospital cases œdema rapidly increases with bubbles of gas, the limbs becoming black; there is generally a mixture with streptococcus infection, and often the anaerobic organism dies out and only streptococcus cultivations can be obtained from the wounds. Active hæmolytic change is shown by straining of limbs, also by the brilliant orange tint of serous exudations. Benefit has been claimed from the method of injecting peroxide of hydrogen, though Sir Henry Makins did not support this view. So that here antiseptics are required as well as simple oxidants. Commonly associated with the microbes of tetanus and gangrene are other pathogenic species, some not anaerobic, such as *B. aerogenes capsulatus* (Welch's bacillus), *B. perfringens*, and *B. enteritidis sporogenes;* their spores are liable to be present in large numbers in dust and mud. The projectile or other weapon may have been more or less antiseptic, but the wound becomes rapidly invaded by pathogenic microbes either from the earth or from the skin itself. Swabbing with powerful agents like iodine tincture or liquefied carbolic acid[1] secures superficial asepsis, but does not reach the organisms when they have had time to colonize within the wound. Therefore the great need that applications should be immediate, and this is only possible when soldiers have themselves the remedy at hand. We shall recur to the point subsequently.

Dr. Rowland's bacteriological work resulted in the isolation of the specific bacillus of gas gangrene; a culture injected into a guinea-pig caused death in eighteen hours with gangrenous cellulitis, from which the organism was recovered. It was first thought to be that of malignant œdema, but further examination at the Lister Institute by Martin and Arkwright made it out to be an allied species called the bacillus of Ghon and Sach. It appears that there are some ten different organisms that have been isolated from gas gangrene in man, all closely allied and all anaerobic spore-bearers. A sample of earth from a trench was examined. Shaken with water and the liquid inoculated into a guinea-pig, the latter died in eighteen hours with gangrenous cellulitis, and contained a spore-bearing anaerobe of the above group. There were the same symptoms of offensive odour, dark colour, and gas production. Gangrene is thus due to infection at the time of the wound. For washing the wounds peroxide of hydrogen is one of the best antiseptics. The Lister Institute succeeded in preparing a suitable antitoxin. The group of

[1] See Sir Watson Cheyne's valuable review of the subject in his presidential address to the Royal College of Physicians, November, 1914.

anaerobes causing gangrene are spore-bearers, and the spores are especially difficult to kill by any antiseptic solution, *or even by boiling*. Consequently, in order to sterilize infected instruments, etc., other measures are required: (*a*) autoclave at 120° C.; (*b*) boiling one hour in 1/20 carbolic or 1/10 lysol. The last named, being made from cresol, has a stronger germicidal power than carbolic, and is similar to the British preparation, cresol soap solution (Liquor cresolis saponatus, B.P.C.), which can replace it with advantage. "Parabolic," used at the Netley Hospital, is another of the British equivalents to the German lysol. For field convenience, attention has been called to one of the earliest (it was described in the *Edinburgh Med. J.*, 1890), and still about the simplest of portable sterilizers for dressing, etc., introduced many years ago by Surgeon Cathcart of the Edinburgh Infirmary. It is cubical in shape, and can be heated over gas or fire. Diagrams of its modern form are given in the *Brit. Med. J.* of December 19, 1914, 1056.

For sterilizing the hands before and after operations the German Army used a soap containing 80 per cent. of alcohol, which had been proved to kill *staphylococci*, *streptococci*, *B. coli*, and *B. diphtheriæ* in half a minute. The soldiers' wounds were treated by irrigating with hydrogen peroxide, applying iodine tincture, and plugging with iodoform gauze.[1] Dr. Linkenheld fixes the tincture of iodine with a varnish composed of 1 part oil of turpentine with 50 parts each of colophony, resin, and ether;[2] these additions have a supplementary antiseptic power, but they tend to absorb the free iodine. For protective dressings "mastisol" is largely employed, made by Dr. Ottingen of Berlin; mastic and other resins are dissolved in benzene with a small quantity of an ester. Cheaper is dammar dissolved in benzene. The resin lodges in the pores of the skin and prevents the passage of organisms.

Some other curative agents for wounds have been used and advocated in our armies. Dr. A. Wilson states that salicylic acid is very successful.[3] Dr. Stephens recommends spraying with petrol. Simpson and Hewlett show by their experiments that colloidal silver is an active germicide;[4] it would probably be suitable for wounds, and would have no irritant action. The germicidal power of soluble mercury compounds is well known, but the commonest of them, mercuric chloride, "corrosive sublimate," has its irritant properties against it for the present purpose. The late Sir Victor Horsley preferred sublimate lotion (1 of $HgCl_2$ in 1,000 of distilled water), using also hydrogen peroxide of 20 volume strength

[1] Feldärzliche Beilage, *Münch. Med. Wochenschr.*, No. 1. [2] *Ibid.*, No. 6.
[3] *Brit. Med. J.*, December 5, 1914, 999.
[4] *Lancet*, December 12, 1914, 1359.

and petrol "as a cleanser." Colonel Makins, in his already-mentioned report of November 12, 1914, records that cures have followed under different conditions when wounds have been irrigated with hydrogen peroxide, painted freely with iodine tincture, dressed with carbolic, mercuric chloride, creolin, or lysol, and covered with mercuric bicyanide gauze. Subcutaneous injections of 2 per cent. carbolic have been a favourite treatment in English and French hospitals.

Sir A. Bowlby, in his letter to the *Lancet* of December 19, observes that the usual routine is to paint the skin far around with iodine tincture, and to wash the wound with carbolic 1 in 20, iodine tincture diluted to half or a quarter strength, or strong hydrogen peroxide; dressings are always mercuric cyanide gauze and absorbent wool. For the naval wounded at the Haslar Hospital, Surgeon Wildey states that he has been using with great success only two antiseptics; the wounds were first cleaned with a solution containing 1 in 1,000 of mercuric iodide (dissolved, of course, in about an equal weight of KI), and then treated with iodine tincture. He recommends an iodine spray-producer with hook attachment fastened to the belt or coat for ambulance work in the field.

R. Lambert,[1] as a result of a series of experiments with various germicides, including $HgCl_2$, $KHgI_3$, KCN, NaOCl, C_6H_5OH, tricresol, H_2O_2, C_2H_5OH, and iodine, on living tissues infected with staphylococci, found that iodine was the only effective germicide, and did not injure the cells or tissues.

We have seen that the pathogenic microbes with their toxins develop so rapidly as to very often render cases beyond relief on arrival at field centres. It was important, therefore, for the soldier to carry carbolic or iodine, which could be packed into the wound at once, so as to stop growth of bacteria before the patient reached the base hospital. Surgeon Lenthall Cheatle, of the Haslar Royal Naval Hospital, mentions some other portable remedies. He soon learnt in the Boer War that "wounds should receive disinfectant treatment as soon as possible after infliction. Lord Lister gave me a powder of zinc mercury cyanide, but wind and rain made it impracticable. Therefore I made the powder into a paste by mixing it with 1 in 20 carbolic dyed with $\frac{1}{2}$ per cent. rosaline, and found it wonderfully successful. The paste was mounted in collapsible metal tubes, and was squeezed out on the wound and on surrounding skin, on which it retained its position for days. I found that all shell wounds in South Africa were septic, except those to which the cyanide and carbolic paste had been applied almost immediately after the injuries, when it dealt effectually with the spore-bearing

[1] *J. Amer. Med. Assoc.*, 1916, **67**, 1300.

anaerobes. I now use also a mixture of equal parts of 1 in 20 carbolic and 1 in 500 of mercuric chloride in alcohol, coloured with rosaline. The dye indicates the persistence. No case of mercurial or carbolic poisoning has occurred. The solution can be carried by the soldier, and is better than iodine, more efficient and less irritating."[1]

Every combatant should therefore be provided with portable emergency means of at once sterilizing wounds.[2] Suitable for the purpose are "friable ampoules," brittle tubes, hermetically sealed, of glass, 6 millimetres diameter, and 6 to 7 millimetres long, contracted near one end, with a file-mark on the neck. There is a small cotton brush by which the wound can be painted, and the whole is enclosed in a little cardboard box. The entire apparatus is not much larger than a pencil. By a private agency many thousands of these ampoules have been sent into the firing-line at a small cost. with very great benefit.[3]

Dr. Highet[4] says the "asepto" should be placed in a small glass capsule packed in a gauze pad. When occasion arises, the capsule is broken, the gauze becomes saturated with the solution, the wound is swabbed with it, and is used as a first dressing. "The whole should be packed in impervious paper, so that if the capsule be accidentally broken the solution will be absorbed by the gauze and still be available. Such capsules are being made up for general and Voluntary Aid Department use."

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[1] *Brit. Med. J.*, December 12, 1914, 1006; and December 26, 1119.

[2] These means should also be at hand in civil life, and their use taught in the first-aid classes that are now so common and serviceable.

[3] *Lancet*, November 7, 1914, 1115.

[4] *Brit. Med. J.*, December 26, 1914, 1120.

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CHAPTER VII

NON-BACTERIAL PARASITES

Animals.

An obvious difficulty in dealing with parasites is that many agents, when powerful enough to extirpate the intruders, may also inflict injury on higher life; this clearly imposes limitations both as to materials and methods, and especially applies to internal parasites. Incidentally it may be mentioned that neither drying, smoking, nor salting of food secures safety against the ova of organisms like trichina, tapeworm, etc. Nothing but thorough cooking will do so.

Pediculi, or lice, causing the disease *phthiriasis*, are of three distinct species—*P. corporis*, *capitis*, and *pubis*, living respectively on the body, head, and genitals. The first kind hide in the clothes, and are easily dealt with by removing these cautiously over a sheet, boiling them for half an hour with soap and water, and ironing, particularly attending to the seams, where the eggs or "nits" are laid. Baths with soap and water and rubbing zinc ointment on the parts most affected complete the cure.

For treating *P. capitis*, "white precipitate" ointment (Unguentum hydrargyri ammoniati, 1 in 10) is frequently used, but has the common danger of mercurial applications—that the mercury may be absorbed and cause salivation and other objectionable effects. In place of this, the following safe and thorough method should be at once adopted: The hair is well saturated with "paraffin" (kerosene) oil twice a day for three days, wrapping in cloth for the first twenty-four hours. This will kill both the vermin and their eggs. It is never necessary to cut the hair. At the end of each twenty-four hours the hair should be thoroughly washed with soap and water, and any skin sores treated with a little zinc ointment, which is allowed to remain unmoved for about twenty-four hours before the next application of kerosene.

Pediculus pubis, the "crab" louse, is the most difficult to destroy, and often requires a mercurial unguent. The best is *Oleatum hydrargyri*, which does not salivate unless used in excessive quantity (Martindale), but its use should be carefully watched at frequent intervals. *Oleum staphisagriæ* (the expressed oil of stavesacre seeds, *Delphinium staphisagria*), mixed with 6 to 12 parts of olive

or almond oil, is said by the *Medical Press and Circular*, ii., **85,** 551, to effectually kill pediculi of all kinds, but it is very poisonous, and the above treatment is much preferable.

In institutions, steam-disinfecting machines are employed for killing all parasites in clothing; ten to fifteen minutes of full heat are necessary. Vermin and their eggs can be killed by careful heating in an oven (Klein).

Scabies, or itch, is caused by a minute insect, the *Acarus scabiei*, which bores under the epidermis. It has been treated successfully by rubbing the patient all over with strong soap, followed by a hot bath for at least an hour, then applying sulphur ointment. A more effectual application is beta-naphthol, used as follows: β-naphthol 15 parts, sapo viridis (soft or potash soap) 50 parts, prepared chalk 10 parts, lard up to 100 parts. This destroys the acarus and cures the injuries.

Several other burrowing parasites are met with, especially in tropical countries, and if they have not gone too deep can be remedied in a similar manner. Mercurial ointments are often effectual if used carefully.

There are many volatile substances whose odour is very obnoxious to insects, and therefore drives them away; these are **insectifuges,** not insecticides. Camphor and many essential oils can, moreover, actually kill insects. A useful insect powder is made from pyrethrum. The vermifuge action is one reason for the adoption of perfumes and incense.

Naphthalene is also much disliked by vermin, but has an unpleasant smell. It is a good preventive of moth. Carbolic and coal-tar soaps are a popular remedy against insects, but their efficiency is not high as generally employed. Wood creosote has been beneficially used (with care) in many parasitic cutaneous diseases.

The trenches in warfare often become infested with body vermin. Belts are manufactured containing substances of strong odour to be worn near the skin, and are said to keep these pests away from the person. Essential oils drive lice away, but the latter are only killed by such substances if they remain a long time in the vapour of the oils, and the eggs are not killed at all. Wintergreen oil appears to be the most active of the class; then follow camphor, bergamot, fennel, eucalyptus, and rosemary.[1]

According to a research by Dr. A. Zucker:[2]

(*a*) *Lice are driven away by :* Essential oils; menthol; turpentine oil; Peru balsam; solution of carbolic acid; precipitated sulphur; infusion of tobacco; black pepper; fatty acids.

[1] *Chem. and Drug.*, June 12, 1915, 34; November 27, 1915.

[2] *Centr. Bakt.*, 1915.

(*b*) *Lice are killed by:* Cresol powder (3 per cent.); sulphurous acid; mercury ointment; ether; benzine; benzol; petroleum; carbon disulphide; cresol-soap solution; carbon tetrachloride; solution of corrosive sublimate (1: 1,000); naphthalene; anisol; dichlorbenzol.

(*c*) *Inactive are:* Formaldehyde; acetylene; illuminating gas.

For the soldiers in the field the author recommends a solution of anisol in carbon tetrachloride (1: 9), and naphthalene or cresol powder. Clothes are best disinfected by exposing them to heat—*e.g.*, in a steam apparatus or by ironing them. For disinfection of rooms, Dr. Zucker prefers sulphur dioxide obtained by burning sulphur in a stove constructed for this purpose by Professor von Walther, Dresden.

Ringworm is caused by a fungus, *Trichophyton* or *Tinea tonsurans*. Citrine or red precipitate ointments, well rubbed in, will usually cure it. The juice of the herb *Siegesbeckia orientalis* is recommended as a topical application (Martindale). Dockrell has also had considerable success with a plaster containing hydronaphthol.[1]

Flies have in late years been proved to be carriers of all kinds of contagion. Dr. Halford Ross, of the Lister Institute, points out that "the decision against fly-breeders granted by Lord Justice Warrington in the Court of Chancery in the summer of 1914 placed a legal handle in the power of public health officials when such may be needed in dealing with persistent offenders." One of the earliest campaigns against the danger was initiated by the Bermondsey Borough Council on the advice of their medical officer, Dr. Brown. The municipality of Stockton-on-Tees started a similar work early in 1915. The Local Government Board urged other local bodies to follow suit, and recommended instructions to householders. Kitchen refuse must, as far as possible, be burnt. Dust-bins should have tightly-fitting tops, and all collections of refuse near houses should be disinfected or removed weekly. The fly requires at least ten days to mature, and lays its eggs in garbage, so that if accumulations of refuse are dealt with once a week it cannot multiply.

The most active extirpation should take place in spring, before the few flies that have survived the winter have begun to breed. In houses these yet dormant survivors will be found behind pictures, curtains, etc., and a broom with a towel wrapped round it dipped in "paraffin oil" (kerosene) is an excellent cleanser. After taking the above precautions during 1914 a committee of Surbiton residents stated that "by the freedom we enjoyed from flies throughout the whole summer we proved that the house fly is a local pest remaining

[1] *Lancet*, 1910, ii., 89.

in the neighbourhood in which he was hatched. So that if the inhabitants of any particular district suffer unduly from flies it is largely their own fault."

Some fly-papers contain soluble arsenic compounds, and are to be condemned as dangerous to higher animals. Sticky fly-papers are not recommended. A better remedy is formalin mixed with sweetened milk, and placed in saucers with bread for the flies to alight on. Besides those that are killed by the liquid, a mere trace of the vapour is very offensive to all insects. E. B. Phelps[1] reports favourably on a 1 per cent. solution of sodium salicylate as an insecticide. According to a pamphlet issued in 1915 by the Medical Officer for Westminster, rooms in which there are many flies may be cleared by (1) pouring 20 drops of carbolic acid on a hot shovel; (2) burning cones of Persian insect (pyrethrum) powder on a plate. The cones may be made by moistening the powder and allowing it to dry. In both cases the fumes stupefy the flies, which fall and can be swept up and destroyed.

For sprinkling refuse 2 per cent. carbolic, new slaked lime, or chloride of lime, may be used.

Carriers of special diseases are the phlebotomus fever fly, the hen flea, and some of the deadly mosquitoes.[2] Fleas spread bubonic plague, and also the parasite of "kali-agar" of India and the Mediterranean, and are suspected of other dangers. Rats are also plague-spreaders; they can be exterminated by "Danysz Virus," which was discovered some years ago at the Pasteur Institute, Paris. It is harmless to man, domestic and farm animals, and birds. There is also a "Liverpool Virus." Phosphorus paste and various sugar mixtures made up with extract of squills are among the well-known vermin destroyers.

Infection by Flies and Insects.—During recent years there has been a gradual cumulation of evidence that the common house fly (*Musca domestica*) is responsible for the transmission of diseases, although a plague of flies has from time immemorial been regarded as a visitation from the gods. It is especially active in the transmission of internal diseases such as "residuary" typhoid fever, cholera, and diarrhœa; while Nuttall and Jepson[3] have collected evidence pointing out that it may also act as a carrier for anthrax, diphtheria, ophthalmia, tuberculosis, smallpox, staphylococcus infection, swine fever, tropical fever, and eggs of parasitic worms. The experiments of Buchanan,[4] Firth and Horrocks,[5] and Graham Smith[6]

[1] *Bull. U.S. Public Health*, December, 1911.

[2] See "Insects and Man," by C. A. Ealand, M.A. (Grant Richards), and "Our Insect Enemies," Wood (S.P.C.K.).

[3] *Reports to Local Gov. Board*, 1909, No. 16. [4] *Lancet*, 1907, ii., 216.

[5] *Brit. Med. J.*, 1902, 936. [6] *Local Gov. Board Report*, 1911, No. 53, 34.

have definitely shown that the fly can convey organisms from infected sources to objects upon which they walk, feed, or rest, and that the organisms adhere to the external parts of the flies; and, further, that the organisms so deposited are capable of infecting the substances, such as milk or syrup, upon which the flies are feeding. Nicoll[1] considers that the house fly aids in the spreading of infection from intestinal worms.

Jackson[2] has found over 800,000,000 bacteria on one fly, while Esten and Mason[3] found an average of over 1,000,000 per fly on 414 flies investigated. In carrying out a "kill that fly" campaign it is useful to publish leaflets with recommendations to minimize the fly nuisance by destruction and elimination of their breeding-grounds.

Among such may be mentioned stable manure, spent hops, ash-pit refuse, dirty bedding, waste vegetables, paper, rags, milk, foodstuffs (especially sugar and sweetmeats), fruit, and meat.

The *Councils' Journal* of December, 1908, gives the following list as the principal breeding-places for flies in a manufacturing town:

**Refuse-heaps and "tips."
*Sewage-pools.
**Stables, manure-pits, and "depots."
Dairies, cowsheds, and cow-middens.
Milkshops.
*Slaughter-houses and butchers' shops.
Pail-closets, privies, and ash-pits.
Domestic refuse receptacles (movable).
*Hide and skin brokers' yards.
Triperies.
Bone works (boiling and other).
*Fried fish and chip shops.
Knackers' yards.
Marine stores.
All offensive trades under the Public Health Act, 1875.
*Jam factories.
*Confectioners' shops and manufactories.
Spent hop accumulations.
*Farmyards.
Gut-scraping deposits.
Fish offal deposited in ash-pits by hawkers and others.
Poulterers' refuse and offal.
**Restaurant kitchens and basement cooking-places.
*Kitchens of tenement dwellings, etc.
Any accumulation of decomposable refuse.

Those asterisked (*) are the worst.

[1] *Loc. cit.* [2] *Boston Med. and Surg. J.*, 1908, **159**, 45.
[3] *Bull. Agricult. Exp. Station*, Conn., 1908, No. 57.

Flies should be kept away from infants and invalids, while every active member of the community should take steps entirely to eliminate this insect from the globe. The rapid multiplication of the domestic fly makes this a matter of some difficulty. The number of ova produced by a single fly in a season has been variously estimated at from two to five hundred millions, while under favourable circumstances the maggots hatch in less than twenty-four hours, and complete their growth in from five to seven days. The pupa remains in this resting condition also from five to seven days, so that the life-cycle is completed in from ten to fourteen days, according to the temperature, humidity, and other circumstances.

In sharp contradistinction to the common flies we have examples of certain flies acting as specific carriers for certain specific diseases. This is particularly the case in the protozoid diseases. The disease malaria has been shown to be transmitted by mosquito to man. At the Canal Zone of Panama the species *Anophelene albimanus* has been shown to be the propagator. Both in America and in Italy bovine malaria has been shown to be propagated by the ticks *Ripicephalus annulatus s. Boophilus bovis.* Yellow fever produced by *Paraplasma flavigenium* has been conclusively shown to be propagated by the mosquito *Stegomyia fasciata*, and by no other means, and in particular by no other mosquito. The sleeping sickness of Tropical Africa is produced by the *Trypanosoma gambiense* carried by the tsetse fly *Glossina palpalis;* while Stephens and Fantham have isolated in Rhodesia a similar trypanosome, *Tr. Rhodesiense*, carried by *Glossina morsitans.*

The general prophylactic measures taken against these diseases consist in:

(1) Immunisation of the subjects exposed to the diseases.

(2) Treatment of the subjects when infected.

(3) Destruction and elimination of the intermediate host.

The first method is obviously not by its nature so suitable a preventive measure as the third, whilst the second can only be regarded as the penalty of non-appreciation of proper methods of protection.

During the last twenty years or so active steps have been taken to destroy both mosquitoes and the tsetse fly. This work has been encouraged by the Governments of all the Powers, more especially the Italian in Italy, the British and German in Africa, and the United States in Mexico and the Canal Zone, Panama, where the late General Gorgas accomplished an epoch-making work and made the canal a possibility. For subduing yellow fever and lowering, if not entirely eliminating, the malarial incidence in a district where these are rampant, the following plans of procedure should be drawn up:

1. In country districts and around the towns, jungle brush and grass should be cut away from around each house and burnt.

2. All houses should be provided with a continuous supply of water; if this is not available, all drinking barrels and cisterns should be made mosquito-proof by screens. One of the authors, when engaged in this problem of sanitation at Guayaquil, Ecuador, noticed that although this source of breeding, which is well recognised as one of the most prolific, was well known to the authorities, there was no method of ensuring that the orders issued by the health authorities had been carried out. Weekly visits by duly authorized inspectors are essential at the commencement of any such work, and are continually required where a native population has to be dealt with.

3. Pools and marshes should be as far as practicable drained or filled up.

4. Open water which is not running should be oiled with crude petroleum or compounds such as saprol. It is necessary to repeat the operation about twice a week. Wind also frequently ruptures the oil film.

5. Running water should be guarded against stagnation at any point. Concreted channels are preferable to dug ditches, where grass can grow and produce little patches of still water.

6. Gutters from houses should have a direct fall or should be dispensed with.

7. Houses should be screened, both windows and verandah, the doors preferably with a double screen. The copper gauze used for screening work should have a fine mesh, and be constructed of electrolytic copper; small traces of impurities such as iron cause rapid deterioration in the damp, warm, tropical climates.

8. District inspectors should be instructed to search for breeding-places and be provided with disinfectants for killing the larvæ.

9. Quinine should be taken daily, preferably in a soluble form. Tablets occasionally get hard and nearly insoluble on keeping. A United States Commission appointed to study yellow fever and malaria at Vera Cruz reported in 1904[1] that sulphur dioxide was the best of the gaseous insecticides for destroying mosquitoes, and that formaldehyde was not successful for the purpose. As preventives against bites, naphthalene and eucalyptus oil in paraffin have been used successfully. Quarantine and fumigation of ships, trains, and baggage arriving from infected or suspected places must be rigidly enforced.

The blowfly, while as liable as other flies to transmit disease, is peculiarly objectionable in time of war. It often lays its eggs in

[1] *Bull.*, 1905, No. 14.

the nostrils, ears, and wounds of men and animals lying in the open. During the first hot weeks of August, 1914, several soldiers were found to be in a terrible state from maggots in their wounds. Fortunately, the occurrence of cold weather at once kills the flies. The *Homalomyia canicularis* is often mistaken for the common house fly, with which it is associated.

A great many of the State Boards of Health[1] in the United States have published from time to time official bulletins recommending certain procedures to be adopted in the campaign against flies. They practically all include the recommendations indicated above, and, in addition, screening of houses by means of door and window gauze screens; also the use of sun-blinds over shop windows is sometimes advised. Professor Newstead, of the Liverpool School of Tropical Medicine, recommends the application of 2 ounces of Paris green in a gallon of water to either stable manure or ash-pit refuse to destroy fly larvæ. He finds that 99 per cent. are destroyed by this method.

Mites.—The harvest mite lies among long grass. It can be dislodged from its host by treatment with paraffin or petrol, and is not dangerous to the majority of persons or animals. The itch mite (*Acarus*) burrows a long tunnel in the skin in which it deposits its ova. It prefers portions of the body in which the skin is soft—*e.g.*, the wrists of washerwomen. It can be killed by washing frequently with soap and hot water, and sulphur treatment. The soap and hot water soften the skin and make it more permeable to the sulphur ointment, the grease of which suffocates the insect, while sulphur is a direct poison. Hot baths containing salt, 1 ounce to 4 gallons of water, are also recommended. A practical method used in the bush is said to consist in the application of tobacco juice to the skin, and holding a lighted match near the tunnel. The mite apparently comes out of its hiding-place, and is poisoned by the nicotine in the juice.

Fleas.—The *Pulex irritans*, while annoying, has not yet been conclusively shown to convey any disease. The rat flea of Great Britain lays eggs in rubbish; the larvæ are easily killed at 70° C. and 40 per cent. humidity if exposed, but when buried in the rubbish are not affected. The adult flea has a preference for human blood, but rat's blood is necessary to stimulate the sexual organs. In the absence of a suitable pabulum it can only live one month, while in rubbish it can exist for over seventeen months. Dog fleas can be removed by a bath with carbolic soap and quassia chips in water.

The generally accepted theory that plague is mainly, if not solely,

[1] *E.g.*, State Board of Health, Maine, U.S.A., 1909.

communicated to man from rats through the agency of rat fleas has led to active measures in the extirpation of rats and of the rat fleas.

The work of Hossack,[1] Kitasato,[2] and others[3] has shown that plague transmission is unhappily not confined to the rat and the rat flea, but that other insects, such as dog fleas—possibly also human fleas—and the bed bugs are other modes of infection.

As a general practice, the use of a disinfectant which combines both pulicidal and germicidal powers is advocated.

Where bubonic plague is present, travellers should not be allowed to leave the infected area without a certificate of inoculation with Haffkine serum. All baggage should be disinfected. Trains should be likewise inspected, and washed out with disinfectant solution. In infected ports, ships should not come alongside, otherwise rat fenders must be provided.

Lice, which have been the cause of the devastation of Servia and Montenegro in the European War, are best destroyed by agents such as petrol, paraffin, benzene, xytol, or turpentine, while discarded clothes should be burnt and buried.

Bed bugs, which are also carriers of typhus, are, according to Dr. Shipley,[4] removed by a painter's flare passed along the cracks of woodwork, while houses are disinfected by hydrocyanic acid gas or sulphurous acid.

Sheep Dips.—Among the various parasites which afflict sheep may be mentioned the tick Iscodes, the "scab acarus" Psoroptes, and the maggot Lucilia. The one which causes the greatest amount of damage is the scab-producing mite. Occasionally also are found a red louse, *Trichodectes spherocephalus*, and a wingless fly, the "ked," *Melophagus ovinus*, while of bacterial or protozoic diseases one of the most important is foot rot (?). Attempts to eradicate these parasites were made by rubbing the affected parts with preparations such as mercury or mercury salts incorporated with lard or copper as copper oleate. Zinc salts were also occasionally used. These were soon found to be practically useless, for not only did the more popular mercury ointment rapidly produce symptoms of poisoning, but unhatched eggs and places where the irritation had not developed were not noticed.

Arsenious oxide solution was one of the earliest dips to which some astringent such as zinc sulphate was added. Lime, soda, and sulphur preparations were found to be a cure for scab, but was found to lower the price of the wool, probably owing to the effect of the

[1] Reported, *The Statesman*, Calcutta, August 18, 1909.

[2] Sixteenth Intern. Med. Congress, Budapest, 1909.

[3] *J. Hyg.*, April, 1902, 129.

[4] *Brit. Med. J.*, 1914.

alkali on the wool fibre. The chief defects accompanying the use of an alkaline dip are said to be (*a*) an increase in adsorptive power of the wool for dyes, entailing a heavier expenditure in dyeing; (*b*) a decrease in the elasticity of the fibre, making it difficult to spin; (*c*) actual solution of the wool in the dip; and (*d*) a shrinkage of the wool, making the operation of scouring both difficult and tedious. Nowadays arsenical dips are made of the alkali salts of arsenious acid, arsenic sulphide, free sulphur, and arsenious acid. These are efficient, and also stimulate the skin and are also a safeguard against reinfection. Quibell,[1] in a good résumé of the subject, gives the following as the composition of a typical arsenic sheep dip:

Arsenic trioxide	21·90
Alkali	2·86
Moisture	6·70
Sulphur	68·54

One pound is diluted with 11 gallons of water.

The only other kind of sheep dips used on a large scale are the carbolic acid dips, which are efficient parasiticides, but do not exert any prophylactic action, as is the case with the arsenic dips. These dips are of varying composition; emulsions, semi-solutions containing less hydrocarbon oils, and true solutions of carbolic or cresylic acids are used. The emulsified parasiticide has been found superior to the non-emulsified form, having the same tar acid content; this has also been shown by one of us to hold true for their action on bacteria. Mixtures of tar acid and arsenical dips, the former frequently compounded with sulphonated castor oil or soaps, are found to be very effective, while more or less successful experiments have been conducted on using tobacco extracts and soluble mercury salts.[2]

Disinfection and Preservation of Hides.—Owing to the frequent presence of anthrax organisms in hides, and also owing to the occasional sporadic outbreaks of foot and mouth disease, it has been found advisable to disinfect skins and hides. Older methods include the use of 5 per cent. carbolic acid solution, sulphur dioxide, and pickling sodium arsenate in salt. The carbolic acid and sulphur dioxide methods injure the skins, while the use of sodium arsenate gives unsatisfactory results. The American Leather Chemists Association[3] have obtained good results with a 0·1 per cent. solution of mercuric chloride. The disadvantage associated with this substance is the fact that it forms insoluble compounds with the albuminous compounds in the hides, and such insoluble compounds no longer exert any marked germicidal action. The association

[1] "Sheep Dips," *J. Soc. Chem. Ind.*, 1907, 1266.

[2] See *J. Soc. Chem. Ind.*, 1907, 888.

[3] *J. Amer. Leather Chem. Assoc.*, 1910, **5**, 507.

found that the addition of 0·5 per cent. salt solution, and thus depressing the concentration of mercuric ions, prevented this precipitation. In hides which have been treated with sulphur and lime, the formation of insoluble mercuric sulphide in the interstices of the hide material makes its subsequent removal a matter of difficulty. Sulphuric acid has also been recommended. Kohlstein and Schattenfroh[1] advise the treatment of the hides with 2 per cent. hydrochloric acid in 10 per cent. brine solution. Seymour Jones[2] suggests using formic acid or some other organic acid instead of sulphuric acid, so that disinfection and curing can go on together. He has also suggested a method of soaking the hides in mercuric chloride solution containing 1 per cent. of formic acid, and subsequently washing with lime. This method as well as Kohlstein and Schattenfroh's acid salt process have been favourably reported on.[3]

Hailer[4] has shown that 0·5 to 1 per cent. caustic soda at 15° to 20° C. destroys the spores of *B. anthracis* in hides after seventy-two hours' contact. This treatment was found more effective than 5 to 10 per cent. sodium chloride.

Cupramonium hydroxide and copper alkali tartrate form the basis of some patented hide and skin disinfectants. Various methods have been suggested for preserving hides. The most frequent and probably the most efficient is common salt. Picric acid has been much used in the East Indies, while clay and sodium sulphate or dry alum have been used. Refrigeration has been attended with the production of a loose porous leather. Drying or smoking may result in the formation of a gluey or partially tanned hide.

Recently the Departmental Committee on Anthrax appointed a sub-committee to inquire as to the practicability of disinfection of wool and hair.[5] As reported by the Departmental Committee, "manufacturing processes do not kill the living organisms (anthrax spores) which cause anthrax, and the disease occurs and continues to occur in every process from the entry of the raw material into the factory to the production of the finished goods. The danger to be guarded against is different from that usually met by means of regulations applied in factories, and the committee finally came to the conclusion that this is not a suitable or effective method of dealing with the problem, and, further, that anthrax can only be prevented either by preventing the disease among animals or by the destruction of the organisms in wool and hair. In these circum-

[1] *Collegium*, 1911, 248.

[2] *Leather Trades Review*, 1908, **41**, 540.

[3] *Brit. Soc. d'Encour*, 1913.

[4] *Arbeit. Kais. Gesundh. Chem. Abstr.*, 1916, **10**, 985.

[5] Departmental Committee on Anthrax: Vol. I., Report of the Disinfection Sub-Committee, 1908.

stances it was decided to endeavour to find a process by means of which anthrax spores in wool can be destroyed, and for this purpose a sub-committee was appointed to go into the whole question. The difficulties of disinfection of wool and hair are very great, and it was recognised that the prospects of finding a practicable process were unpromising, having regard to the failure of many previous efforts to find a successful method. The sub-committee has, however, surmounted every difficulty successfully, and their experimental work and its results are fully described in the accompanying report." This report details a large number of experiments carried out, and also a final successful process of disinfection.

The degree of the infection of the materials places them in the following approximate order: (1) East Indian goat hair; (2) East Indian wool; (3) Persian wool; (4) mohair and other goat hair, including cashmere; (5) Egyptian wool; and (6) alpaca. The cause of failures hitherto has been due to the combination of the drastic treatment required to ensure destruction of highly resistant spores, often enclosed in dried or semi-dried blood-clots entangled in the material, and the ease with which the raw substances are damaged, rendered useless, or their value lowered for subsequent manufacture, or the cost of the latter increased. This important point was dealt with by conducting the tests on a commercial scale, the results being checked of course in the laboratory, the treated materials being submitted to the various manufacturers for working up into their finished products; reliable data was thus obtained as to the infliction of any damage, and at the same time the working cost of the different treatments was controlled.

As regards the choice of a disinfecting agent, steam invariably causes damage; although the United States Government have proposed the issue of regulations requiring the exposure of possibly infected wool for fifteen minutes at 212° F., it is found that even the brief steaming that would be necessary to sterilise the wool after the first scouring process—five to eight minutes at 212° to 214° F.—caused obvious damage.

Phenol and cresol compounds are not sufficiently powerful against spores, although their efficiency is increased by heat; chlorine disinfectants rapidly cause damage; mercuric chloride, besides being deficient in penetrative power, is too poisonous. The bulk of the experimental work was conducted with formaldehyde as the disinfecting agent, and the final successful process consists of a hot treatment with formaldehyde after special washing and scouring. This method consists essentially of four stages, which are described as follows:

Stage 1.—*Preliminary treatment*, consisting of agitation (by means of rakes which thrust the wool through liquid as in scouring

machinery) for twenty minutes in a solution of soap in water (preferably also containing an alkali-like sodium or potassium carbonate) at a temperature of 102° to 110° F., assisted by squeezing through rollers. The protection afforded to the spores is by this means removed; the spores are rendered susceptible to the action of the disinfectants and the wool is cleansed.

Stage 2.—*Disinfecting treatment* in which the material is agitated by similar means for twenty minutes in a 2 to 2½ per cent. solution of formaldehyde in water at a temperature of 102° F., assisted by squeezing through rollers. In this stage the bulk of the anthrax spores is destroyed, those only surviving which are embedded in remnants of blood-clots which in a few instances may have escaped complete disintegration during Stage 1, but which become saturated with formaldehyde solution.

Stage 3.—*Drying* in a current of air heated to 160° F. The moisture in the wool is driven off, and nearly all the surviving spores in any blood remnants are destroyed.

Stage 4.—*Standing* for some days to ensure by the progressive action of the formaldehyde which remains in the blood remnants the complete destruction of the few weakened spores which have survived Stage 3.

The strength of the formaldehyde solution is recommended to be maintained between 2 and 2½ per cent.; there is apparently no gain by increasing the strength above 2½ per cent.; a reduction of the formaldehyde below 2 per cent. is unsatisfactory as regards greatly increasing the period of treatment required to ensure disinfection. The authors of the method are satisfied that in practical work the subsequent successful disinfection of the anthrax depends upon the thoroughness of the first mechanical washing, and although the experiments were conducted on an extensive scale, they were to some extent necessarily handicapped with inefficient machinery. In actual practice the preliminary washing and squeezing would be done by specially constructed scouring plant, which, while avoiding any damage to the wool, would adequately break down any protective covering of the spores, which are then destroyed in the second stage. The third and fourth stages of drying and standing would act as checks, ensuring the sterility of the anthrax spores.

As already stated, infected wool and animal hair, besides grease, earthy matter, and excrement, is frequently soiled with dried blood adhering to the material. Highly resistant anthrax spores deeply buried in hard dried blood-clots formed the infected test material in all these investigations.

An exposure of twenty minutes in the formaldehyde solution at a temperature of 102° F. kills all unprotected anthrax spores;

this somewhat surprising conclusion is vouched for by Professor Delépine, who worked in co-operation with the committee as an independent investigator.

No damage to the treated test materials submitted to the manufacturers was reported, and only differences equal to those occurring within the ordinary range of variations in such materials were observed; a further satisfactory point is that the danger to the operatives is reduced to the minimum, the raw material being entirely manipulated by machinery after entering the plant. The only possible sources of contamination would be at the opening up of packets of raw materials prior to treatment and the waste liquor from the scouring machinery. With regard to the former, experiments were made in the direction of an attempt to disinfect unopened parcels, but were not successful. The second source of danger can be dealt with and the Anthrax Committee in their report advocate the sterilisation of all such waste liquors before being allowed to pass into the drains, although they do not indicate what treatment is to be adopted for such effluents.

The cost of the disinfection treatment is modified by the fact that part of the process—*i.e.*, Stage 1—to a large extent displaces the usual preliminary cleaning and shaking in the worsted, woollen, and felt trades, and the recovery to some extent of the formaldehyde, the disinfectant used. Further, as pointed out, the whole process is highly technical and requires skilled supervision; it would be advisable to deal with the matter at a large central station for safety and economy; no steps should therefore be taken by interested manufacturers until a decision has been reached on these points. The estimated cost of treatment, calculated on pre-war prices, lies between 0·54 and 0·82 penny per pound of the various untreated materials.

It is interesting to note that this is one of the first attempts by a Local Government Board in England at the systematic disinfection of raw materials coming into the country.

Domestic and Farm Animals.—To keep down parasites, general cleanliness and avoidance of overcrowding are essential. Walls should be thoroughly lime-washed with *fresh-slaked lime* and water, and gone over with a rather weaker wash at intervals of not more than three months. It is often overlooked that the inside of roofs and beams should be similarly treated, since they are equally a harbour for vermin with the walls. The lime-wash is rendered more lasting in effect if about ½ per cent. of crude carbolic acid or similar disinfectant be added in the mixing.

Against fleas and lice, which are a pest to all animals, pyrethrum powder is effective. Dr. R. S. Macdougall[1] recommends "creolin-

[1] Stephen's "Book of the Farm," 1909.

ated water, a 10 per cent. solution," also stating that sawdust soaked in a solution or emulsion of naphthalene placed in the nests of birds will give them peace. If pine-wood shavings or wood wool are placed in a nest, no lice or fleas will live in it, on account of the aromatic odour.[1] It is said also that bracken makes a good lining, as it is disliked by insects.

For *Phthirius inguinalis*, the crab-louse in animals, a remedy is found in stavesacre ointment. For Acari (mites), that so frequently infest birds, a 2 per cent. solution of carbolic is a preventive as well as a curative. Chloroform water (1 to 6) is also of service. Other remedies are sulphur ointment and benzene (used very carefully). Fowls can be dusted with sulphur. Worrall found *Izal* effective against sheep acarus.

Mange is due to the parasite *Sarcoptes scabiei* and other species. It is treated by a lime and sulphur wash made as follows: 25 pounds of flowers of sulphur, 12½ pounds good quicklime. Triturate to a smooth cream. Transfer to a boiler, make up to 20 gallons with water, boil and stir half an hour. Make up to 100 gallons.

A powerful insecticidal soap is described by Gouthiére and Ducancel.[2] Quinoline bases are made to combine with fatty acids (oleic, sulphuricinic, etc.) and with resins, with or without the addition of copper compounds. To these soaps, toxic salts such as arsenites or arsenates of lead, sodium, iron, etc., may be added. Or mixed soaps may be obtained by neutralising the basic substance with a mixture of fatty acid and arsenious or arsenic acid.

For **Warble fly** in cattle, equal parts of Archangel tar and paraffin oil are as effective, with less injury to the hide, as the old composition of train oil, sulphur, and spirit of tar.[3]

Favus is a fungus affection which is now rare in man, but frequent among domestic fowls, also attacking dogs, cats, and rabbits; it is very common in rats and mice. It is caused by *Achorion Schoenleinii*, and is exceedingly contagious. The Board of Agriculture (Leaflet 67) prescribe washing with warm water and soft soap, and then rubbing in an ointment of vaseline containing 5 per cent. of silver nitrate. A 10 per cent. solution of carbolic acid has also proved curative.

Worms in fowls can easily be expelled by a dose of *thymol*—1 grain made up into a dough pill and administered morning and night. Similar good results have sometimes been obtained by the use of 3 grains of santonine given in the same way.[4]

[1] Leaflet 57, Board of Agric. and Fish., p. 5.
[2] Fr. pat. 444,021, 1911 and 1912.
[3] *J. Roy. Agric. Soc.*, 1913, Annual Report of the Zoologist.
[4] Leaflet 58, Board of Agriculture.

Plants.

It has been estimated that insect and fungoid pests reduce our vegetable and fruit crops by at least 25 per cent. in value every year.[1] The best preventive is to keep the cultivation area as clean as possible, and to use soil dressings and fumigants freely at the proper times. Vegetable débris should on no account be allowed to accumulate; it is even unsafe to dig it into the ground, but is better to burn it as soon as possible and restore the ash to the land. Attend to the suppression of weeds (especially those allied to the cultivated plants), as these also harbour vermin and fungi.

To combat the lower forms of animal life, a knowledge of their habits is necessary. The most effective procedure is to destroy their eggs, but unfortunately these are protected by their natural coverings, so that agents strong enough to penetrate the envelopes will almost certainly injure the plant which is their host. When, on the other hand, the eggs are laid on bark, on walls, or in soil, they can be strongly treated. A number of species, however, breed in stagnant water, and some in clear lakes and streams.

Although the *mature* forms of a few insects (*e.g.*, turnip fly and weevils) are actively injurious, as a rule they are only destructive in the larva state—as caterpillars, grubs, or maggots. This is usually the longest period of their lives, lasting in many cases for more than one season. In the pupa or chrysalis stage they are more difficult to destroy, as they are enveloped in a tough jacket, occasionally in a cocoon, and hidden in the earth or in some obscure place. Wire-worms, leather-jackets, and various larvæ spend months, and even years, in the soil, and do enormous damage to roots. But insects may pass the winter in either of their three states: (1) As larvæ, still feeding on what remains of vegetable matter, or even lying dormant in the soil; (2) as pupæ or chrysalides in a condition of quiescence; or (3) sleeping in the perfect form in some sheltered place. The last indicates that all possible shelters for hybernating flies should be searched out and, as far as can be, syringed. Immediately after such crops as peas have been gathered, the ground should be dressed with a preparation capable of killing the larvæ which have dropped off the crop fully fed and purposing to remain in the soil till next spring. Most of them can be killed by lime and soot forked in, but for certainty another dressing of lime must be given in winter, digging or ploughing in deeply.

In infested hop-land and fruit-land, where the plants are permanent, besides constant hoeings and the application of caustic

[1] Lloyd's "Practical Gardening," seventh edition, p. 13.

materials in May and June, the soil immediately round the plants should be treated in the autumn with lime and soot, or earth, sand, or ashes saturated with kerosene at the rate of 4 or 5 pints to the bushel. See Board of Agriculture Leaflets 2 and 19 (weevils[1]), 14 (raspberry moth), 62 (sawfly "slug-worms"). In 19 (pea and bean weevils) and 22 (diamond moth caterpillars), dressing infected plants with 2 to 6 bushels per acre of a mixture of 1 part lime to 3 parts soot is also prescribed. For "surface caterpillars" (*Agrotis*), Leaflet No. 33 recommends dusting thoroughly with fresh soot alone, and sprinkling a mixture of 3 or 4 of finely powdered lime to 1 of soot close to the infested plants. Quicklime is still the most effective agent known against club root or "finger and toe" in turnips, cabbages, and other cruciferous root crops, due to a slimy fungus, *Plasmodiophora Brassicæ*. A dressing of 5 to 7 tons per acre is given in autumn either six or eighteen months before the sowing. According to Leaflet 77, the latter interval is the better, with a corn crop between.

Light soils require discretion in the use of lime, but for heavy ones a good proportion is 1 ton per acre every winter. Unless it is at once dug in, it loses its strength or causticity by absorbing CO_2 from the atmosphere. Ordinary lime may be applied at any time from the autumn to the spring within a few weeks of planting or sowing. "Gas lime," though less caustic, contains tarry and sulphuretted compounds, therefore is more potent against insects and fungi, and especially wire-worms. But it is for some time injurious to plants, hence after using it the soil cannot be cultivated for a considerable interval. When the recommended dose of ½ cwt. per rod (1·85 pounds per square yard) is applied in the late autumn or early spring, the interval must be at least two months.[2] Common salt has been used for the same purpose in the proportion of 7 pounds per rod for autumn and half that quantity for spring dressing, well dug or forked in. But we may remark that salt, sodium chloride, is not generally favourable to *land* plants; they require a preponderance of soluble *potassium* compounds. A top dressing of kainit (which is a potash mineral), 3 to 5 cwt. per acre, has been found effective against "surface caterpillars" (Agrotis), pear midge,

[1] Curtis says "nothing but boiling water and turpentine seems to affect the mature weevil," so the object must be to kill the grubs and to trap the perfect insect with tarred boards. Pushing a light wide framework with boards well tarred on the under surface fastened on it, so as to come just over the plants, has been found to catch many destructive insects, which, being disturbed, jump up against the tar. Many acres may be got over in a day (Leaflet 3, Board of Agric., p. 4). Blossoming fruit bushes should be shaken over tarred boards or sacks soaked in kerosene (see *J. Roy. Agric. Soc.*, 1913, 388).

[2] Lloyd's "Gardening," pp. 13, 16.

woolly aphis, cranefly grubs, and others, besides being a good manure.

In reference to "eel-worm" (*Tylenchus*), which causes failure in clover and other crops, Miss Ormerod reported in 1897 that *sulphate of potash* at the rate of 1 cwt. per acre stopped the disease in oats; and, again, that at Rothamstead on an eel-worm-infested clover field "a mixture of sulphate of potash 3 cwt. and sulphate of soda 1 cwt. per acre was applied on April 3; the disease ceased, and the clover made a very vigorous growth."

Many preparations safer than gas lime are sold, such as "Vaporite," "Kilogrub," "Fumisoil," "Clift's Manurial Insecticide," and others. Some kinds, when mixed with the soil, gradually evolve vapours and act partially by virtue of these, but principally as contact poisons.

A well-informed correspondent, however, writes: "At our trial ground we have conducted experiments with various commercial soil sterilizers, several of which consist principally of crude naphthalene, and others of hydrocarbons[1] emulsified with soap. Our results have been uniformly unsatisfactory." We have not up to the present in our own practice found any substance of this class that has been recommended in any of the horticultural and agricultural papers which gives uniformly satisfactory results.

The gradual liberation of active vapours is only vigorous in porous ground. But the most effective way of clearing insects from soil is to pour carbon disulphide into holes about 1 foot deep and 2 feet apart, 2 ounces in each, the holes being then covered and the vapour left to act. This method has been successful in France against Phylloxera; it is, however, expensive, and very dangerous from the inflammability of the bisulphide (a spark would cause an explosion) and its poisonous action on higher animals.[2]

Nitro-explosives in cultivation for making soil porous were first introduced in the United States, and it was thought also that the nitrous fumes would get rid of insect pests; but Professor Durham found[3] that plants put in on the site of explosions were infested with slugs a fortnight later, although the fumes had been seen issuing from amongst the roots.

The plumber's blow-lamp is used as a garden tool in France for

[1] Kerosene ("paraffin") is, of course, a hydrocarbon.

[2] Experiments might be made with *thiophosgene*, $CSCl_2$, prepared by the action of chlorine, and then stannous chloride, on CS_2. It is a red, mobile, strongly fuming liquid "of sweetish taste," which attacks the mucous membrane. It boils at about 160° F., is hardly inflammable, and is only slowly decomposed even by hot water. For a number of trials by the Roy. Agric. Soc. with lime, soot, vaporite, CS_2, etc., see report of the zoologist, *J. Roy. Agric. Soc.*, 1913.

[3] *J. Roy. Hort. Soc.*, August, 1914, 7.

destroying the woolly aphis (*Schizoneura lanigera*), turnip fly, pests like the raspberry weevil which fall to the ground when disturbed, ants' nests, etc.

Acids are germicidal to wire-worms; the following figures indicate the concentrations required to kill by five minutes' contact. It is interesting to note that the concentrations are by no means equivalent in the hydrogen-ion concentrations in solution.

Acid.	*Concentration per Cent.*
HCOOH	1·16
CH_3COOH	2·4
C_6H_5COOH	0·28
$C_6H_4(OH)COOH$	0·24
H_2SO_4	0·42
$NaHSO_4$	1·8

Gaseous insecticides such as hydrocyanic acid and sulphuretted hydrogen (this is apt to injure plants). and the vapour of volatile liquids like carbon disulphide, benzene, formalin, and nicotine, are employed in confined spaces, as in greenhouses, by *fumigation.* Fumigation with hydrocyanic acid has been extensively used in America against insects in fruit trees, San José scale, etc. In England it seems to be the only remedy for black-currant mite, *Phycoptus ribis*, but in other respects Leaflet No. 1 (published 1894, revised 1901) of the Board of Agriculture and Fisheries says "fumigation with hydrocyanic acid, as largely used for scale attack abroad, has not met with the success which at one time was thought likely. Further experiments may, however, show it to be useful as regards the cleaning of young plants." *Nicotine* is the strongest insecticide that can be used with safety under precautions that bear in mind its very poisonous nature to higher animals. In a strength that will kill all lower animal life it is quite harmless to vegetation; its vapour will not injure the bloom of the most delicate fruit, nor the perfume or colours of flowers.[1] Incidentally it may be mentioned that it does not kill bacteria, but these produce only a few diseases of plants, although certain species (chiefly *Bacillus amylobacter*) cause wet rot of potatoes, also rot of onion bulbs, and the pink decay of wheat.[2]

Nicotine has a high boiling-point (250° C.), and easily oxidizes, hence to vaporize it alone would be difficult and wasteful. Therefore it is mixed with a more volatile substance which will carry off its vapour without change, and evaporated from a metal dish over a small lamp. It is cheaper to buy the fumigating liquids ready made, as they are manufactured in bond from duty-free

[1] G. E. Williams, *J. Roy. Hort. Soc.*, September, 1902.

[2] Dr. Fream's "Agriculture," *Roy. Agric. Soc.*, 1912.

tobacco. They should be purchased of guaranteed strength; an example of quantity and cost is ½ ounce per 1,000 cubic feet, costing 4½d. Another method is often practised, by mixing it or tobacco juice with combustible fibrous material such as rags or paper, adding a little nitre to promote combustion, igniting the dried mass, and allowing it to smoulder away in a greenhouse. Some simply burn dry tobacco leaf in the ordinary manner. Both these methods are unreliable, and likely to injure plants.[1] Another compound, *pyridine*, is produced which is distinctly injurious to plant life.

In fumigation the house should be kept tightly closed for six hours; then open the door and windows, and do not enter till the house is thoroughly ventilated.

The small amount of nicotine contained in tobacco accounts for the high price of the preparations, but on the other hand for fumigation a little goes a very long way, while for efficient spraying the dilution with water may be often more than 1,000 times. As an instance, Spencer Pickering, at a conference of fruit-growers held at the South-Eastern Agricultural College, Wye, Kent, said he had found that for Psylla (apple sucker) a solution containing 0·075 per cent. (1 part in 1,333) of nicotine was in all cases efficacious, and that the occurrence of slight rain within a few hours of spraying did not nullify that effect.[2]

When it is required to apply nicotine directly to the plant, other substances are usually mixed with the solution, causing it to adhere to the leaves; the mixture is then diluted with water. A syringe with a fine nozzle is used, or, better still, a spraying apparatus. So applied, it brightens the foliage, does not stain, and will not injure the roots or retard the growth of the plants so treated.

The importance of addition agents necessary to cause the wash or spray to adhere to the leaves of the plants can scarcely be over-emphasized. We are indebted chiefly to Pickering and his researches on the stability of oil-water emulsions for drawing attention to the rôle played by surface tension in these cases. It is evident that a suitable spray should possess the following desiderata: firstly, it must spread the suspension of the fungicide over the whole of the leaves and stem, and not collect in small globules or roll off—*i.e.*, it must wet the plant; and, secondly, the suspension, when once deposited on the plant surface, must not be washed off by any accidental shower.

The first of the conditions involves a study of the surface tension

[1] G. E. Williams, *ut supra*. He justifies at length the condemnation of the combustion procedure.

[2] See also Pickering and Theobald's "Fruit Trees and their Enemies," and the eighth and tenth reports of the Woburn Experimental Farm of the Roy. Agric. Society.

of the spray; sprays with low surface tension will spread more easily than those possessing a greater surface energy, which will tend to keep the wash in the droplet form. The surface tension of sprays can be adjusted by the addition of substances such as soaps or saponin, which lower the surface tension, so that an effective spreading will be obtained. The recent work of Langmuir, Harkins, and others (see Chapter IX.) has indicated that this effect may not be entirely physical in its action, but is pseudo-chemical in behaviour, and the use of addition agents which will form loose adsorption compounds with the cell wall of the plant may prove effective spreading agents. The second point—viz., the subsequent adherence of the suspension to the plant surface—presents greater difficulties. It is evident that the fungicide must be slightly soluble to prove effective, but must not be washed off by rain falling on the leaves. To accomplish this end, attempts have been made to coat or protect each particle with substances like glue or gelatine, which will adhere to the plant surface more firmly than the unprotected particle; in other words, the surface energy of the area of contact between the plant surface and particle must be very much less than the sum of that between plant surface and water and the particle and water. The preparation of an ideal wash thus entails the presence of two addition agents: one in the suspension medium which will ensure the spreading of the medium carrying the particles of fungicide over the surface of the plant, and a second one protecting or coating the fungicide particles ensuring a firm adherence to the leaves. It is possible that one agent could perform the two functions, provided that it contained suitable chemical groupings within its molecule to form adsorption compounds with the plant surface and with the fungicidal particles.

A dressing to destroy eggs, etc., of insects on the bark of trees or on old walls or fences is made by adding $\frac{1}{2}$ pound of tobacco, $\frac{1}{2}$ pound flowers of sulphur, and $\frac{1}{4}$ peck of lime to 3 or 4 gallons of water, and stirring well at intervals for six to ten hours; syringe with the clear liquid. Some moths, such as *Zeuzera pyrena*, which infest fruit-trees, deposit their eggs to a considerable depth in the crevices of the bark, hence old or rough bark (also lichens and moss) should as far as is safe be scraped off before syringing.

Caustic alkaline washes are most successful in cleaning the trees of an orchard (also bushes) in winter and destroying pests, the best time for the spray being about the middle of February, as then it will kill the majority of the eggs. *Preparation:* Dissolve 1 pound of commercial caustic soda and 1 pound of crude potash (carbonate) separately in water; mix and add $\frac{1}{2}$ pound soft soap, and make up with soft soap to 10 gallons. It has been said that alkaline washes

cause the living bark to crack, and undermine the health of trees, but the Board of Agriculture (Leaflet 70) have not found this.

There are a number of spraying liquids that, although less powerful than nicotine, are often of service (*e.g.*, for apple sucker, Psylla). Soft soap is itself useful; some recipes containing it are: (1) 5 parts quassia chips stirred with 100 of hot water, then add 6 of soft soap and 4 pints carbolic No. 5 (for red spider and a great number of other pests); (2) 10 pounds quassia and 7 pounds soft soap to 100 gallons water; (3) 8 pounds soft soap, 2 pounds ground hellebore, 3 pounds kerosene, well stirred together in 100 gallons boiling water (*care as to inflammability*); (4) boil in 2 quarts of soft water 1 part of soft soap; while still boiling, remove to a distance from the fire or flames and add a pint of "paraffin" (kerosene); work the whole thoroughly together by means of a hand pump or syringe and add 10 gallons of water. No. 4 is an effectual wash for green fly (aphis), white fly, etc., also by spraying during April and May to prevent maggot in onions; for red spider[1] add ¼ ounce of liver of sulphur per gallon. Quassia extract mixed with soap solution is a good insecticide for roses. Nos. 1, 2, and 4 above have the advantage of being non-caustic and non-poisonous to higher animals, which is a consideration when dealing with fruit and vegetables. Nicotine and other poisons can be absorbed through the skin, unless india-rubber gloves are worn. Repeated spraying with dilute solutions is more effective than a single application in more concentrated form, besides being safer for the tender growths of the plant.

Particularly for root crops, it is useful to soak the seed in kerosene—or, better, turpentine (Leaflet 3, Board of Agriculture)—before being sown; this keeps "fly" away from the seedlings. Spraying the ground, and even the seedlings, is sometimes further necessary.

Dusting with various powders such as a mixture of tobacco dust and sulphur, pyrethrum, hellebore,[2] and others is sometimes practised, but is neither sure nor cleanly. The only one of practical value is quicklime, and this injures plants.

Parasites that have protective coverings, like mealy bug, scale, cuckoo spit, and "tent caterpillars," demand greater force in syringing, which is made more effective by brushing, also by using the liquid warm, at 110° F. (43° C.).

For the codling moth and leaf-eating caterpillars, as well as

[1] Red spider is not properly an insect, as it has eight legs, not six, and does not go through the three transformations; it belongs to the *Arachnida*, or spider group. The wash has to be applied with considerable force, to break up the web which protects the eggs and mites.

[2] Hellebore *wash* is used successfully against gooseberry sawfly and some other species: 1 ounce of the powder and 2 ounces flour to 3 gallons water, kept stirred, and sprayed.

turnip "flea" beetles, and many other intractable pests, *arsenate of lead* is used. It can be purchased as a paste, which, when properly made, remains a long time in suspension, and does not scorch the foliage. To prepare the spray, 1 ounce of sodium arsenate dissolved in 16 gallons of (preferably rain) water is mixed with a solution of 3 ounces of lead acetate and 2 pounds of treacle added. Some kerosene emulsion may also be added with advantage. Trials at the New York Agricultural Experimental Station[1] showed zinc arsenite to be three times as effective as lead arsenate. When used in conjunction with lime or Bordeaux mixture it caused no injury to apple foliage. But more or less spotting occurred when it was used alone or with lime-sulphur or glucose, and these also caused severe "burning" of grape foliage; laboratory tests indicated that this "might be due in part to the solubility of the zinc arsenite in CO_2 contained in the moisture on the leaves." Zinc arsenite or lead arsenate with Bordeaux mixture, soap, or glue, remained efficient for twenty-five days; at the end of that period the poisonous properties had disappeared and the protection had ceased. It was observed that lime-sulphur solution does not resist wet weather as well as does Bordeaux mixture. Tartar and Bundy[2] remark that while soap has been recommended for keeping lead arsenite in suspension (instead of treacle), practical trials have shown that sometimes the foliage is considerably injured by the mixture.

Paris green, a copper arsenite, has been employed extensively in the United States, and is also approved by the British Board of Agriculture and Fisheries, when used with care, for turnip and cabbage flea beetles; sawflies; "surface" and "tent" caterpillars, and those of the codling, winter, and pith moth; "slug-worms" (*Eriocampa*), and other insects as difficult to kill. The wash is prepared by adding $\frac{1}{2}$ pound Paris green to 100 gallons water and thoroughly mixing with 1 pound lime; the whole must be kept well stirred. It can be bought as "Blundell's Paste," which is more easily mixed with water than the powder. The Board prefer lead arsenate, which will kill the larvæ, as Paris green sometimes damages the leafage. *London purple* is another arsenic preparation, used with lime as above. None of these poisons must be used for six weeks before the fruit is gathered, green or ripe,[3] nor where vegetables for early use are grown under the trees.[4]

Banding trees with sticky compositions, better put on rings of grease-proof paper fitting closely to the trunk, is necessary to entrap those vermin that ascend the stems from the ground. It is of especial

[1] *Technical Bulletin*, March, 1913, No. 28.
[2] *J. Ind. Eng. Chem.*, 1913, **5**, 561.
[3] Leaflet 12, p. 3.
[4] Leaflet 4, p. 4.

benefit in early autumn. The bands must be watched, the captures removed, and the composition kept adhesive, otherwise the process becomes ineffective.

Fungoid Parasites of Plants.—Much valuable work has been done during recent years in combating and controlling the fungous diseases of plants. The enormous losses caused by them in French vineyards led to their extensive study, and to experiments proving that certain salts of copper (especially the famous "Bordeaux mixture" and its varieties), sulphur in various forms, and alkalies were beneficial, and there seemed to be a prospect of the eventual control of the troubles caused by fungous diseases generally.

Sulphur in the form of "flowers of sulphur" has been largely used for hop mildew. Dusted over the plants, it leads to the slow formation of SO_2, which in hot weather can be smelt where the powder is widely used. But at ordinary times it often fails, therefore it has been generally replaced by copper salts. A special use is described in Leaflet 64, Board of Agriculture. If wilting of the leaves of trees suggests root rot (caused by the fungus *Rosellinia necatrix*), an examination should be made at once; if white mycelium is found, the roots should be exposed and covered with sulphur, and this should also be mixed with the soil used for filling in, which should be *fresh* and free from mycelium. The infected soil is removed and sterilized by adding quicklime or gas lime.

The fungicidal activity of sulphur is to be attributed to the formation of thio-acids with atmospheric moisture under the influence of light, the primary reaction being in all cases the formation of hydrogen sulphide and sulphur dioxide according to the reaction—

$$3S + 2H_2O \rightleftharpoons 2H_2S + SO_2.$$

Although the equilibrium point of this reaction is at normal temperature on the left-hand side, yet the small quantities of the products formed are withdrawn from the sphere of action by secondary reactions. Ground crystals of sulphur adhere to the plant surface better than flowers of sulphur, yet the latter are more reactive with moisture and generally possess an insignificant quantity of various thio-acids adsorbed on their surfaces.

Lime-sulphur washes prepared by the solution of sulphur in lime-water consist essentially of mixtures of calcium penta- and hexa-sulphide; these readily undergo decomposition into disulphide and free sulphur, which reacts as above. The calcium disulphide also reacts with the atmospheric carbon dioxide with the production of free sulphur and calcium thiosulphate.

Sulphur vapour is a good destroyer of mildew and other diseases of plants under glass. Campbell's vaporizer is a vessel heated by a

lamp; the stem of the funnel outlet is loosely closed by a hollow glass ball, which rises and falls so as to allow the vapour to escape, but at the same time prevents the boiling sulphur catching fire from the entrance of hot air; 6 ounces of sulphur is sufficient for 10,000 cubic feet. *Potassium sulphide* ("liver of sulphur") spray, in the strength of ½ ounce to the gallon of water with ½ ounce soft soap, is the best remedy for gooseberry mildew, and for cucumber and melon leaf blotch.

Copper Salts.—The most successful fungicides which have achieved a wide popularity are those containing copper salts in suitable form. It is estimated that over 12,000 tons of copper are used annually in France to combat the Phylloxera on the vines.

Bordeaux mixture is essentially cupric hydrate suspended in water, and is made by precipitating a solution of copper sulphate by (usually) milk of lime. If too little lime is added, free copper sulphate will be left in solution and will injure the plants, while if the solution is too strong in lime it is also harmful. Since the theoretical proportions are: crystallized copper sulphate ($CuSO_4,5H_2O$) 249, quicklime (CaO) 56, it will be seen by the following standard recipes that a decided excess of lime is prescribed by experience. The *Eleventh Report of the Woburn Experimental Fruit Farm* (Royal Agricultural Society) says: "No direct fungicidal action is possible without the risk, and indeed almost the certainty, of some damage to the plant." But in instances of apparent scalding, the appearance is really due to the destruction of the fungus by the fungicide, so that the supposed injury is actually a benefit. In any case the fungus *must* be antagonized, and does far more harm than the chemical remedy.

MODIFICATIONS OF BORDEAUX MIXTURE.

	Bordeaux Mixtures.				*Burgundy Mixtures.*		"*Cupram.*"	*Woburn Winter Wash.*
	A.	B.	C.	D.	E.	F.	G.	H.
Crystallized copper sulphate, 98 per cent. (pounds) ..	12	8	12	12	20	12	—	15
Copper carbonate (ounces) ..	—	—	—	—	—	—	10	—
Quicklime (pounds)	8	8	6	10	—	—	—	5
Washing soda (pounds) ..	—	—	—	—	25	15	—	—
Caustic soda (pounds) ..	—	—	—	—	—	—	—	20
Liq. ammon. fortiss. (pints)	—	—	—	—	—	—	5	—
Treacle (pounds)	—	—	—	10	—	—	—	—
"Paraffin" (solar dist.) (pints)	—	—	—	—	—	—	—	50
Water (gallons)	100	100	100	100	100	100	100	100

A, B, E, and H are given by Wrightson and Newsham, whilst C, D, F, and G are from Leaflet 23, Board of Agriculture. A is "for potatoes"; B "for fruit-trees"; and C, D, E, and F for general use.

To make Bordeaux mixture, dissolve the copper salt in 80 gallons of the water in a wooden or earthenware vessel (iron would be attacked); slake the lime and make into a cream with the other 20 gallons of water; strain this and pour it into the copper solution with constant stirring. A stronger wash composed of 30 pounds copper sulphate and 15 pounds lime to the 100 gallons water is recommended for vine mildew, *Peronospora viticola*.

Mixture D, which adheres better to the leaves, especially in showery weather, is prepared by making the cream of lime as before, but with *hot* water, stirring in the treacle, heating if possible till the lime and treacle have combined, and pouring the liquid into the copper solution. The result is a green *solution* of copper sucrate, which precipitates copper carbonate on exposure to air.

For Burgundy mixture, dissolve the copper salt in 90 gallons of water, the washing soda separately in 10 gallons; add the latter to the former with agitation.

For "Cupram" (G), add the ammonia to 4 or 5 gallons of water and throw in the copper carbonate little by little, stirring vigorously till dissolved; then dilute with the rest of the water, when a clear blue solution is formed which never clogs the nozzles of the sprayers. It can be made up and kept in the concentrated form in stoppered glass vessels and diluted when wanted, whereas the other mixtures deteriorate after a few days. It is particularly suited to sprayers and work under glass.

The wash H cleanses bark, removes moss and lichen, and is strongly fungicidal. Applied early in February, it destroys a number of parasites, such as woolly aphis ("American blight").

The other sprays should be applied at the end of June and repeated in about three weeks. The average quantity is 120 gallons per acre. The lower side of the leaves must be sprayed, as well as the upper.

With regard to potato disease, the report for 1913 of the botanist to the Royal Agricultural Society states that while the usual kind, due to *Phytophthora infestans*, is cured by Bordeaux mixture, for other kinds, "wet rot" from *Bacillus amylobacter* and "black stalk rot" from *Bacillus melanogena*, no curative measures are known at present. Tomatoes under glass are sometimes attacked by Phytophthora; then a temperature of 75° F. checks it.

The effect of copper or other antiseptic agents is not to destroy spores, which indeed live through the application. But when the spores germinate, the delicate young hyphæ find themselves in a medium which is fatal to them, and the disease is thus remedied.

Sulphate of iron (ferrous sulphate or copperas) is a remedy for some species. The canker fungus, *Nectria ditissima*, in its white

stage can be killed by brushing with a solution of this salt—1 pound to a gallon of soft water, which will also destroy lichens and moss. *In all cases, wounds in trees must always be at once coated with tar to prevent spores entering.* A new destructive grass parasite, *Cladotrychium graminis*, was first noticed in 1908 in Kent. By watering the soil with ferrous sulphate, ½ pound to the gallon, the spread of the disease is checked.[1] For brown rot of fruit, *Sclerotinia fructigena*, the trees and also the ground should be thoroughly drenched with this solution: Sulphate of iron 25 pounds, sulphuric acid 1 pint, water 50 gallons (not placed in an iron or zinc vessel, as the acid would act on it). A spray of the same should be used in January or February *before any leaf-buds begin to swell.* When these are expanding, and at intervals as required, the trees should be sprayed with weak Bordeaux mixture. This treatment must be followed for at least two seasons.

Soft-soap mixtures are sometimes of value against fungi, as, for example, the fungus *Eutypella prunastri* which seriously injures fruit-trees, and is recognized by horizontal clustered cracks in the bark (see figure, Leaflet 87, Board of Agriculture). To prevent the spores germinating on the bark and entering the wood, paint the entire stem with a mixture made thus: Reduce soft soap "to the consistency of thick paint" by adding a strong solution of washing soda; add 1 pound of powdered quicklime to every 5 gallons of the preparation, and thoroughly mix. This generally lasts one season.

The *carbolic* family of disinfectants have generally uncertain value as fungicides. Cyllin soap is found by many rose-growers to prevent mildew.

Seed Sterilizing.—Fungous diseases of grain crops are generally caused by spores of the fungi becoming mixed with the seed, and then germinating with the latter and producing a mycelium (thread growth) which attacks the young plants. The commonest are rust (*Uredo*), mildew (*Puccinia*), smut (*Ustilago*), and bunt (*Tilletia*).[2] It is always desirable to treat the seed before sowing with a "steep" or "pickle," the most usual kind being a solution of sulphate of copper, "bluestone." The grain may be poured into a vessel (*not of iron or zinc*) containing a ½ per cent. solution, and stirred up frequently for twelve to sixteen hours. In this country the more common method is to sprinkle the dry grain with a 10 per cent. solution of the copper salt, 2 pounds in 2 gallons of soft water sufficing for ¼ cwt. of corn (Fream). The liquid is distributed over the seed

[1] *J. Board of Agric.*, November, 1913.

[2] The report of the botanist to the Royal Agricultural Society for 1913 records that travelling threshing-machines are often contaminated with spores of burnt fungus.

spread on the barn floor, and the whole well mixed up with a *wooden* shovel or rake, and afterwards turned over two or three times. As it dries, a thin coating of the sulphate is deposited on the grain. Fream states that this treatment is less successful against smut than it is against bunt. "Seed wheat is thus dressed on most farms to protect the crops against bunt, which gives a fishy taste to the flour, yet wheat sometimes suffers as much from smut as barley and oats, which are never dressed"—because the process prejudices their germination. They are treated by Jensen's hot-water method, which depends on the fact that if seed be immersed for five minutes in water at 127° to 133° F., its vitality is not impaired, but smut is prevented. Leaflet 92 (Board of Agriculture) gives the following directions: About 10 gallons of boiling water are placed in a tub, and cold water added (about an equal quantity) till a temperature of 130° to 135° F.—*not over nor under*—is reached. One bushel of seed in a sack or closed basket is dipped for five to seven minutes, then removed and spread out to dry. We must emphasize that there is a chance of recontamination by spores during the desiccation; this is less if it is done *on a drained floor which has just previously been sterilized by hot water and allowed to cool and become partially dried.* There is not the same danger in the copper and formalin methods, in which some of the disinfectant remains on the seeds. For treating seed oats or barley the same leaflet states that a similar dipping for ten minutes in 1 pint of 40 per cent. *formalin* to 36 gallons of water has of late years been used with great success, this quantity, costing about 2s., being sufficient for 40 to 50 bushels of seed.

In each of these processes the vitality of a certain percentage of the grains is destroyed, but only of those that would tend to produce weak plants. The loss in copper treatment may be diminished by dusting with powdered lime after steeping. Chloropicrin in the proportion of 20 c.c. per cubic metre of space has recently been proposed as a parasiticide in grain stores. The following data for certain salts indicate the relative concentrations necessary to destroy barley seeds on prolonged contact:

Salt.	*Concentration.*	*Salt.*	*Concentration.*
$CuCl_2$	1 in 7×10^8	$Ba(NO_3)_2$	1 in 4,200
$HgCl_2$	1 in 3×10^8	$MnCl_2$	1 in 1,000
$CdCl_2$	1 in 1×10^8	Borax	1 in 1,000
$AgNO_3$	1 in 1×10^6	CaI_2	1 in 1,000
$ZnCl_2$	1 in 46,000	$CaBr_2$	1 in 1,000
$TiCl_3$	1 in 12,000	$CaCl_2$	1 in 260

In testing for seed vitality the sowing method is usually adopted; care, however, must be taken to ensure the removal of the fungicide before planting out. It seems probable, however, that in the near future the somewhat tedious sowing method will be supplanted by the electric "blaze" current method, in which vitality is indicated by the response of the seed to electrical stimulation.

Weed Killers.—We shall have occasion to note that many germicides function through their plasmolytic action on micro-organisms. This conception has been extended to plant life, for whilst most plants are destroyed by drastic treatment such as by 5 per cent. sulphuric acid, 1·5 per cent. of sodium arsenite, or 1·75 per cent. of calcium sulphide, it is possible to differentiate between plants possessing relatively thick cell walls and those, such as *Ginapis arvensis* (common charlock), in which the cell walls are comparatively thin, and thus more susceptible to poisons. The following strengths of solutions have been suggested for the selective removal of charlock from growing crops: 3 per cent. copper sulphate, or 10 to 12 per cent. of ferrous sulphate, using 40 to 70 gallons per acre.

Soil Sterilization.—Russel[1] at the Rothamstead Experimental Station has shown that by treatment of soils with mild germicides such as chloroform, toluene, or carbon disulphide in suitable concentrations it is possible to selectively remove or at least diminish the protozoan population of the soil. The immediate result is a great increase in the number of soil bacteria, and especially the nitrogen-fixing organisms.

The following concentrations of volatile antiseptics and disinfectants are stated to be sufficient to exert the selective action:

$C_6H_5CH_3 + CS_2$	0·09 per cent.	C_6H_6	0·16 per cent.
Cyclohexane ..	0·17 ,,	CCl_3H	0·23 ,,
Ethyl ether ..	0·74 ,,	Hexane ..	0·86 ,,
Ethyl alcohol ..	4·6 ,,		

Gruzet finds that a hydrogen-ion concentration of N/1200 is germicidal to over 99 per cent. of the soil bacteria.[2]

In the near future an extension of this method to the farm is to be anticipated.

A report by the Minister of State for External Affairs, Melbourne, in 1914, observes that in Australia, on the whole, "the losses through animal and insect pests are, except in rare cases, insignificant. By the enactment of drastic laws they are being entirely stamped out in some districts and diminished in others." Similar laws are

[1] See *J. Soc. Chem. Ind.*, 1913, **32**, 1132.

[2] *Soil Science*, **3**, 199, 289.

enforced in France and many other countries. In 1890 the Intelligence Department of the English Board of Agriculture was empowered to conduct investigations and publish a series of reports on injurious insects and fungi, "so as to give timely notice as to their appearance and the measures for restricting their ravages." More than 300 leaflets on different branches of the subject have since been gratuitously distributed by the Board from 4, Whitehall Place, and contain valuable information and illustrations; of one of them as many as 35,000 copies were issued. The reports on investigations at the Woburn Experimental Farm of the Royal Agricultural Society are likewise very valuable; so are the records of similar work in Ireland, on the Continent, and in America. See especially a pamphlet of forty-one pages "on the effect of spraying with disinfectants on plant growth."[1] Miss Ormerod's "Manual on Injurious Insects and their Prevention" gives detailed descriptions, and Dr. Fream's "Agriculture," chapter xviii., has about the latest list of insect pests.

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[1] U.S. Department of Agriculture, *Bulletin* No. 7.

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CHAPTER VIII

WOOD PRESERVATION

THE subject is very complex on account of the multitude of processes and the great variety in methods of procedure. In common with many other branches, it has been overburdened with patents, which have led to contradictory and unreliable statements.

Among destructive agencies to which wood is exposed, that of fire is beyond our province. It is sufficient to say that in some patents, ostensibly put forward as preservative, which soak the timber in solutions of inert salts—*e.g.*, alkaline silicates[1]—these have only value as making the material less inflammable, other partial preservation only occurring when heat is applied in the injection. On the other hand, methods like creosoting increase the inflammability, and cause a dense and acrid smoke to be evolved in burning. Hence creosoted sleepers have a special danger in railway tunnels.

As to the action of air, although it is well known that the substances which constitute the main framework of plants—lignin and cellulose—when pure and dry, are very permanent, yet damp wood is apt to be considerably weakened by oxidation; this is decreased by such organic applications as have an avidity for oxygen themselves. In green wood the changes in the fibre are promoted by vegetable ferments or enzymes existing in the juices. These substances are coagulated and rendered inert by all effective methods of preservation. At the same time, seasoned timber can be treated so much better than green, and wood should be seasoned for at least six to twelve months before treatment.

Water swells, and to a certain extent softens, the fibre, and can assist the penetration of oxygen and of many vegetable and animal destructive agents, hence *waterproofing* is the real basis of a large number of processes. Thus in Enrodi's (1913) "the wood is immersed in molten waxes and cleansed with a solvent." This would be expensive, and only applicable to special purposes. Lerach (1908) claims to preserve wood from splitting and rotting by coating with plaster (calcium sulphate), resin oil, and benzine varnish (10 per cent. colophony in benzine). A cheaper process uses a mixture of asphal-

[1] *J. Soc. Chem. Ind.*, 1913, 946.

tum with mineral oils "to stop up the open wood cells." But by itself waterproofing is not usually sufficient.

The same may be said of simple mechanical sterilization by dry or moist heat. Dry heat makes the wood shrink or warp, and injures the fibre. Moist heat (steam) properly applied kills any organisms in the wood, and also extracts its putrescible juices, which are the chief food of moulds or insects. To exclude such enemies permanently we must use at the same time an agent which will be poisonous to them.

In some cases, however, waterproofing is almost all that is demanded. Seidensehnur[1] remarked that phenolic compounds are not necessary; "old sleepers only contained neutral oils;[2] lubricating oil has no preservative action; pure neutral anthracene oil is good." The Santa Fé test,[3] with a crude "non-antiseptic" petroleum (Bakersfield) proved the preservation of timber for a number of years by mere waterproofing. In the same year the *Engineering Record*, N.Y., stated that waterproofing, rather than preserving from decay, is the chief object in saturating wood-paving blocks (probably because, owing to wear and tear, they have to be renewed so often).

"Vulcanizing," according to Howard's U.S. patent of 1909, consists in heating the wood gradually *in vacuo* up to 250° F., then with steam at 230° F., finally raised to 380° F. Later Wallis-Tayler[4] describes "vulcanizing or Haskinizing" as roasting wood, which has been previously dried by steaming, to a temperature high enough to coagulate its contained albumins (given as 71° to 94° C.), and to resolve some of the fibre and sap with the production of wood creosote.

Many impregnating patents have claimed a large number of inorganic solutions as germicides or preservatives which are neither; the substances are of little or no use, beyond that some of them give the small and inadequate protection of a coagulating effect. Early instances of the numerous almost useless prescriptions are acetates of aluminium and lead with glycerine, and sulphites.[5] Later examples are: waste sulphite liquors (1913); salts of magnesium, aluminium, or iron;[6] "preservation" by soaking in ammonia for a fortnight, when it is washed away.[7] Among complicated patents of doubtful utility are, in 1907, Effendi's "pectic acid," Ellis's "copper carbolate," Soc. Anon. per Conserv. del Legno (combined

[1] *Chem. Zeit.*, 1909, **33**, 701. [2] We shall examine this statement later.
[3] Report *N.Y. Railway Age Gazette*, August, 1910.
[4] *J. Roy. Soc. Arts*, 1914, **62**, 286.
[5] Patents 17,814, 1887; 3,356, 1893; 14,599, 1894.
[6] *J. Soc. Chem. Ind.*, 1908, 1021; 1909, 1250. [7] *Ibid.*, 1911, 1214.

processes and apparatus). Others employ sulphur or sulphides, which are of little value for the purpose—*e.g.*, Deditius' German patent of 1906, sulphuretted petroleum; Chisholm, 1909, lime polysulphides (these injure metallic bolts, nails, etc.).

In Russia brine is frequently used for impregnating railway sleepers, as much cheaper than creosote, though not comparing with the latter in efficiency.[1]

The use of metallic salts has some danger of their decomposing into basic compounds and free acids, the latter acting harmfully on the wood tissue. To avoid this, the temperature should be sufficient to coagulate albumin, and not high enough to injure the wood—*i.e.*, between 60° and 98° C. This simple precaution has actually been claimed as a novel invention by a French patent, No. 376,798 of 1907. English patent 19,241 of 1906 neutralizes by alkaline solutions which are at the same time antiseptic, containing, for example, cresols, naphthols (as wash waters from petroleum and resin-oil refineries), fluorides, or silico-fluorides. Beaumartin in 1911 steeped wood in copper sulphate, then in lime-water, which precipitated the copper as hydrate. This was converted by treatment with carbonic acid water into cupric bicarbonate, which was soluble and preservative, while not being injurious to the wood.

It must be remembered that as a rule chemical substances manifest their activities in solution, and are almost quiescent in the solid state. Therefore all the recipes for injection of emulsions of solids, or for their precipitation within the wood, involve loss or absence of activity.

In the most effective treatment, a preservative liquid is made to enter the lower end of the wood, to follow the natural course of the sap and replace it, at the same time acting on putrescible substances so as to prevent putrefaction, destroying organisms that may be present, and rendering the material unsuitable for the entry of fresh ones. The liquid may be either (1) made to enter by a head of fluid; (2) forced in by additional pressure; (3) drawn in by encasing the top with india-rubber or leather and establishing a vacuum above, while the lower end dips in the preservative liquor; or (4) the timber may be enclosed in a strong cylinder which is exhausted and filled with liquid several times. A possibly cheaper but less efficient method was patented by Nelson in 1909. Timber is heated to 100° C., so as to convert the contained moisture into vapour; the whole is then at once covered by the (cold) preserving liquid, which condenses the steam, and the contraction sucks in the preservative, but the sap is not replaced.

The second of the above methods is the quickest, but the first

[1] *J. Soc. Chem. Ind.*, 1910, 1311.

is said to give the most uniform penetration. The progress of the operation should be tested at intervals. If it has been properly conducted the timber is proof against insects and against the mycelium of disintegrating fungi such as *Merulius lachrymans* (dry rot). Where wood has been already attacked by this organism, care must be taken not to spread the spores, and the most potent remedy is to spray with a hot 1 in 250 solution of mercuric chloride (corrosive sublimate). The parts of the syringe must not be made of copper, brass, or iron, as these metals precipitate mercury. But barriers to the use of this salt for sterilizing wood are not only its cost, but its poisonous nature to higher life. Marked salivation has been suffered by the inmates of rooms where the wood has been so treated. A similar objection of toxic danger applies to arsenic, which figures in a few patents—*e.g.*, Somermeier's of 1914. Wallis-Tayler, in the paper already quoted, mentions a **saccharine solution**[1] or **Powellizing** process as suitable for the treatment of green wood, the solution consisting mainly of sugar with a small percentage of arsenic. But, as we have remarked elsewhere, although arsenic is so powerful a poison to higher animals and insects, it has little effect on lower forms of life.

Impregnating with solutions of *fluorine* compounds has been recommended as effective and cheap;[2] they are included in several wood-preserving patents, such as the one of 1906 which we have described earlier. Brase's of 1908 preserves sleepers with a mixture of zinc chloride, a fluoride, and tar. F. Bub's of 1913 is somewhat similar. Nowotny in 1913 asserted that sodium fluoride and acid zinc fluoride, $ZnF_2,2HF$, are stronger antiseptics than copper sulphate, also that their freedom from colour and odour gave them an advantage over creosote.[3] The latter point would only be of importance in rare cases such as ornamental work. But soluble fluorine compounds, although preservative and germicidal, and possibly useful as adjuncts in other treatment—*e.g.*, when mixed with nitrophenols[4]—are, by themselves, neither sufficiently powerful nor lasting for wood preservation, and have the objection that they are precipitated by lime and by some other metals, and so rendered inert. Malenkovic's patent of 1908[5] has this fault of insoluble deposition that we have condemned above.

[1] See also Suchard, *J. Soc. Chem. Ind.*, 1911, 364.

[2] Seventh Internat. Congress of Appl. Chem., London, 1909; the same paper mentioned attempts to use the strong fungicidal properties of organic *dinitro compounds*; they have not been economically successful (see *J. Soc. Chem. Ind.*, 1909, 711; see also a full report by Teesdale, *Proc. Amer. Wood Preservers' Assoc.*, 1916 and 1917).

[3] *J. Soc. Chem. Ind.*, 1913, 1110. [4] Nowotny, *Oest. Chem. Zeit.*, 1912, **15**, 100.

[5] *J. Soc. Chem. Ind.*, 1908, 1114.

Formaldehyde, acetone, and some allied bodies, ingredients in a few of the proposed mixtures,[1] are negatived by cost, volatility, and feeble action on moulds.

The only metallic salts that are practical germicides for this purpose are, in increasing order of power, those of zinc, copper, and mercury, and we have already given the objections to the last.

Zinc chloride is more powerful than the sulphate, and at the same time more acid in its character. A 2 per cent. solution was patented in 1838 by Sir W. Burnett for preserving timber, hence the method is called "Burnettizing." It is usually conducted by first steaming, then impregnating with a 2 to $2\frac{1}{2}$ per cent. solution of zinc chloride under a pressure of 7 to 8 atmospheres. On the Continent it is commonly termed Pfister's process. The sleepers on the Hungarian State Railways were treated with this reagent forced in by steam pressure, but the distribution was found to be somewhat irregular.[2] In the *zinc-tannin* or Wellhouse process, treatment in a partial vacuum follows the preliminary steaming; a small percentage of glue is added to the zinc chloride, and after impregnation for two and a half to six hours at 100 to 125 pounds per square inch, the timber receives a final treatment with a 0·5 per cent. solution of tannin under the same pressure for two hours.[3]

According to tests made by the Austrian Postal and Telegraph Bureau[4] with pine, fir, and spruce poles, acid zinc fluoride is more efficacious than creosote. Dilute solutions were very quickly absorbed, variations of temperature below 50° C. having no effect. Another product for treating timber is mentioned, called "bellite," which is a mixture of sodium fluoride, dinitrophenol, and aniline.

Investigations carried out by the United States Forest Service seem to indicate that railway cross ties are somewhat weakened by the process unless carefully conducted. They also found that a light injection of creosote greatly added to the effectiveness of the zinc chloride treatment.

In the determination of the amount of zinc chloride in treated wood, E. Bateman notes[5] that extraction by leaching also gets out organic substances, while incineration drives off some zinc. The Wellhouse method is to destroy the wood with potassium chlorate, nitric and sulphuric acids; and then to determine the zinc with ferrocyanide. We have found sulphuric acid alone, as in the ordinary Kjeldahl, sufficient and less dangerous, driving off the excess of acid.

The U.S. Department of Agriculture[6] test the penetrative power

[1] Baekeland's French patent, 1908; Pages Camus et Cie., 1909, etc.
[2] *Dingler's Polytech. J.*, **271**, 230, and **278**, 22.
[3] *Wallis-Tayler, loc. cit.*
[4] *Génie Civil*, **58**, 465.
[5] *J. Soc. Chem. Ind.*, 1914, 138.
[6] Circular 190, 1911.

of zinc chloride treatments by immersing discs of the treated wood into a 1 per cent. solution of potassium ferrocyanide for ten seconds. The excess of liquid is removed by a filter-paper and the block then dipped into a 1 per cent. solution of uranyl acetate and allowed to dry. Untreated wood will appear dark brown treated white This method, it is claimed, will detect 0·2 pound of zinc chloride per cubic foot. The method is not suitable for red oak. Modifications may be introduced for the determination of the penetration of copper, iron, and mercury.

Copper Salts.—Kyan was the first to systematically use sulphate of copper for injecting timber to kill destructive fungi, hence the process is called " Kyanizing." This salt is less caustic and more antiseptic than zinc chloride, but it is more expensive. It was the earliest agent used, and it is still found effectual, although the corrosion by galvanic action of any iron nails, screws, or bolts embedded in the treated wood is a serious disadvantage, and iron tubes cannot be used in the injecting apparatus. A strength of 1 per cent. is somewhat stronger in efficiency than the 2 per cent. zinc solution, but at the same time more deleterious to higher animals.

The Hasselmann process uses a mixture of cupric, aluminium, and potassium sulphates heated to 118° to 127° C. under a pressure of 35 pounds to the square inch. The alum is added to prevent the precipitation of copper by lime in the water.

Finely divided copper[1] suspended in various oils forms the basis of a number of wood preservatives.

Ammonia precipitates zinc and copper solutions, but an excess of it redissolves the precipitate. Such a liquid is employed in Gerlache's patent of 1909, presumably to avoid any weakening action of the ordinary solutions on the wood fibre; but it cannot be recommended, on account of the extra cost, and also because of the liability of the metallic compounds to become insoluble and almost inert within the tissue.

A bulletin of the U.S. Department of Agriculture in 1911 on wood preservation methods in America states[2] that there is an increase in the use of creosote, a decrease in that of zinc chloride, and that small quantities are used of corrosive sublimate, water-gas tar, crude oil, and refined coal tar.

According to Wallis-Tayler, the zinc chloride process more than doubles the life of wood; creosoted wood lasts 25 to 50 per cent. longer than wood treated with the zinc salt, but costs three or four

[1] English patent, 22,802.

[2] *Oil, Paint, and Drug Rep.*, August 7, 1911; *J. Soc. Chem. Ind.*, 1911,1059 Out of the eighty-five wood-treating plants in the U.S., sixty-five employ creosote or tar oils as a preservative (Chas. N. Forrest, *N.Y. Chem. Club*, November, 1910).

times as much. The amount of preservatives injected into 1 cubic foot of various classes of timber ranges from about 3 pounds of mercuric chloride in the case of hard woods to about 6 pounds for moderately hard and 10 pounds for soft woods, the corresponding amount of creosote oil being 3, 10, and 20 pounds respectively. The average costs of preserving timber with zinc chloride, creosote oil, and mercuric chloride, are approximately 1¼d., 5d., and 8d. per cubic foot respectively.

Creosoting Processes.—One of the earliest prescriptions is that well-seasoned timber is placed in a vessel so constructed that a more or less perfect vacuum can be obtained by an air-pump. The oil previously heated to 35° to 50° C. is allowed to enter the exhausted receiver, and pressure of 100 to 180 pounds per square inch is then applied by pumps in order to effect the better penetration of the antiseptic fluid. In S. B. Boulton's improved method, the exhaustion is continued after the entrance of the creosote, which is heated to a temperature between 100° and 130° C. The moisture in the wood is thus volatilized and sucked out, so that the oil subsequently penetrates unmixed and very thoroughly in the quantity of about a gallon per cubic foot. A great advantage of this process is that wet timber can be at once treated without being previously seasoned. The smell of the liquid is much disliked by the lower animals (white ants, etc.), while certain of the constituents have a powerful antiseptic action. Boulton and Coisne proved[1] that in the course of a few years the lower tar acids (phenoloids) in the railway sleepers may completely disappear by dissolving and by volatilization, whereas the semi-solid constituents, such as naphthalene and the higher-boiling oils (above 315° C.) remained, and could preserve the wood for sixteen to thirty-two years. Hence these bodies are more lasting in their action than the lower phenoloids, carbolic and cresylic acids, but the latter are of value in coagulating the organic matter present in the sap, and should be present in sufficient quantity to accomplish this.

Quantity and Character of Creosote in Well-Preserved Timbers.[2]—The creosote oils extracted from timber which had been in use many years showed an average of 32·9 per cent. of distillate below 270° C., and 66·8 per cent. of oils of high boiling-point. The defects of most modern creosote preservatives are deficiency in basic oils of high boiling-point and the substitution for these of tar or otherwise viscous substances. Under proper conditions of distillation a

[1] *Proc. Inst. Civil Engineers*, May, 1884. For later information see Lunge's "Coal Tar and Ammonia," and Church, *J. Soc. Chem. Ind.*, 1911, 191.

[2] G. Alleman, *Proc. Amer. Wood Preservers' Assoc.*, 1914, 88; through *J. Soc. Chem. Ind.*, 1914, **33**, 832.

stable, heavy creosote oil (specific gravity 1·10) could be manufactured from coal tar, containing nothing which boils below 210° C.; for general purposes not more than 50 per cent. of the total should distil below 315° C., and for wood-paving blocks not more than 35 per cent. The qualities demanded are penetrating power, stability, and preservative and waterproofing value. All these are possessed in a high degree by pure heavy creosote oil. Tar has a very low penetrating power, even when injected at a high temperature, and wood treated with a mixture shows a separation of the components, oil, tar, and carbon, at the margins of the close-grain rings, the depth of impregnation of each constituent varying inversely as its viscosity. As regards stability, losses occur owing to volatilization, extraction by water, and crystallization in wood impregnated with light creosote oils. Preservative value may depend on direct antiseptic action or permanent adhesion of a stable oil-coating to the walls of the minutest cells; external filming without penetration is of little account. In the light oils the antiseptic constituents predominate, but are volatile and largely soluble in water. The heavy oils are sufficiently rich in the higher homologues of cresols, both these and the protective oils being far more stable. Waterproofing also depends on the complete coating of the cell walls with an oily deposit which excludes moisture.

Teesdale, in a paper on *the absorption of creosote by the cell walls of wood*,[1] found from described experiments that wood swells in this treatment, causing a weakening effect.

Weiss in 1911 made a long series of tests on the different disinfectants and their constituents in preventing the growth of fungi in wood. He concluded that:[2]

1. The neutral oils of creosote are strong antiseptics, and—
2. The middle fractions of these, boiling at 235° to 270° C., are the strongest.
3. High boiling bases are strong antiseptics.
4. The same is true of coal-tar acids, "the efficiency rising with the boiling-point."
5. Solid hydrocarbons like naphthalene and anthracene have a low value.
6. Addition of filtered tar to creosote does not much affect the antiseptic value.
7. Paraffin has no antiseptic value.[3]

[1] *J. Soc. Chem. Ind.*, 1913, 235.

[2] *New York Section of Chemists Club*, November, 1910, and *J. Soc. Chem. Ind.*, 1911, 190, 1348.

[3] This has a bearing on Devaux's patent of 1911 (*ibid.*, 1061): "Paraffin or stearic acid, etc., is dissolved in the creosote when hot, and, cooling in the wood, go solid, holding in the antiseptic liquids." But they would also reduce the activity.

8. Coal-tar creosote is much better (in the ratio of about six to one) than water-gas tar distillates and petroleum residues as an antiseptic preserver.

The U.S. Department of Agriculture[1] investigated the effect of mixed cresols on specimens of sap loblolly pine. The following fractions of the distillate of a coal-tar creosote were used, and the loss of weight taken over several months:

0° to 205° C.	250° to 295° C.
205° ,, 250° C.	295° ,, 320° C.

They found that the lighter undistilled residue material fractions taken, separately injected, volatilized quicker than those combined in the original creosote. This can be explained by the outer cells getting filled up and sealing the inside. S. Cabot[2] found that the higher-boiling coal-tar phenols, on exposure to air, became converted into tarry substances insoluble in benzene, but soluble in acetone. Of this tar, a part is insoluble in 10 per cent. soda, but soluble as an alkaline salt in water; a portion also forms with alkali, a salt which undergoes hydrolysis on dilution; and a third is practically unattacked. He concluded that the higher-boiling phenols remain in creosoted wood as complex oxidation products. These phenols have considerable preserving powers, are not volatile, and are also markedly fungicidal.

In 1912 Weiss[3] investigated the effect of the viscosity of the creosotes on the depth of penetration, and found that the depth of impregnation varied inversely as the viscosity. It is therefore essential for good penetration to work with hot preservatives, and, owing to the low thermal conductivity of wood, the treatment should not be too rapid. With the coal-tar creosote fractions, those of the greatest stability are the least toxic. He also showed that wood treated with saline preservatives is generally more easily ignited than untreated woods, but preservation makes it slow burning and more easily extinguishable. Coal-tar creosote and copperized oil had the least deleterious effect on steel. Metallic salts, on the other hand—*e.g.*, zinc salts and fluorides—had a more pronounced action, while certain wood tars were highly corrosive owing to the presence of free acetic acid.

Dean and Downs[4] compared the fungicidal properties of coal-tar and water-gas creosote on *Polystictus versicolor*, one of the common wood-rotting fungi. They found that coal-tar creosote was stronger than the water-gas product, and that the value of the

[1] Forest Service Circular 188, October 17, 1911.
[2] *J. Ind. Eng. Chem.*, 1912, **4**, 266.
[3] Eighth Int. Cong. App. Chem., 1912, Section VIA.
[4] *Ibid.*

coal tar depends upon the presence of tar acids and tar bases. Water-gas tar creosote was found to be the same as the coal-tar oil with the tar acids removed.

Charitschhoff[1] showed that creosotes, even when freed from all phenols by extraction with strong caustic soda, still exerted a decided germicidal and antiseptic power when tested on *Merulius lachrymans* and *Penicillium glaucum*.

A good many modifications of the creosoting process have been called by the inventors' names, thus:

Curtis-Isaacs: The timber and creosote are heated to above the boiling-point of the sap at ordinary pressure in a vessel having vents open to the air; the vents are then closed, and the creosote is forced into the wood under pressure.

Rueping: Compressed air is forced into the wood at a pressure of 80 to 100 pounds on the square inch, and then at a higher pressure creosote oil, without relieving the air-pressure.

Lowry: Treatment with the oil at 77° to 82° C. at 180 pounds per square inch, followed by draining and a rapid vacuum treatment.

Rutger or *zinc-creosote* process: An emulsion of ½ pound of zinc salt (called "dry zinc") with ½ to 4 pounds creosote per cubic foot of timber is used, and is kept continually agitated.

Guissani: Wood is heated in a mixture of melted anthracene and pitch to 140° C. until freed from moisture and "sap," then successively treated with cold, heavy tar oil, and cold zinc chloride solution.

The *creo-resinate* process is said to be specially suitable for wood-paving blocks; the wood is first heated to 121° C. in air at a pressure of 100 pounds per square inch, then a hot mixture of 50 parts creosote oil, 48 of resin, and 2 of formaldehyde is forced in, followed by lime-water at 100° C. and 150 pounds pressure.

Although the oils are more powerful when in the concentrated state, much creosoting is done by steaming the dried timber before heating under reduced pressure, then running in the oil and raising the pressure to 100 to 180 pounds per square inch. Piles and wood-paving blocks can be readily injected with the most viscous tars to the extent of 15 to 20 pounds per cubic foot.

Many attempts have been made to diminish the *cost* of creosoting, but the result is almost inevitably to decrease the efficiency.[2] Such would be the case with Chateau and Merklen's patent of 1907, impregnating with a small quantity of the agent—*e.g.*, creosote—

[1] *J. Russ. Phys. Chem. Soc.*, 1912, **44**, 345.

[2] See Kempfer, *Bull.* 84, *U.S. Dept. of Agriculture*, 1911, on the preservative treatment of poles.

then with a liquid like water, "which carries the disinfectant to all parts, thereby economizing it."

Creosote Testing and Characteristics.—Great Britain is still the chief producer and shipper of creosote, and should adopt a uniform system of testing. Tars originate from the manufacture of coal and water gas and coke, and give by their distillation liquids called collectively creosote; the word may mean a product from gas tar, wood tar, oil-gas tar, producer-gas tar, or coke-oven tar. Chemically they have great similarity in their content of aromatic hydrocarbons; we have already given Weiss's estimate of the relative antiseptic powers of the coal-gas oil and water-gas oil. The most important difference is the absence in the latter of those oxygenated or phenolic compounds which occur in the former, but the water-gas products could be made available for wood preservation by adding a small percentage of crude coal-tar acids. Forrest says that a mixture of the water-gas and coal distillates forms the bulk of the creosote now used in America.

The subject is well treated up to the date in Allen's "Commercial Chemical Analysis," vol. iii. There are also able papers by Charles N. Forrest, *New York Chemist Club*, November, 1910; R. Estor, *Les Matières Grasses*, 1911, **4**, 2209; E. Sage, *J. Soc. Chem. Ind.*, 1911, 588; and S. Collins and A. Hall, *ibid.*, May 15, 1914.

Circular 98, U.S. Department of Agriculture, is on the "Quality and Character of Creosote in Well-Preserved Timbers." A number of other bulletins deal with standard methods of testing.

1. **Specific Gravity** should be taken at 60° C., as some of the products are thick at lower temperatures; Forrest's 38° and the ordinary 15° are not so convenient as a standard.

2. **Coefficient of Expansion.**—100 c.c. at 40° C. are warmed to 80° C. in a flask with graduated neck. Sage finds the usual increase of volume to be 1 per cent. for each 13·3° C. This figure is sometimes of great importance, and it enables the specific gravity given at one temperature to be calculated at another.

3. **Fluidity or Condition.**—Keep 100 c.c. at 15° C. for six hours, adding a small crystal of naphthalene (to avoid supersaturation) and stirring occasionally. Report as "fluid," "quite solid," "some deposit," etc., also whether it is completely liquid after keeping for a specified time at 40° C. Estor's quoted specification—"should not deposit more than 25 per cent. of naphthalene or other product solid at 15° C."—refers to difficulty in injection unless a higher temperature is used. The determination of *viscosity* is not so important, as in creosoting the presence of traces of insoluble carbon has far greater influence than slight differences in viscosity.

4. **Solubility in Benzene.**—Crude tars may contain 5 to 40 per cent. of matter insoluble in benzene or CS_2, commercially called "free carbon." This would be concerned in waterproofing rather than in antiseptic action. Most creosotes, being distillates, contain little or none, and in no case should more than 0·25 per cent. be passed without comment. Some specifications say "must dissolve completely in benzene."

5. **Flash-Point.**—Sage considers the Pensky-Marten apparatus more suitable than Abel's, and finds the usual point 186° to 190° C. It has relation to safety in use.

6. **Solvent Tests.**—Pitch and a great part of tar are insoluble in a mixture of alcohol and petroleum naphtha; creosote is mainly soluble. For distillates, Forrest recommends a dimethyl sulphate test described by Dr. Sommer as "dissolving benzene and pyro-distillates, but not paraffins or olefines."[1]

7. **Biological Tests** with the organisms destructive to timber are long and difficult, but have conclusive value.

8. **Distillation.**—The method is often detailed in the contracts, but a usual process is to distil 100 grammes in a weighed 250 c.c. hard glass distillation flask with the bulb of the thermometer opposite the end of the outlet tube. The fractions are collected in stoppered graduated cylinders, which are also tared for convenience.

Water is measured in the fraction distilling under 180° C. by diluting with an equal volume of benzene to facilitate the separation. If necessary, from the benzene solution the solvent can be driven off at 81° C., and the remainder separately examined.

The main distillation is continued to 316° C., noting specially the volumes coming over near 205°, 215°, 220°, 245°, 271°, 300°, and 316° C. What remains undistilled is weighed, and is generally put down as "pitchy residue." Creosote does not enter timber easily with much pitch.

The tar acids (and the phenoloids) are extracted from the whole distillate by three lots of 12 per cent. caustic soda of 25 c.c., 15 c.c., and 10 c.c. respectively. The soda extract is washed three times with ether, the ether collected and washed with 5 c.c. of soda, which is then added to the main soda extract; this is warmed and shaken till all the ether is expelled, then placed in a 200 c.c. burette, cooled, and carefully acidified with 50 per cent. sulphuric acid. After again cooling, the volume of tar acids is read off. The tar bases (pyridine, etc.) can be determined similarly by extraction with sulphuric acid; they are very antagonistic to organisms, but are volatile.

[1] *J. Ind. Eng. Chem.*, **2**, 186.

Estor adduces two examples of French specifications for wood-preserving creosotes:

FRENCH INDUSTRIAL SOCIETIES.

1. Completely liquid within thirty minutes at 40° C.
2. Specific gravity at 15° C., 1·04 to 1·05; at 50° C., 1·015.
3. Must dissolve completely in benzene.
4. Contain at least 10 per cent. of tar acids soluble in soda, 1·15 specific gravity.
5. Not to deposit more than 25 per cent. of naphthalene at 15° C.

CAMPAGNIE DES CHEMINS DE FER DE L'EST.

1. Specific gravity not less than 1·05 at 15° C.
2. Distillation fractions: below 150° C., less than 3 per cent.; 150° to 235°, less than 30 per cent.; 150° to 355°, more than 85 per cent.
3. At least 5 per cent. of phenols.
4. Not more than 30 per cent. naphthalene.

Naphthalene can be separated from the fractions boiling below 270° C. by cooling, filtering through cloth, and pressing, and can then be weighed. Picric acid precipitation gives too high a result, as it precipitates other hydrocarbons.

Collins and Hall[1] find the best method for the assay of creosote is carefully to distil it, using a long (20 discs) Young's "rod and disc" still-head up to 271°, and then a shorter one to 316°. The naphthalene comes over between 205° and 220°, solidifies in the receivers, and on cooling can be weighed and the melting-point taken. They find crude naphthalene a splendid preservative for timber, but so much is absorbed that the expense is great. Its evaporation seems limited to the surface. Creosote disappears from the exposed portions of a post, and also from the point, but the middle part keeps its creosote well, as shown by tests after twelve to fourteen years. The more volatile portions are easily lost. While the creosote remains, the wood will be preserved.

In the report of the Committee on Wood Preservatives (Creosote Oil),[2] the definition of creosote oil is revised, and comprises all distillate oils boiling between 200° and 400° C., obtained by direct distillation from tars consisting principally of compounds of the aromatic series, and containing well-defined amounts of phenoloids. The most important tests are for moisture, specific gravity, and distillation. Additional tests are for free carbon, tar acids, sul-

[1] *Loc. cit.*

[2] *Proc. Amer. Wood Preservers' Assoc.*, 1914, 58-76; through *J. Soc. Chem. Ind.*, 1914, **33**, 832.

phonation; the Hempel distillation test, refractive indices, and specific gravities of the fractions. These tests are described in detail, together with the apparatus employed. All temperature observations must be made with a standard thermometer of specified dimensions: length of stem from 0° to 400° C., 295 mm.; bulb, 14 mm long and 6 mm. in diameter. Readings to be uncorrected. No recommendations have yet been formulated as to standard specifications for creosote oils, but the specifications enforced by several consumers' associations are reprinted collectively for comparison.

Leaflet No. 284 of the British Board of Agriculture, issued 1914, on "The Preservation of Outdoor Timber," mentions under *surface applications* that simple painting may do more harm than good, as the moisture is prevented from escaping, and conditions favourable to decay are thereby maintained. A tar coat is more or less elastic, and allows the contraction and expansion of wood by changes of temperature; but a coating that cracks readily obviously permits the entrance of destructive agents. It alludes to the primordial device of superficial *charring*, in which the wood is destroyed to the depth of half an inch or so, the resins, gums, tannins, etc., contained being driven in front of the heat till they saturate a layer and form a protecting mantle to the deeper tissue, and observes that mere singeing or scorching will again do more harm than good, as causing the wood to crack and be penetrable to the dangers. The destruction of material necessarily involves so much weakening of the structure, therefore "it is doubtful whether, on the whole, the charring of posts is a profitable process."

Consequently, impregnation of wood throughout with preservatives by such processes as we have indicated is the only safe resort, and of these the foremost at present is the application of creosote. The objections stated to others, such as copper sulphate, zinc chloride, or corrosive sublimate, are cost, poisonousness to animals, liability to be washed out by water, or injurious action on metals. The railway companies generally specify that each cubic foot shall contain 1 gallon of creosote, costing at least 4d., and there is little advantage in increasing this quantity. One economic benefit is that by prolonging the life of timber for twelve to fifteen years it makes useful, for fencing and other purposes, much material that would otherwise be too perishable. Leaflet 284 gives good directions for the creosoting process.

CHAPTER IX

THE CHEMICALS EMPLOYED IN DISINFECTION

CHEMICAL CONSTITUTION AND GERMICIDAL ACTIVITY

This branch of therapeutic chemistry has not yet been the subject of any systematic treatment. Investigators in the field have been at once confronted with the usual difficulties that beset observers when experiments on living organisms are being carried out. Confusion between disinfection or actual germicidal activity and antiseptic value has frequently arisen, and the concept of activity and antiseptic value of the disinfectant has been masked by side reactions between the chemical investigated and extraneous matter, either organic, such as serum, blood, or pus, or inorganic (*e.g.*, sodium chloride) present with the bacteria. Although for practical purposes the stability of a germicide in the presence of extraneous matter is usually desirable, and should be determined, yet, owing to the great variety of possible contaminating substances, for the purely scientific problem of the relationship between chemical constitution and germicidal activity these complications had best be avoided.

The first point of interest in the subject is that undoubtedly selective action takes place; thus not only will two different organisms show different resistances to the same germicide, but unfortunately their relative resistances to two different germicides will not be the same, whilst the phenomenon of gradual immunity or acclimatization to disinfectants introduces still another factor. Thus Harde and Jackson[1] showed that staphylococci treated with 1 : 200 phenol for three periods of one and a half hours each would then withstand 1 : 100 phenol for one and a half hours, whilst the untreated organisms died within three-quarters of an hour on immersion. Attention must be paid to the standardizing of the growth of a particular organism for testing purposes, and having defined the medium, the nature of the organism, and method of culture, comparable results with different germicides may be obtained.

Whilst the practical methods of testing disinfectants will be dealt with later, it is important to bear the above points in mind when discussing the results of different observers.

It is well known that certain chemicals possess the power of

[1] *Compt. rend. Soc. Biol.*, 1918, **81**, 635.

stimulating the growth, arresting the growth, and finally destroying the growth of different micro-organisms with increasing concentrations of those reagents, properties utilized in culture growing, antisepsis, and disinfection respectively.

Under the usual conditions of testing where solutions are made use of, the germicide may be in solution or in the colloidal state in the medium, and any theory of disinfection which is applicable to ionized solutions must be also capable of extension to non-ionized solutions, emulsions, and other colloidal systems.

Bacterial Suspensions.—An emulsion of bacteria is not, strictly speaking, an emulsion at all. A micro-organism, of which the average diameter, excepting the ultra-microscopic bacteria, is about 1 to 1·5 μ, is composed of a chitin envelope[1] containing, in addition to organic compounds of high molecular weight, which consist of polypeptides, lipoids, and carbohydrates, also enzymes, as well as salts, chiefly sodium chloride, in strength approximating to that of physiological salt solutions, together with a cell nucleus containing the chromospores and chromosomes of unknown chemical constitution. We must rather regard the " emulsion " as lying between a suspension and a suspensoid in size. Practically all bacteria will exhibit Brownian movement, and may therefore be regarded as of colloidal diameter. The bacteria are feebly precipitated by cations; thus hydrion and the polyvalent elements, iron and aluminium, as well as the heavy metals, mercury, copper, and silver, precipitate them, but they are practically unaffected by the alkali and alkaline earth cations. In this respect—namely, insensibility to a great number of cations—they resemble emulsoids rather than suspensoids. A further resemblance is shown in that bacteria are but feebly protected from precipitation by the ordinary protective colloids such as gelatine and isinglass. It is therefore more legitimate to regard bacterial suspensions as suspensoid nuclei coated by or containing an emulsoid.

If we add to a suspension of bacteria serum taken from an inoculated animal, we obtain agglutin bacteria complexes. These have entirely lost their emulsoid properties, and exhibit the properties of suspensoids.

The reaction between agglutin and the bacteria, similar to the reaction between toxin and antitoxin, resembles in many respects either the combination of a very weak acid and a weak base, the excess of either constituent, when equilibrium has been attained, being given by the general equation—

$$C_1C_2 = KC_3,$$

[1] Cellulose, hemicelluloses, and carbohydrates of the pentosan group are, however, present in the cell walls of many fungi, whilst with certain amœba the cell wall appears to be lacking.

where C_1, C_2, C_3 are the concentrations of the reacting constituents. This view has been advanced and supported by Arrhenius (Immunochemie), but may also be interpreted equally well on the usual absorption formula—

$$\frac{C_3}{C_1} = AC_2^{\frac{1}{n}}$$

in cases where n is near unity. Experimental evidence is not sufficiently accurate to distinguish between the two.

Recent work[1] has gone far to indicate that the usual adsorption formula has no theoretical significance, and that there is no difference in mechanism between physical and chemical adsorption for dilute concentrations; if concentrated solutions be used, there is a possibility that the substance adsorbed may build up a second or more layers above the more firmly adhering single layer, and thus give rise to the "adsorption" formula. The Danysz effect must be regarded as a phenomenon of this kind.

The conditions determining physical adsorption, and especially the influence of electrical charges on suspensoids, have been discussed more especially by Freundlich,[2] W. Gibbs,[3] Pawlow,[4] Donnan, Bancroft, and others. It may be noted that suspensions of bacteria always acquire an electric charge.

A very sharp distinction between these reactions and ordinary weak acid base neutralization is the specific nature of the reaction. Each toxin requires its own particular antitoxin, and each bacteria species its own agglutin. This, of course, is characteristic of enzyme reaction, and the usual example cited—namely, "a key for every lock"—holds good.

We can thus distinguish between the following types of action:

1. **Absorption of cations** (ionic disinfectants), with simultaneous absorption of anions which may affect the activity.

2. **Mutual action between two colloids** (reactions between emulsified disinfectants and organisms).

In this connection, although mutual absorption is said to take place, the mechanism may also be regarded as one of "protection," for the following reasons:

The finer the emulsion, the more efficient the germicide. This is directly observable under the microscope; solutions are not so germicidal.

Taking the diameter of an average organism as $1{\cdot}0\,\mu$ diameter, and assuming approximately spherical shape, we require 10,000

[1] Langmuir, *J. Amer. Chem. Soc.*, 1913; Williams, *Proc. Roy. Soc.*, November, 1919, 287.

[2] *Kapillarchemie.*

[3] Scientific Papers, 2.

[4] *Zeitsch. Physikal. Chem.*

molecules to coat the organism with a molecular thickness of the emulsified disinfectant; 10,000 molecules in the spherical form have a diameter of 0·15 μ, which is the lowest limit of direct visibility. Now the ratio of volume and weight of organism to emulsion particle is as 1 to 0·001 approximately. Zzigmondy has found that the weights of protective gelatine to gold is as 0·001 to 1. It therefore appears that the relationship may be of significance, and that the most desirable emulsoid disinfectant will be a protective colloid to the organism. From these considerations it is at once evident that an emulsion of, say, a cresol in water may be more powerfully germicidal than the same amount of cresol in solution.

3. **Direct absorption of non-ionized substances in solution.** The adsorption of phenol by anthrax and the partition of phenol between water and organisms has been found to obey the regular adsorption law.[1] Alterations in the surface tension of proteins and sera by the addition of phenol and water indicate also the adsorption of phenol. A point to be noted, and one not usually recognized, is that the degree of adsorption is dependent on the degree of curvature of the envelope. With decreasing size—*i.e.*, increased curvature—the adsorption must get less, since in the limiting case the solution must become uniform in composition.

Animal charcoal has long been used as an adsorbant for micro-organisms, and when fresh and "active," especially those varieties prepared for gas masks, it undoubtedly removes micro-organisms and their ferments. In the Vienna hospital it was found that proteolytic ferment produced by *B. pyocyaneus* was completely adsorbed, and that a bacterial suspension shaken with fresh charcoal was rendered completely sterile. Methods of wound treatment were likewise elaborated during the war, usually consisting of a preliminary washing with hydrogen peroxide, followed by dry dressings of charcoal changed every day. Deep wounds were syringed with a 2 to 3 per cent. suspension of charcoal. It is stated[2] that the method proved successful, and that no ill effects were observed.

When we inquire a little more closely into the mechanism of disinfection, instead of referring it purely to "adsorption," irrespective of the germicidal activity of the substance adsorbed, we are at once confronted with a variety of hypotheses as to the nature of the forces involved.[3]

The early experiments of de Vries on plasmolysis of plant cells (especially *tradescantia*) and of Hamburger on plasmolysis of the red blood-corpuscles indicated quite clearly that many substances

[1] Küster and Bojakowsky, *Disinfektion*, 1912, **5**, 193.

[2] *Brit. Med. J.*, June 19, 1917.

[3] *Jahresbuch. für wiss. Bot.*, 1884, 14.

could not diffuse into the interior of the cells, whilst others could. The work of de Vries on both non-permeable electrolytes and non-electrolytes was, in fact, the starting-point of the present concept of osmosis and the theories of solution (for which we are chiefly indebted to Van't Hoff and Arrhenius).

The peculiarly selective action of blood-corpuscles in their permeability to substances was investigated in detail by Gryns,[1] who showed that the sodium salts of the following acids: HCl, HBr, HF, H_2SO_4, CH_3COOH, $CH_3 \cdot CH_2 \cdot COOH$, and the ammonium salts of HNO_3, H_2SO_4, HCNS, H_3PO_4, were not permeable in the blood-corpuscles, whilst the ammonium salts of HCl, HBr, HI, HF, HBO_3, $CH_3 \cdot COOH$ readily penetrated. Hedin,[2] by determining the relative lowering of the freezing-points of equal volumes of serum and blood on addition of equal amounts of the various salts, investigated whether the serum or the blood adsorbed the salt more easily. In the case of the alkali salts an equal adsorption was noted, and similarly with sugars, alcohols, and amino-acids and some aldehydes, whilst ketones, ethers, and esters were more strongly adsorbed by the blood than by the serum.

Overton and H. Meyer,[3] in their studies on narcosis, were more successful than these former observers in correlating permeability with other physical properties. They proved that narcosis was produced by readily permeable substances such as ether, chloroform, and strychnine, which also, on account of their permeability, produced no plasmolysis. This striking result at once brought up the question in an acute form as to why the cell was permeable to some very large molecules like strychnine and impermeable to some very small ones such as the ions of the simple salts. Overton attributed this lack of permeability of certain substances in part to chemical reaction with the cell wall, but at the same time considered even more important the interesting fact that permeable substances were soluble in fats, fat solvents, and lipoids, and relatively insoluble in water, whilst the impermeable substances were relatively very soluble in water and lipoids. Thus special emphasis was laid upon the value of the partition coefficient—

$$K = \frac{\text{solubility in oil, fat, or lipoid}}{\text{solubility in environment, water, or serum}}.$$

Large values for K, the partition coefficient, would indicate a penetratable substance and an effective agent, which would readily dis-

[1] *Pflüger's Archiv*, **63.**

[2] *Ibid.*, **68.**

[3] *Vierteljahrschrift der Naturs fors.*, Zurich, 1895, 1896, 1899; *Studien über Narkose*, 1901.

solve in the lipoid material of the cell and affect the vitality of the organism.

Thus urea, $CO<^{NH_2}_{NH_2}$ penetrates into the cell wall with extreme slowness, but by replacing the hydrogens by alkyl or even aryl groupings the rate of permeation increases very considerably; simultaneously there is an increase in the ether solubility.

Oxygen-free alkaloids penetrate with readiness and are fat soluble, but their salts do not diffuse, and at the same time are fat insoluble.

Ether soluble basic dyes penetrate with ease, whilst the water soluble sulphonated dyes do not. Germicides such as mercuric chloride, iodine, and formic acid are appreciably fat soluble. Attempts[1] to convert non-trypanocidal metals such as copper or silver into trypanocidal agents by combining them with a lipoid soluble group such as acetic ester or peptone yielded, however, negative results.

Numerous investigations on yeast cells, such as those of Herzog and Betzel[2] and Gössl[3] have shown a very close connection between antiseptic disinfecting power and lipoid or protein solubility. It is of interest to note that lipoid soluble substances will be absorbed by dead as well as living cells, and thus adsorption is not diagnostic of life in the cell. Further, that death does not always result from such adsorption or lipoid solution, since the aliphatic and hydroaromatic hydrocarbons possess a large partition coefficient, but are not germicidal. The action of sodium chloride in elevating the germicidal activity of phenol and of alcohol in depressing it can be attributed to the alteration of the $\frac{\text{lipoid}}{\text{water}}$ partition coefficient, the former elevating it by decreasing the solubility of the phenol in water, and the latter lowering it by increasing the water solubility. The germicidal power of phenol in such solutions is directly proportional to the activity or fugacity of the phenol. Salts affect the germicidal powers of phenol to different extents; thus in order of increasing activity are KNO_3, KI, NH_4Cl, KBr, KCl, NaCl.

As has already been pointed out, adsorption by the colloid appears to be the primary action in disinfection, and the factors governing this adsorption must influence the germicidal activity of a disinfectant. The influence of electric charge has already been noted, but of even greater significance is the influence of the germicide on the surface tension of the medium. It was shown by Willard Gibbs that in those cases where the solute lowered the surface tension of a solvent the solution would be more concentrated at the surface than in

[1] *Archiv. Internat. de Pharmacodynamie de Thérapie*, No. 3, 1913, **12**, 73.

[2] Hoppe-Seyler, *Zeitsch. Physiol. Chem.*, 1910, **67**, 309; 1911, **74**, 221.

[3] *Loc. cit.*, 1913, **88**, 103.

bulk; thus round each micro-organism there will exist a film of medium richer in germicide than the bulk of the medium. We can thus postulate that efficient germicides will lower the surface tension of the medium in which the organisms are dispersed.

This relationship between the lowering of the surface tension and the germicidal activity is very well exemplified in the somewhat insoluble organic hydroxyl derivatives. Thus thymol, camphor, and menthol exert a greater depressing action than the cresols, and cresol than phenol, on the surface tension of the water, and the same order is found in their molar germicidal activity. Phenol is more effective than resorcin, resorcin than hydroquinone, this latter than phloroglucin and pyrogallol in both respects.

A remarkable correlation is found in the nitrophenols and nitrobenzaldehydes; in the former the para position is stronger than the ortho, and in the latter the converse is true. Their action on the surface tension of water follows in the same order.

The hydrocarbons possessing a high lipoid water partition coefficient have an almost negligible germicidal activity, and scarcely affect the surface tension of the water.

Brown and Tinker have likewise shown[1] that in the case of barley seeds immersed in dilute aqueous phenol there is a direct relationship between the adsorption and the surface tension.

From the physical standpoint there are thus two criteria which may be applied to test the efficiency of a germicide—the partition coefficient between a fat or liquid and the medium, and the effect of the germicide on the surface tension of the medium. These facts alone are, however, not sufficient to account for the anomalous cases of permeability noted by De Vries, Hamburger, and Overton. This latter observer somewhat modified his earlier physical theory[2] by postulating the existence of active groupings which inhibited permeability, and thus promoted plasmolysis. Ionized substances do not permeate with readiness, whilst substances like aniline, aldehydes, methyl alcohol, acetone, and phenol do. In the case of glycerol, succinimide, and acetamide plasmolysis will set in to commence with, but afterwards disappear, indicating a slow diffusivity. In decreasing order of diffusivity or extended period of plasmolysis can be mentioned glycerine, urea, and, slowest of all, erythrose.

It is thus evident that the metals existing in the form of ions in solution as simple salts can be made to diffuse into the interior of the cell by means of a complex attached to the ion; thus we find certain organic mercurials much more germicidal than mercuric chloride for the same concentration of mercury.

By simple substitution of various groupings in permeable organic

[1] *Proc. Roy. Soc.*, 1915, 389. [2] *Loc. cit.*

substances Overton[1] was able to show that certain groupings retarded the rate of permeation very considerably, and frequently made the compound completely plasmolytic. In order of decreasing activity he noted the following: Amido-acid group, carbonyl, acetamide, alcoholic hydroxyl, aldehyde.

Thus glycocoll, alanin, and leucin, containing an amido-acid grouping, do not penetrate the cell appreciably; one hydroxyl scarcely hinders penetration, although $CH_3CH(OH)CO.NH_2$, lactamide, penetrates far less readily than acetamide or propionamide. With the introduction of further hydroxyl groups penetration is much slower, as is instanced by ethylene- or propylene-glycol, glycerol, erythrose, and the pentoses and hexoses, which do not penetrate at all.

Ketone, ester, ether, halogen substitution, and nitrile groupings appear to have little effect on the permeability.

Of significance is the fact that ammonia and the amines penetrate with readiness, whilst the quaternary nitrogen bases do not. Pyridine, quinoline, piperidine, and oxygen-free alkaloids are permeable, whilst oxygen-containing alkaloids usually do not penetrate. Butschli showed that only certain dyes, such as carmine and hæmatoxyline, were capable of staining the bacterial nucleus, and were thus permeable. This observation has been confirmed and considerably extended in the development of specified reagents for the treatment of trypanosomic and similar infections.

In addition to the conditions necessary to bring about surface adsorption, with subsequent surface reaction or penetration of the cell, we have the specific toxicity of the substance or of certain groups in the substance to consider. Whilst the above short review of the former factors indicate that something, if indeed but little, is known, it is clear that the relationship between germicidal activity *per se* and constitution is as yet practically an unworked field. This is in part due to the fact that pharmaceutical preparations have usually an ulterior motive, such as the possession of a narcotic, sedative, or other activity, germicidal activity being itself usually merely a desirable auxiliary, and in part due to the discrepancy of results obtained by utilization of non-uniform methods of testing, confusion between antiseptic and germicidal activity, the complications introduced by the considerations noted above, as well as the pronounced selective action shown by many substances.

Certain generalizations may be formulated, to which, however, there are the inevitable exceptions.

In the case of the simple ionized acids, bases, and salts certain regularities are apparent.

[1] *Loc. cit.*

J. Blake[1] pointed out that in isomorphous groups the toxicity increased with the atomic weight, whilst a variation in the anions of metallic salts had but little effect on the toxicity. In the case of the non-metals this relationship does not hold; thus in the case of the halogens the toxicity appears to increase in the order I_2, Br_2, Cl_2, and for the sodium halides NaCl, NaBr, NaI, and NaF.

The valency of the metallic ion is also an important factor in germicidal activity; thus trivalent ions are more potent than divalent, divalent than monovalent ions. Again, unsaturation augments the germicidal power; thus trivalent arsenic is a much more efficient spirillocide than pentavalent, as are the stibnites as compared with the stibnates. An interesting fact noted by Loeb[2] is that the presence of a divalent ion will promote the activity of a monovalent ion, a typical case of promoter action. In the case of ionized disinfectants such as calomel Hg_2Cl_2, Dresner[3] was the first to note that the greater the concentration of mercury in solution, the greater was its action on yeast cells; the observation was confirmed by Scheurlen and Spiro[4] who showed that the toxicity of certain mercury compounds decreased in the following order: $HgCl_2$, $Hg(CN)_2$, $Hg(CHS)_2$, $K_2Hg(S_2O_2)_3$, this last being scarcely antiseptic. It remained, however, for Krönig and Paul[5] to explain these results in the light of the ionic theory. These observers showed that in the case of simple salts the germicidal activity, as measured by the agate method (see Chapter XIII.), was directly proportional to the ionic concentration of the cation. A very large number of experiments were carried out, and this rule was found to hold in practically all cases, especially for the following germicidal ions: Hg, Ag, Aü, Cü, Fe.

Thus they found the germicidal activity of mercuric chloride depressed by the addition of the common ion Cl, as is evident by the following figures from experiments on anthrax spores:

Solution.	*Organisms Alive after Six Minutes.*
$HgCl_2$ +	8
1NaCl	32
2NaCl	124
3NaCl	282
4NaCl	382
6NaCl	803
10NaCl	1,087

The addition of other anions forming less dissociated salts than the chloride in the solution likewise brought about a decrease in the germicidal activity, as shown in the following table:

[1] *Proc. Roy. Soc.*, B, 1881, **14**, 299. [2] *Pflüger's Archiv*, **88**, 68; **93**, 246; **96**, 248.
[3] *Archiv. Exp. Path. Pharm.*, 1893, **32**, 406.
[4] *Münch. Med. Wochenschr.*, 1897, 4.
[5] *Zeitsch. Physikal. Chem.*, **21**, 419; *Zeitsch. Hyg.*, **25**, 1.

Solution.	*Organisms Alive after Ninety Minutes.*
$HgCl_2$ 1 gramme mol./16 litres	0
+4NaCl	0
4KBr	0
4KCNS	173
4KI	431
4KCN	795

Here, again, the germicidal action falls off with decreasing ionic concentration. Scheurlen and Spiro[1] give the following figures for the iron salts with *B. typhosus:*

Solution.	*Organisms Alive after—*			
	One Minute.	*Ten Minutes.*	*Two Hours.*	*Twenty-four Hours.*
1 per cent. ferric chloride ..	0	0	0	0
1·71 per cent. potassium ferrocyanide	600	700	600	800
1·71 per cent. ferrous sulphate ..	100	0	0	0
2·00 per cent. potassium ferrocyanide	800	800	700	800

It is important to note that germicidal value is measured in these experiments, and not antiseptic power. For the hydrogen ion present in dissociated acids the generalization of Krönig and Paul does not hold with great rigidity. The work of Horrocks and Kitasato on the germicidal activities of acids indicated that their disinfectant action was roughly proportional to their strength—*i.e.* their hydrogen-ion concentration—in equal dilutions. Kahlenberg and True[2], Heald[3] and True[4] came to somewhat similar results with experiments on the toxicity of acids to the seeds of plants such as *Lupinus albus*. Clarke[5] and Stevens[6] found in the case of fungi that the fungicidal power of an acid was in several cases not proportional to the acid strength; thus acetic acid and the chloracetic acids were found to be more effective than hydrochloric acid.

These conclusions have been repeatedly confirmed by other observers[7]; Crozier came to the conclusion that the "penetrative" power of an acid, as measured by the colour change effected on the blue integumentary pigment of *Chromodoris zebra*, was a function of its ionization as well as the possibility of union of the acid with one of the constituents of the cell wall; in weak monobasic fatty acids this constituent is of a fatty nature.

[1] *Loc. cit.* [2] *Bot. Gaz.*, 1896, 22. [3] *Ibid.*
[4] *Amer. J. Sc.*, **9.** [5] *Bot. Gaz.*, **58.** [6] *Ibid.*, **26.**
[7] See Haas, *J. Biol. Chem.*, 1916, **27**, 225; Crozier, *ibid.*, **26**, 217.

Paul and Krönig,[1] in the course of their investigation with anthrax spores, noted that in completely ionized dilute acids there was scarcely any selective effect due to the anion, but with stronger solutions the germicidal power was by no means proportional to the hydrogen ion concentration; marked anion effects were noted in the case of hydrofluoric, nitric, hydrochloric, and oxalic acids, which were all found to be abnormally strong germicides.

Norton[2] not only showed that the addition of a common ion generally lowered the germicidal activity of an acid, as is to be anticipated on Krönig and Paul's hypothesis of ionic activity, but that the addition of other salts frequently raised the germicidal strength; he regards the anions as positive catalysts, and the undissociated molecules as negative catalysts for the rate of germicidal action (see Chapter XII.). These results are also, of course, capable of a tentative explanation on the salting out effect or partition coefficient theory of Overton. In addition it should be noted that for relatively concentrated solutions the differences between the thermodynamic and actual concentrations may be quite marked (see p. 187).

The activity of the hydroxyl ion is some five times less than that of the hydrogen ion; thus Krönig and Paul showed that the strong alkalies KOH, NaOH, LiOH were practically equally effective, the feebly dissociated ammonium hydroxide being far less germicidal, its antiseptic power being only one-seventh that of caustic soda. For non-ionized disinfectants the problem is somewhat complicated by other factors such as penetration or impermeability to the cell wall, which we have seen is partly governed by the possession of a high lipoid-water partition ratio, a marked depression on the surface tension of the medium, and the absence of certain specific groupings.

O. Loew adopted the theory that the organism itself, especially in the cell wall, possessed certain groupings with which the disinfectant reacted; this point of view merely supplements Overton's theory that the disinfectant may possess certain groups which react with the organism; the nature of the groupings postulated by these different observers is, however, somewhat different. Loew confines himself to the amido, $-NH_2$, and aldehyde groupings which are the active groups in the living cell organism and in protoplasm to which the disinfectant molecule must attach itself. These groups are extremely reactive or labile, especially with other amido, aldehyde, or hydrogen groupings. Thus hydrazine, NH_2-NH_2, possesses a higher germicidal power than NH_3, phenyl hydrazine, $C_6H_5.NH.NH_2$, than aniline, $C_6H_5.NH_2$. Phenyl urea, $CO<^{NH_2}_{NH.C_6H_5}$ is as antiseptic as sublimate, but diphenyl urea,

[1] *Loc. cit.* [2] *J. Infect. Diseases*, 1916, **18**, 2.

$CO<^{NH.C_6H_5}_{NH.C_6H_5}$ possesses scarcely any antiseptic action. Likewise an increase of activity has been noted in the following substances, the last being least active:

$$HN=C<^{NH_2}_{NH_2};\quad OC<^{NH_2}_{NH_2};\quad OC<^{OC_2H_5}_{NH_2}.$$

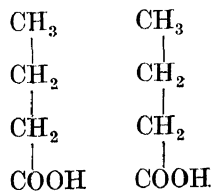
Unsaturated compounds with these groupings are likewise more reactive than saturated ones; thus a marked decrease in germicidal activity is noted in the following:

$$IC{:}CI > IHC{:}CHI > CHI_3.$$

The work of Emil Fischer on the activity of various organisms on the sugars went far to support Loew's theory of specific chemical groupings in the organism to which the reactant attached itself. This point of view was strongly emphasized and extended by Ehrlich in his work on trypanocides (see later).

A path to the solution of the problem of correlation of chemical activity and these factors has, however, been indicated by a study of the relationship between chemical constitution and surface tension, especially by the late Lord Rayleigh,[1] Milner,[2] Marcelin,[3] and Langmuir.[4]

It seems probable that, since the introduction of certain groupings such as $-OH$, $>CO$, and $-COOH$, or of a double or treble bond into an organic hydrocarbon molecule renders the substance more soluble in water, these groupings react with the water by secondary valencies or oxonium linkages, whilst the hydrocarbons do not.



Thus if a fatty acid be distributed over the surface of the water, the carboxyl groups will be immersed in the water and tend to pull in the hydrocarbon nucleus which is not wetted. Short hydrocarbon chains can be totally immersed by the active grouping, and the substance becomes soluble (*e.g.*, $CH_3.OH$, $CH_3.COOH$), whilst the reactive grouping has usually not enough energy to pull in very long chains (*e.g.*, oleic acid). We have thus direct evidence that

[1] *Phil. Mag.*, 1899, **48**, 331.
[2] *Ibid.*, 1907, **13**, 96.
[3] *Ann. Phys.*, 1914, **1**, 19.
[4] *Proc. Nat. Acad.*, Washington, 1917, **3**, 251.

the surface films consist of orientated molecules, and that solubility in various solvents such as lipoids, nuclein, water, or serum is conditioned by the presence of certain particular groupings in the molecule. Overton's partition theory, the hypothesis of surface tension activity, and the Loew-Ehrlich theory of the presence of particular chemotropic groupings in the organism and parasito- or microbotropic groupings in the disinfectant are thus brought into unison by the adoption of this physico-chemical hypothesis of molecular orientation.

The manner in which the normal metabolic functions of the organism are destroyed by the germicide is unknown. We have already noted that many physical and physico-chemical factors are involved in the process of disinfection, reactions proceeding prior to death. The view generally advanced as to the final action of the germicide in causing death by precipitation or coagulation of some protein constituent in the organism is probably not universally applicable to all germicides. This hypothesis is, however, of utility in that it visualizes the dynamic nature of the process. Thus a small concentration of the germicide within the organism will cause a little coagulation to take place; the metabolic activity of the organism will naturally increase in order to reject or repeptize the coagulated material, and it appears likely that a general and not limited augmentation in activity will take place, giving rise to the phenomenon of growth stimulation. With increasing concentrations of the poison all the activities of the organism will be devoted to its removal, and growth arrest or antisepsis will result; finally, the mechanism of the organism will break down and death will occur. This hypothesis, however, is limited to disinfectants permeating the cell wall and reacting with a protein constituent inside, but as we have already had occasion to note, lipoid-soluble substances are frequently germicidal, but it is doubtful if in every case these germicides coagulate proteins; whilst still a third type of reaction is to be noted in many germicides, which attack the cell wall alone, and either combine with it or cause precipitation and flocculation of the organisms, thus interfering with the osmotic circulation of the living cell. The metal ions are thus found to be the most effective germicides for spores.[1]

These considerations permit us to draw some interesting deductions; thus in the emulsified disinfectants the protective action of the emulsion is enhanced if the emulsion contains parasitotropic groupings. Thus, although gelatine itself has but a feeble protective action, the incorporation in the gelatine or the conversion of part of the gelatine molecule into a parasitotropic grouping which reacts

[1] Chick and Martin, *J. Hyg.*, 1908

with either a protein or cellulose constituent of the organism enhances the protective action, but the protective action is really an enemy in disguise, for the protector then kills the organism. In some ways the problem is analogous to the action of mordants in dyeing.

The absorption of non-ionized disinfectants can also be made more complete and rapid by similar means. For example, a 1 per cent. chlorine solution has an R.W. figure of about 2·2, but chloramine, NH_2Cl, which not only oxidizes, but possesses the $-NH_2$ group—a group reactive with cellulose or chitin—has for the same 1 per cent. chlorine an R.W. figure of 6·6, being thus three times as strong.

CHAPTER X

THE CHEMICALS EMPLOYED IN DISINFECTION—*Continued*

INORGANIC SUBSTANCES.

THESE may be broadly classified as (*a*) non-metallic; (*b*) derivatives of metals.

(A) NON-METALLIC SUBSTANCES.

Ozone.—Ordinary oxygen acts slowly by the aid of aerobic organisms. Its activity is slightly increased by compression, but it becomes extremely energetic when converted into its allotropic form, ozone (O_3), formed most conveniently by passing an electrical discharge through ordinary air. Since ozone is decomposed by heat, by most metals, and by otherwise inert organic matter, the chief conditions for efficient working are: (1) The production of a silent electrical discharge without sparking; (2) keeping the gas and the apparatus cool; (3) straining the air, and also partially drying when it is desirable to prevent the formation of oxides of nitrogen; (4) parts in contact with ozone must be made of, or lined with, unoxidizable materials; (5) the grosser organic impurities, as well as sulphuretted hydrogen and ferrous iron, should be removed before disinfection. The use of ozone on a large scale for purifying water and sewage is now well known (see *ante*), and the principal types of apparatus for the purpose have been described by Don[1] and by the writers.[2] In the dry state, like chlorine, it has very little action on micro-organisms, and therefore does not act powerfully on bacilli in air. Some American experiments, however, seem to show that 8 grammes per cubic metre of air in a room ordinarily closed attain disinfection in three hours (see *ante*); whilst Heise[3] has found that 95 per cent. of the bacteria on the surface of a culture medium are killed in a similar period by concentrations of 3 grammes per cubic metre. Its use as an adjunct to ventilation has often been proposed, but its irritant action on the lungs, its low

[1] Inst. Mechan. Engineers, January and February, 1909; "Modern Methods of Water Purification," by J. Don and J. Chisholm. Edward Arnold.

[2] "Water Supplies."

[3] *Arbeit. Kais. Gesundh.*, 1917, **50**, 418; *Chem. Zeit.*, 1918, **42**, 137.

penetrative power, and ease of decomposition are grave defects. All observers have found that when moist it is a very powerful germicide. Ozonized air under pressure has been used successfully for destroying moulds and bacteria in brewers' foul casks, and has been introduced into wort in the later part of the fermentation " to destroy noxious germs."[1] On account of its rapid consumption by oxidizable substances. it can only be effective in disinfecting the surfaces of organic solids. A large plant has been in operation for some time at the Pittsburg Homeopathic Hospital for purifying the water supply, and also for sterilizing instruments, bandages, etc., and for dressing wounds and ulcers. In cold storage, it would probably be useful for destroying injurious organisms and odours, thereby possibly lessening the amount of refrigeration required. Many attempts have been made to utilize it for disinfecting, combined with bleaching, textiles, feathers, and other surface-contaminated articles, and have been only limited by questions of expense.

Hydrogen Peroxide.—The earlier experiments showed that this was a bactericide which appeared inert to enzymes[2] such as diastase, ptyalin, pepsin, and pancreatin, and did not injure foods. It is also innocuous and non-corrosive. These properties suggested its use for killing pathogenic organisms, and those that caused change in articles of diet, especially milk, and also as an internal disinfectant. Altehoefer[3] and most later observers state 1 per 1,000 of H_2O_2 is required to destroy pathogenic organisms in twenty-four hours. In 1903 the writers found that in milk raised to 50° C., then treated with 0·6 gramme of H_2O_2 per litre, and the temperature maintained at 52° to 55° C. for eight hours, pathogenic organisms, and even the spores of *B. anthracis* and *subtilis*, were killed; the milk was not physically altered, and kept for over a month unchanged in closed receptacles. Hydrogen peroxide thus aids pasteurization and enables it to be efficient at a lower temperature. Similar results have been obtained by Lewin and others, and by Hewlett.[4]

Peroxide of hydrogen is present in *sanitas* (*q.v.*). *Perhydrol* is a 30 per cent. or " 100 volume " solution of H_2O_2. The use of peroxide of hydrogen in medicine depends partly on its bacterial action. Registered names of solutions are *dioxogen* (3 per cent.), *hydrozone*, *glycozone* (in glycerine), and *pyrozone* (dental practice).

[1] Patent 22,355 of 1898.

[2] The catalytic enzymes present in malt, yeast, milk, and many organic liquids, mutually decompose one another (Van Laer, *J. Soc. Chem. Ind.*, 1906, 439, 550; 1909, 550), but the above statement remains practically true (see also *ibid.*, 1909, 1267).

[3] *Centr. Bakt.*, 1890, **8**, 129. See also Bruns (*Berl. Klin. Wochensch.*, 1900, **19**), Paneth, Bokorny and Paul, and Krönig (*loc. cit.*).

[4] *Lancet*, January 27, 1906.

Peroxides of sodium, magnesium (*hopogen*, *biogen*), zinc (*ectogan* or *dermogen*), and mercury generate oxygen or H_2O_2, and have analogous use. It is more stable in ether than in water; *ozonic ether* is an ethereal solution containing about 1·2 per cent. of H_2O_2, which has been used in whooping-cough and scarlet fever.

Nitric Acid and Oxides of Nitrogen.—The corrosive action of nitric acid limits its value as an active disinfectant, although, in common with all strongly dissociated acids, it is an effective germicide; the anion appears to exert a slight specific activity in solution. Behring[1] gives 0·26 per cent. as the antiseptic concentration for anthrax spores in blood-serum. Paul and Krönig[2] place it second to hydrofluoric acid in activity on anthrax spores, 1 gramme molecule per litre effectively sterilizing in less than two hours. Dr. J. C. Smith used it with success in 1780 for fumigation in a violent outbreak of typhus fever in the British Fleet.[3] Disinfection of rooms by nitrogen peroxide was carried out during the siege of Paris; forty-eight hours was required, and the cost was very high. Severe bronchitis and several deaths from poisoning have resulted from breathing this gas, and nitric disinfection has been replaced by safer methods, except in the local destruction of bacteria, as in laboratories.

According to Heinz[4] nitrous acid is a much stronger germicide than nitric acid, in spite of the fact that it is a very much weaker acid, a dilution of 1 : 100,000 being already toxic to algæ and many bacteria. Its potency must be ascribed to the reactivity of the acid and salts with the $-NH_2$ group of the cell organism.

Sulphur.—The uses of sulphur as a fungicide have already been referred to. The application of sulphur internally is due to its forming sulphuretted hydrogen in the system, and thereby destroying or enfeebling micro-organisms and higher parasites; it possesses the further advantage for internal uses in that it is a phagocytic stimulant.

Sulphur dioxide disinfection is still a subject of controversy, but certain of the unfavourable results adduced have been due to faulty application. Some of the discrepancies may be explained by the observations of Klein and Wynter Blyth, that while most pathogenic microbes do not thrive in an acid medium, some organisms thrive well in weak acids; therefore sulphur disinfection, though generally successful, may sometimes fail. Spores are not generally killed by it, while species like *B. anthracis* are extremely resistant to sulphurous acid. The dry gas has very little effect on micro-

[1] "Infektion u. Disinfektion." [2] *Loc. cit.*
[3] Vallin, "Désinfectants," 1882, p. 265. [4] "Handbuch der Exp. Path.," 1900.

organisms, but it destroys all vermin, and therefore is of special value in combating insect-borne diseases. As to its effects on the lungs, about 5 per cent. in the air has produced fatal results, but ½ per cent. can be tolerated for some time, and a larger amount with the protection of a wet towel alkalized with washing soda. For the uses of sulphur dioxide in room disinfection, see Chapter V.

According to Buchholz, sulphurous acid is a relatively strong bactericide, stronger than sulphuric acid. This must be attributed to the possession of an aldehyde-reacting grouping.

Sulphuric acid, like acids generally, by virtue of its dissociation into hydrogen ions, is antiseptic, and in some cases disinfectant; 0·05 per cent. (which is a palatable strength) is fatal to *Sp. choleræ* in fifteen minutes. Stutzen found that this strength disinfected iron pipes, cleaning out rust and sediment without sensibly attacking the metal. With 0·04 per cent., Ivanoff destroyed cholera organisms in Berlin sewage, and with 0·08 per cent. in that from Potsdam. In our laboratory we found that 0·035 per cent. kills *B. typhosus* in thirty minutes, and 0·07 per cent. in fifteen minutes, in impure water infected ordinarily with typhoid; but with very heavy infections the latter strength requires forty-five minutes. One of the writers recommended 0·09 per cent. as having advantages over heat sterilization in dealing with the drainage from hospitals and other infected areas; the acidity would speedily be neutralized on mixing with the bulk of the sewage.[1] In the Lienur process a much stronger sulphuric acid is used for sterilizing sewage, combined with the recovery of ammonia.

Sodium bisulphate has been introduced by one of the writers and Dr. Parkes as a means of sterilizing drinking-water for armies in the field and for travellers. Fifteen grains of $NaHSO_4$ to a pint of water in fifteen minutes destroys *B. typhosus* and *enteritidis*, *Spirillum choleræ*, and internal parasitic worms. In effervescent tabloids yielding a slightly acid solution it was used with success in the South African and Russo-Japanese Wars, and has been extensively used in the European War. Kenwood and Hewlett found that one tablet per pint of water killed *B. typhosus* and *S. pyog. aureus* in two minutes.[2]

Persulphates give off oxygen when moist, and are useful as hand disinfectants.[3]

Carbon disulphide, if it were not for other properties, would be a valuable disinfectant. As well as its alkaline compounds, the

[1] British Association, 1901.
[2] Martindale's "Extra Pharmacopœia," 1908, p. 932.
[3] *Lancet*, 1905, ii., 1106.

xanthates, it has been found useful against fungi, such as the vine phylloxera. For this purpose it would appear that it may be supplanted by chlorpicrin, which was found by Moore[1] to be over 280 times as effective, requiring a dose of only 0·5 pound per 1,000 cubic feet of space. Ckeandi Bey's lamp burns it safely for generating sulphur dioxide.

The Halogens.

Chlorine, bromine, and iodine act as disinfectants in several ways. They can combine directly with organic substances or replace the hydrogen in them, precipitating albuminous substances and rendering them imputrescible, killing organisms by combining with and coagulating protoplasm, removing their food or rendering it unsuitable, acting to them as irritants or direct poisons, also producing substances which have that effect.

Chlorine and the hypochlorites, like other oxidizers, are consumed by otherwise inert organic and inorganic matters present, but in ordinary disinfection leave behind them as substitution compounds which maintain the germicidal powers, the chloramines, hydrazine, and the chloroproteins.[2] In dilute solution the R.W. coefficient is 2·18 for 1 per cent. of available chlorine; this is increased to 6·36 by the addition of an equivalent of ammonia. It remains near this level for twenty-four hours, and even after seventy-two hours has an enhanced value. Therefore, since the coefficient of chlorine itself averages 220 units, that of ammonia less than 0·7, and ammonium chloride nil, that of the chief product, chloramine, NH_2Cl, must be over 600 units; hence, this substance, but for its instability, would probably be the most valuable of disinfectants. It has a pungent odour, hitherto often mistaken for chlorine or hypochlorous acid, and gives the blue reaction with potassium iodide and starch. With excess of ammonia, as in sewages, it gradually disappears, forming a salt of hydrazine, which still has a germicidal value (R.W. coefficient of the base at least 24). The action of chlorine on nitrogenous organic compounds gives compound chloramines, many of which are insoluble; they have a tendency to become fixed on cellulose, and in this way attack the envelopes of organisms. Chlorine in the free state has been generally disused in disinfection, with the exception of water sterilization (see p. 80), on account of difficulties in practice. Preparations must be tested as to the amount of "available chlorine." Chloride of lime, or "Calx chlorinata," about 33 per cent. available chlorine, has some advantages from being solid, but is quickly deliquesced and decomposed by air, takes some time to dissolve, and gives a quantity of insoluble

[1] *J. Econ. Entomol.*, 1918, **11**, 357, 443.

[2] Rideal, *J. Roy. San. Inst.*, 1910, **31**, 2.

waste. There is in many respects a preference for sodium solutions: chlorinated soda, or *Eau de Labarraque* (often called *Eau de Javel*, which was originally the potash salt), about 2·5 per cent. available chlorine; *Chloros*, 10 per cent. available chlorine; and the electrolytically prepared hypochlorites, up to 11·5 per cent. available chlorine. *Hermite fluid*, used successfully at Poplar, employs magnesia as an adjunct in the electrolysis, and contains free hypochlorous acid, 4·2 per cent. available chlorine. The effective strength for local disinfection is 0·35 per cent. available chlorine, which kills non-sporing organisms in five to ten minutes, and anthrax and enteritidis spores in one and a half hours. Chloride of lime has the objection that it leaves the surface for a long time damp from the presence of sodium chloride. The same salt imparts its bitter taste and increases the hardness when it has been applied to the purification of drinking-water, while the sodium preparations tend to soften the water and are not sensible in the flavour.

Hypochlorous Acid.—For medical purposes various modifications of the original Dakin's solution have been prepared. These preparations all owe their germicidal activity to hypochlorous acid liberated by the action of a slightly stronger acid from bleaching powder or sodium hypochlorite. In order to ensure that the hydrogen-ion concentration of the solution shall not change in storage, thus obviating the danger of a too acid or alkaline reagent being brought into contact with living tissue, and at the same time minimizing the rate of decomposition of the acid, a buffer salt—*e.g.*, a borate—is added to the solution.[1] It would appear that hypochlorous acid itself exerts its germicidal activity by the formation of substituted chloramines with the nitrogenous constituent of the tissue according to the general reaction:

$$>NH + HOCl \rightarrow >NCl + H_2O.$$

Amongst the many preparations containing free hypochlorous acid and a buffer salt may be mentioned *eupad*, a powder consisting of equal weights of bleaching powder and boric acid; *eusol*, prepared by the solution with the subsequent filtration of 25 grammes *eupad* in a litre of water.

For medical purposes, in addition to their uniformity of composition, these stabilized solutions of hypochlorous acids possess other advantages in that they are hæmolytic, do not dissolve dead tissue, are non-irritant, and have a high penetrative power. Dakin[2] suggests the following mixture as suitable: bleaching powder,

[1] H. D. Dakin, *Brit. Med. J.*, December 4, 1915.
[2] *J. Soc. Chem. Ind.*, 1915, 919.

200 grammes mixed with water (10 litres) containing 140 grammes sodium bicarbonate, and the following liquid made neutral with from 25 to 40 grammes of boric acid. Excess boric acid is to be avoided. Staphylococci were found to be killed in two hours by 1 : 500,000, whilst these organisms in blood were destroyed by 1 : 1,000 to 1 : 2,000.

Pastes have likewise been prepared on the same principle; thus Monziols[1] suggests a paste of the following composition: 10 grammes H_3BO_3, 15 grammes talc, 2 grammes chloride of lime with a little water. It is claimed that it will sterilize the hands in three minutes.

Dr. Cash, from experiments on anthrax and tubercle, maintained that the quantities of chlorine, bromine, and iodine required for disinfection under the same circumstances were nearly in the ratio of their atomic weights. Iodine is, however, a more immediate poison to protoplasm than chlorine.

Bromine is a powerful disinfectant, a saturated aqueous solution having a carbolic acid coefficient of 64, but its use is obviously limited by its danger. In 1897 Altmann patented a solution of bromine in potassium bromide with five minutes' contact and removing excess by ammonia; the potassium salt has disadvantages. Braithwaite introduced a dry mixture of sodium or potassium bromide and bromate with sodium bisulphate, which with moisture liberates bromine. Schumberg, of the German Army, about the same time recommended free bromine in thin sealed tubes for the same purpose,[2] in the proportion of 60 parts per million with five minutes' contact, removing excess by thiosulphate. Braithwaite advised about the same amount, 57 parts; Schüder[3] and others have stated that this treatment is insufficient to sterilize and the presence of residual bromides is against the process.[4] It was tried in the Sudan campaign of 1898. The writers found that 20 parts per million of bromine sterilized *B. typhosus* in less than half an hour.

Iodine owes many of its uses to its germicidal action, as in parasitic diseases, a saturated solution of iodine having a carbolic acid coefficient of 100. Grossich,[5] in 1908, adopted the tincture as a cutaneous disinfectant before operation, the surface being previously cleansed by a 1 per cent. solution of iodine in benzene.[6] Instead of tincture, Chassevant[7] suggested the solution in iodoform, as it does not, like the former, cause desquamation; its use is specially

[1] *Compt. rend. Soc. Biol.*, 1918, **81**, 600.

[2] *Zeitsch. Hyg.*, 1900, 53.

[3] *Ibid.*, **37**, 306.

[4] See also Parkes and Rideal, *Trans. Epidem. Soc.*, 1901, **20**; Frazer, *Public Health*, September, 1902.

[5] *Centr. Chirurg.*, No. 4.

[6] Bogden, *ibid.*, January 15, 1910.

[7] *Lancet*, March 26, 1910.

advised prior to hypodermic injections.[1] During the Sikhim and Thibet expedition iodine (in some cases as tincture), followed by sodium sulphite, was successfully employed for sterilizing drinking-water; and Lieutenant Nesfield recommends triple tablets of (*a*) iodide and iodate, (*b*) citric or tartaric acid, followed after two minutes' contact by (*c*) sodium sulphite, and states that, used in this way, 3·8 to 5 parts per million of free iodine sterilizes the organisms of typhoid, cholera, and dysentery. The writers, in 1905, confirmed this result as regards distilled water infected with 20,000 per c.c. of *B. typhosus;* the (*a*) and (*b*) tablets, used as directed, gave 4·75 parts of iodine per million.

Fumigation of sick-rooms with iodine, sometimes in conjunction with other disinfectants, by burning prepared candles or lamps has been tried, but apart from the fact that the method is unsatisfactory, no chamber can be disinfected while occupied.

Iodine trichloride was introduced by Von Langenbach for sterilizing the hands and instruments and for other surgical uses. The writers find that 50 parts per million are required to kill typhoid in thirty minutes. A saturated solution of iodine trichloride in water has a carbolic acid coefficient of 94. Its activity is but little impaired by the addition of albumin or salts.

Iodine cyanide is said by Kobert to be universally destructive to lower forms of life, and is suggested for preserving biological specimens.

Fluorides.—Hydrofluoric acid is one of the most germicidal of the acid group of disinfectants. Paul and Krönig stated that sterility in anthrax spores was produced in less than two hours by a concentration of 1 gramme per litre. The specific activity of the fluorion is noted by the fact that fluorides are powerful antiseptics, but not germicides. This activity can in part be accounted for by the fact that it is a specific reagent for calcium, which is to be found in cell nuclein.

As food preservatives they are only moderately efficient, and are not innocent physiologically, as they hinder pancreatic digestion. Sodium silico-fluoride (*salufer*) and boro-fluoride have been tried. Effront introduced the use of hydrofluoric acid and its acid salts for checking injurious fermentations, and J. Brand[2] states that a 0·5 per cent. solution of acid ammonium fluoride is largely used for disinfecting rubber hose in breweries.[3] Fluorides form the active principle in certain mouth washes.

[1] *Brit. Med. J.*, February 6 and August 14, 1909; *Lancet*, April 16, 1910.

[2] *Zeitsch. Brauw.*, 1904, **27**, 115.

[3] See also Hehner, *Analyst*, 1902, 173; Richmond, "Dep. Comm. on Preservatives," Appendix XXXII.; Thresh and Porter, "Preservatives," 1906, p. 873.

Halide Acids.—HCl, HBr, HI are relatively strong germicides, their activity being proportional to their dissociation; the anions appear to exert but little selective action.

Cyanogen and Hydrocyanic acid (a weak acid) are more destructive to insects than to lower organisms. Fumigation of fruit-trees with hydrocyanic acid is extensively practised in America, and is considered better than spraying. For greenhouses zinc capsules containing sodium cyanide are made; they are placed in a vessel of dilute sulphuric acid, when the zinc dissolves, while the operator has time to retire.

Boric acid, which is feebly dissociated, is not a disinfectant, but has a power of restraining bacteria which act injuriously in foods. Rideal and Foulerton found that 1 in 2,000 of a boric mixture containing 3 parts of H_3BO_3 and 1 part of crystallized borax keeps milk sweet for twenty-four hours without appreciable effect on digestion. Koch noted the relative antiseptic concentrations for anthrax spores were 1/2,000 for borax and 1/1,250 for boric acid. The British Departmental Committee, already referred to, recommend that the only preservatives allowed to be used in cream, butter, and margarine be boric acid or mixtures of boric acid and borax in proportions of 0·25 per cent. of H_3BO_3 for the former, and 0·5 per cent. for the latter two. Its carbolic acid coefficient is less than 0·1.

Carbonic acid seems to have a certain amount of disinfectant action, since "aerated" beverages have been shown to be in many cases sterilized, and carbonic acid under pressure preserves food.

H. Colin[1] shows that both time and pressure are required to effect sterilization by carbon dioxide. Thus, water contaminated with *B. typhosus* was sterilized in twenty hours at 10 atmospheres, in eight hours at 15 atmospheres, at from three to four hours at 20 atmospheres, and from three to six hours at 25 atmospheres of carbon dioxide.

B. coli was found more resistant, requiring more than five days' contact at 25 atmospheres. The *B. choleræ* was easily destroyed in ten hours at 10 atmospheres, and ordinary Seine river-water almost completely sterilized in a few hours at 25 atmospheres.

B. Metallic Derivatives.

The Alkaline Metals.—The ions of the alkaline metals exert but little selective effects on micro-organisms. Blake[2] noted an increase in physiological activity with increasing atomic weight, but

[1] *Compt. rend.*, 1915, **161,** 652.
[2] *Proc. Roy. Soc.*, 1891, **14,** 394.

C. Richtet[1] gives the equivalent toxic ratios for lithium, potassium, and rubidium as 1·1 to 0·5 to 1·0.

In the simpler salts the additive effects of the relatively inert anions and cations can be noted in the increasing activity displayed by NaCl, NaBr, NaI, NaF. Strong brine is preservative but not disinfectant, and the practice, formerly frequent, of washing out milk cans and other utensils with it is not a safe one. Lode[2] showed that 50 per cent. salt solution does not kill spores of moulds.

The hydroxides in the form of alkaline lyes are to be classed amongst the most ancient of disinfectants. They effect sterility in the proportion of not less than 2 to 5 per cent., and the carbonates in from 5 to 10 per cent. concentration. At 60° C. a contact of five minutes ensures the death of most organisms,[3] hence washing soaps which undergo partial hydrolysis in their solutions possess a slight disinfectant value (see p. 108). Caustic soda has even been suggested for destroying *B. anthracis* in hides (see p. 147). The germicidal activity of these solutions is proportional to the hydroxyl-ion concentration,[4] which has a specific germicidal activity of about one-fifth of the more active hydrogen ion. The feebly-dissociated base ammonium hydroxide has but slight value as a germicide.

The Alkaline Earths.—Of the alkaline earths, lime, as quicklime, is the only compound which has been used extensively as a germicide. Its activity is to be attributed to its caustic and hygroscopic properties when dry, and to the presence of hydroxyl ions when in solution or suspension. No definite evidence for any specified activity of the calcium ion is on record.

Quicklime is fatal to bacteria when it comes in contact with them in an almost dry condition, and has been much used where there is a considerable space and bulk of material to be dealt with. It is not safe, however, to trust entirely to the old method of burying infected bodies in lime, as on disinterring the live spores may again be diffused, unless a long period has elapsed. The disinfecting power of milk of lime and whitewash has been much overrated; as to milk of lime, Liborius[5] stated that 74 parts per million of CaO destroyed typhoid bacilli, and that 246 parts per million were required for cholera organisms, while 2 per cent. of dry lime was needed for cholera discharges, with in each case "a few hours'" contact. When lime is added to sewage, a great number of bacteria are carried down, but are not killed, and the supernatant liquid is not sterilized.

[1] *Compt. rend.*, **101**, 667. [2] *Chem. Zentr.*, 1902, i., 1122.

[3] *Zeitsch. Hyg.*, 1903, 349.

[4] Strictly the "activities" or thermodynamic concentrations and not the actual concentrations should be employed in all cases where comparative data are required. For dilute solutions the two are almost identical.

[5] *J. Soc. Chem. Ind.*, 1915, 632.

The Heavy Metals.—Some metals in the free state are antagonistic to germs. Dievert[1] states that agitation with granulated zinc kills *B. typhosus* and *coli* in a few hours, and Baeyer's method of treating polluted waters with zinc dust, charcoal, and lime causes, according to Margosches,[2] practical sterilization. Rankin[3] shows that clean strips of aluminium, zinc, or copper in air-free water do not reduce the number of coli, while, when air is bubbled through, there is a great reduction after one hour. Except with copper, peroxide of hydrogen was produced, but the amount of this and the metal dissolved is too small to account for the germicidal effect, which is ascribed to the oxide and metal together. Metallic iron has long been used for purifying water, as in Anderson's[4] process; in this case electro-chemical action, resulting in the formation of flocculent hydroxides, comes largely into play, but Frankland proved that the metal itself was to a certain extent bactericidal.

Old Hindu writings direct water to be kept in vessels of copper; among modern observers, Nageli, Galeotti, Israel, and Klingman hold that there is formed a colloidal solution that renders the water toxic to many algæ and bacteria. In 1904 the U.S. Department of Agriculture reported that 1 square centimetre of bright copper per 100 c.c. of water was sufficient to exterminate uroglena and some forms of spirogyra, and Kraemer showed that the same treatment destroyed colon and typhoid bacilli in four hours, while colloidal copper was quickly fatal to these organisms. For household purification he recommended the use of strips of copper about $3\frac{1}{2}$ square inches to each quart (2 square centimetres to 100 c.c.) immersed in the water for about six to eight hours. In a similar way Rideal and Baines[5] obtained sterilization of *B. typhosus*, *B. coli*, and *Sp. pyog. aureus* in less than twenty-four hours. Bassett Smith[6] found that in a bright copper vessel *B. typhosus* was still living at twelve hours, but dead at twenty-four hours, and that of ordinary water organisms, 1,020 per c.c. at first, only 8 per c.c. (none of them liquefying) were left after twenty-four hours. He also found that clear iron or zinc was nearly equal to copper in first effect, but soon lost the power by oxidation.

Colloidal Metals.—For medical purposes a great number of colloidal metals have been proposed, especially those in which the ions of the metals are powerfully germicidal, such as mercury; silver, *collargol*, *argoferment*, *syrgol*, *albargin*, *lysargin*; copper, *cupriase*, and copper oxide, *cuprase*; arsenic, and others.

[1] *Compt. rend.*, **136**, 707.
[2] *Leipz. Monatsh. Textil.*, 1901, **6**.
[3] *Proc. Roy. Soc.*, 1910, B, **82**.
[4] *J. Soc. Arts*, February 14, 1896.
[5] *J. San. Inst.*, 1904, 594.
[6] *J. Prevent. Med.*, July, 1904.

The colloidal metals themselves, prepared by electrical dispersion or by chemical reduction methods, are too unstable for practical work, being rapidly precipitated by electrolytes *in vitreo* or in the blood-serum. It is thus necessary to protect the colloidal metal with some suitable protective colloid. Protective colloids, such as protalbic and lysalbic acids, are the most used, owing to their great protective powers, but it is customary not to isolate these materials in the pure state, utilizing instead proteins and nucleins. Less efficient as protecting agents are gelatine and the starches which occasionally find application. The importance of the nature of the protective colloid employed cannot be over-estimated, since it is highly probable that the colloidal metal is germicidally operative by a gradual decomposition into ions, which are the active germicides. The rate of this gradual ionic disintegration or chemical solution is governed by the protective colloid. The function of a protective colloid appears to be twofold: first, a peptizing action on the colloid which ensures a high dispersivity essential for the economic utilization and the uniform distribution of the agent; and, secondly, a coating action on the sol, through which the reagent and the ion have to travel before the latter can become germicidally active. A well-protected colloidal metal is non-toxic, owing to the very slow release of ions through the protective agent, whilst an unprotected sol is usually extremely toxic. This difference in the degree of protection would seem adequately to account for the anomalous results obtained with colloidal arsenic from different sources.[1] Thus the protective agent should be varied with the power of the patient to excrete toxic ions, since, naturally, the ionic concentration should be raised as high as is compatible with safety to the health of the individual.

Both colloidal mercury, silver,[2] and gold[3] have been used with success for disinfection *in vivo;* they may be injected intravenously, intramuscularly, or hypodermically in the peripheral zones of the infected region.

Copper salts have a distinctly poisonous action on lower organisms, partly from their property of coagulating albumin and combining with many of the constituents of the tissues. Kroncke considered cuprous chloride to be the most active of the salts; he treated Elbe water containing 40,000 to 50,000 organisms per c.c. with 50 per million of cuprous chloride and 20 parts of ferrous sulphate, allowed six hours' contact, then agitated with 10 parts of lime. After settling and filtering through sand, the water was sterilized, clear and colourless, and free from iron and copper.

[1] See Sorev, *Compt. rend. Soc. Biol.*, 1918, **81,** 563.

[2] Marshall, *Brit. Med. J.*, June, 1915. [3] M. Pollard, *Lancet*, May, 1915.

Schumberg[1] corroborated the sterility at the end of the six hours. The efficiency of soluble cupric salts is generally dependent on their percentage of copper,[2] but the sulphate is commonly used as most convenient. For disinfecting sewage effluents, American investigators conclude that copper sulphate "is not so efficient as chlorine compounds, is more seriously affected by carbonates, and is much more expensive."[3] Disinfection of excreta and morbid products, even with considerable quantities of copper salts—*e.g.*, 5 to 10 per cent. of the sulphate—is not reliable. Copper soap washes for trees and *Bordeaux mixture* (copper sulphate and lime) for vines are well known; Chuard[4] estimates that 2,000 tons of copper are thus consumed annually in France, and expresses anxiety as to the result of its accumulation in the surface soil, and with a view to reducing the quantity states that a ½ per cent. aqueous mixture of the oxychloride is as adhesive and effective as the usual 2 per cent. paste of the sulphate.

Mercury Salts.—Mercuric chloride, "corrosive sublimate," has long been recognized as one of the most powerful of disinfectants, and a 1 per 1,000 solution is a kind of standard for comparisons. Apart from cost, points limiting its utility to special purposes are (1) its poisonous effect on higher animals and plants; (2) its precipitation by so large a number of substances, such as hard water, alkalies, and numerous salts, metals, sulphides, and many organic bodies, causing its action to be liable to great variations and inconveniences. It will often form a pellicle over organisms without killing them, and it is inapplicable to the disinfection of sputum, excreta, and the like, since it produces a coagulum which prevents further penetration. Sodium chloride is sometimes added to increase the stability, but considerably diminishes the germicidal power. The Local Government Board recommended for disinfecting purposes: Mercuric chloride, ½ ounce; hydrochloric acid, 1 fluid ounce; aniline blue (a colouring for safety), 5 grains; water, 3 gallons (1 in 962). Krönig and Paul's work in 1897 showed that mercury salts follow a general rule that the germicidal power depends on the metallic ion, and is in proportion to the degree of ionization, so that a 1 in 500 solution of mercuric chloride is much less than twice as active as a 1 in 1,000 solution; moreover, the chloride is more active (in equivalent solutions) than the bromide, and four times more active than the cyanide, which is almost unionized. Solutions of the oxycyanide have been used in surgery, have a slight alkaline

[1] *Chem. Zentr.*, 1900, ii., 203.

[2] Green, *Zeitsch. Hyg.*, 1893, 495; Rideal and Baines, *loc. cit.*

[3] U.S. Geol. Survey, Water Supply, Paper 229 of 1909, p. 32; also *Bull. U.S. Dept. of Agric.*, No. 100, 1906.

[4] *Compt. rend.*, 1910, **150**, 839.

reaction, and only slightly precipitate albumin; in a strength of 1 in 1,500 it is antiseptic, does not readily attack instruments, nor irritate sensitive parts. Mercuric iodide, dissolved in potassium iodide, is a powerful disinfectant, and is made up in tablets as "Iodic hydrarg." It is less affected by albuminoids and less irritant than the chloride, and can be incorporated in soaps. Mercury zinc cyanide, *Lister's antiseptic* has the disadvantage of being of variable composition.[1] A great number of organic mercurial compounds introduced into medicine and surgery owe part of their effect to an antiseptic or germicidal action. *Sublamin*, mercuric ethylenediamine sulphate (43 per cent. Hg), is easily soluble in water, is much less irritant than mercuric chloride, does not coagulate albuminous solutions nor precipitate soap, and is a valuable hand disinfectant. *Protectyl*, according to Drs. Aufrecht and Feibes, contains about 96 per cent. water, 1 per cent. salicylic acid, 0·2 per cent. mercury, and about 3 per cent. gelatine.

Silver Salts.—Silver nitrate stands next to mercuric chloride in germicidal power, and has the same limitations in use, with the additional one of being precipitated by chlorides. The writers found that in distilled water 1 in 1,000 killed *B. coli* and *S. pyog. aureus* in twenty-four hours, but a small quantity of chloride or organic matter prevented the effect. Martindale gives 1 in 2,000 for killing in two and a half minutes. Among other silver salts are the citrate, *itrol*, recommended as a non-irritant antiseptic dusting for wounds;[2] *actol*, the lactate for antiseptic injections; *argentide* (silver iodide), used as a precipitant and germicide for water; *tachiol*, silver fluoride, easily soluble, and said to be a powerful non-toxic bactericide, specially suitable for use in the urinary tract (1 in 1,000 to 1 in 5,000). Chiefly with the object of avoiding irritant action, incompatibility with chlorides, and coagulation of albuminoids, a large number of organic preparations of silver have been introduced, which will be enumerated later.

Zinc Salts.—Zinc chloride, *Burnett's fluid*, formerly in high repute as a disinfectant, is not reliable in its effect, and ranks below copper sulphate and mercuric chloride. The sulphate is still less active.

Aluminium Salts.—Aluminium chloride, *chloralum*, was classed by Miguel between zinc chloride and copper sulphate. *Alsol*, a solution of aluminium acetotartrate, is recommended in treatment of eye diseases.

Iron salts, especially ferrous sulphate, were at one time in vogue for sanitation, but are comparatively ineffective.

[1] *Trans. Chem. Soc.*, 1892, 666. [2] *Pharm. Centralblt.*, **38**, 460.

Permanganates and Manganates were first introduced as *Condy's red* and *green fluids*. Like oxidizers generally, they are largely consumed by otherwise inert matters before attacking organisms, and as complete disinfection cannot be ensured unless an excess of reagent remains, evidenced by the pink colour, which is not always visible owing to the brown oxide of manganese produced, their use may be very costly, and the result is frequently imperfect. The writers carried out an experiment in street watering of two similar areas of ordinarily soiled asphalt roadway, (*a*) with water alone, (*b*) with permanganate solution 1 in 5,000 (six times the amount then customary), and examined the liquid from the surface. The permanganate was almost immediately decolourized. The sample (*b*) was nearly inodorous, on keeping became much less foul than (*a*), and the reduction in the number of organisms was 96 per cent., but the survivors included a large proportion of dangerous forms.[1] For polluted water Rosenau recommends adding permanganate drop by drop till the pink colour persists for twenty-four hours. "Pinking" of wells was many years ago adopted by Hankin in India as a precaution against cholera. Permanganates, used in various ways, are still being patented, chiefly for water purification.

Arsenic Salts.—The inorganic salts of arsenic have but a limited application as germicides on account of their toxicity. The organic arsenicals, on the other hand, which permit of slow liberation by hydrolysis of arsenious ions within the organism, are amongst the most potent of the trypanocides and spirillocides yet discovered. Trivalent arsenious derivatives are more germicidal than the pentavalent compounds; thus arsenious acid was found to be three hundred times as germicidal as arsenic acid on isolated organisms,[2] trypanosomes were destroyed by concentrations of 1 : 20,000 of the former, but 1 : 100 of arsenic acid was required. Friedenthal[3] found arsenious acid a stronger disinfectant than boric acid. Similarly sodium arsenite was much more antiseptic for yeast cells than the sodium arsenate.[4] Green and Kestell[5] find instances of selective action of the arsenites on micro-organisms; thus to a 0·05 per cent. solution *B. subtilis*, coliform organisms and three out of four strains of cocci were found sensitive; *B. putridium* was found insensitive.

Arsine is apparently much less active than arsenious acid, as instanced by its action on infusoria.[6]

[1] Rideal's "Sewage," 1906, p. 177.
[2] Joachimoglu, *Biochem. Zeit.*, 1915, **70**, 144.
[3] *Biochem. Zeit.*, 1919, **94**, 47.
[4] Joachimoglu and Friedberger, *Biochem. Zeit.*, 1917, **79**, 136.
[5] *S. Africa. J. Sci.*, 1919, **15**, 360.
[6] Fühner, *Arch. Exp. Path. Pharm.*, 1917, **82**, 44.

Arsenic, like cyanogen, has more effect on higher than on lower forms of life, and is the basis of valuable insecticides, such as the sheep-dip solutions of arsenious oxide or sulphide in soda, frequently associated with tar products or nicotine (see p. 145), and the copper compounds, *Paris green* (accto-arsenite), and others, used for spraying or dusting trees. In the latter case the actions of arsenic and copper are combined, and the fineness of the powder is of great importance.

Antimony.—The antiseptic and germicidal powers of the stibnites and stibnates are much more feeble than those of the corresponding arsenicals. In this case also the derivatives of trivalent antimony are more powerful than the pentavalent compounds. Colloidal antimony and stibnous acid, $Sb(OH)_3$, exert a definite but weak germicidal action, a 30 per cent. emulsion of the latter, *trixidin*, having been used with success as a spirillocide. The thiostibnate, Na_3SbS_4, is likewise stated to be trypanocidal. Behring[1] found that the double fluoride of antimony and potassium was nearly as effective as mercuric chloride.

Bismuth.—A number of compounds containing bismuth oxide have been prepared and utilized as internal astringents and disinfectants. Their antiseptic power is, however, low, and they possess but little, if any, germicidal activity. Their action is in most cases confined to a protective action. Amongst the more usual preparations of this type may be mentioned *bismona*, a colloidal bismuth oxide, and *bismuthose*, containing the oxide incorporated with albumin. The organic derivatives are enumerated later (p. 278).

Osmic acid was found by Koch and Klein to be powerfully bactericidal; it is very poisonous and a strong oxidizer. The former stated that an extremely dilute solution of potassium auricyanide, 1 part in 2,000,000 checked the growth of *B. tuberculosis*, whilst Behring noted that anthrax was destroyed *in vitreo* by a concentration of 1 in 1,000,000.

Chromic acid, although a powerful oxidizer and instantly coagulating albumin, is excluded by its cost and poisonous and corrosive nature from the list of useful disinfectants or of preservatives; $2\frac{1}{2}$ per cent. solution kills *B. coli* in two and a half minutes.

[1] "Infektion und Disinfektion," Leipzig, 1897.

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CHAPTER XI

THE CHEMICALS EMPLOYED IN DISINFECTION—*Continued*

ORGANIC SUBSTANCES: ALIPHATIC DERIVATIVES.

Hydrocarbons.—The saturated hydrocarbons of the paraffin or petroleum series, such as heptane, C_7H_{16}, and the petrols, C_5H_{12},C_6H_{14}, possess no distinct germicidal power, but have long been used as insecticides in horticulture.

Acids.

The antiseptic power of the aliphatic acids, as well as the dissociation constant, generally decreases with increasing molecular weight.

Formic acid, HCOOH, has a higher antiseptic power than the next homologue, acetic acid, due not only to the greater dissociation, but also to the aldehyde grouping, although Kitasato's results, as summarized by Horrocks, gave acetic acid a slightly higher activity in nutrient media, probably owing to interaction of the aldehyde grouping with $-NH_2$ groups in the medium. He states that with *B. typhosus* the amounts per cent. in cases of (1) growth, (2) growth restrained, (3) no growth, were respectively: Formic acid, 0·22, 0·278, and 0·356; acetic acid, 0·2, 0·225, and 0·3; with *Sp. choleræ:* formic acid, 0·11, 0·167, and 0·22; acetic acid, 0·1, 0·153, and 0·2. But very different results were obtained in water and most organic solutions. In our laboratory it was found that *B. typhosus* is killed by 0·5 per cent. of formic acid in less than fifteen minutes, and by 0·1 per cent. in about thirty minutes, and the R.W. typhosus coefficient of formic acid is many times higher than that of acetic acid. We have also found the preservative action to be higher; with vegetable substances 1 per cent. of formic acid was found to be equal in effect to 5 per cent. acetic acid (time of trial two months). Raw fish were mounted in 0·53 per cent. formic, in 5 per cent. acetic, and in 0·3 per cent. boric acids, heated for twenty minutes at 80° C., and the jar closed with cotton-wool; the last was brownish, disintegrated, and uneatable, though not distinctly putrid, in a week; the first two kept sweet and of a natural character for three months. Experiments with a bread pulp infected with a mixed mould growth proved that 0·1 per cent. of formic acid is sufficient

to entirely inhibit the growth of moulds for several days even under the most favourable conditions of culture. But in the destruction of the spores formic acid is less effective than formaldehyde. Lebbin[1] efficiently preserved different classes of foods by 0·15 per cent. of formic acid, and specially recommends it for fruits and syrups. The writers, Lebbin, and others, have proved that in the quantities mentioned above it is physiologically harmless, the taste is more pleasant than acetic acid, and the odour is not noticeable. B. H. Smith[2] preserved vegetables with formic, salicylic, and benzoic acids in unprotected jars. Under conditions in which the untreated samples became mouldy and sour in two days, 0·1 per cent. formic acid preserved them for seven days, 0·3 per cent. for twelve to eighteen days, 0·5 per cent. for twenty-five to thirty-four days, 0·7 and 1 per cent. for forty-five to eighty-five days, and 2 per cent. for over eighty-five days. He states that 0·1 per cent. of benzoic acid kept his samples for eighty-five days, while with the same quantity of salicylic acid it was sour in nine days. In ordinary preserving practice, as we have seen, the articles would have remained good for the longer time with the lesser quantities of formic acid, which, even if it must be applied in a somewhat higher proportion, is for physiological reasons preferable to salicylic or benzoic acids. The chief formic acid preservatives used in commerce, mainly for fruit preparations, are *werderol* and *fructol*, 10 to 14 per cent. formic acid, "1 to 1¼ per cent. of the liquid to be added"; and *alacet* (made synthetically from carbon monoxide and sodium hydroxide at the Nitritfabric, Köpenick), about 50 to 60 per cent. formic acid, "use 0·3 per cent. of the liquid." The result in the three cases would be about 0·14 to 0·18 per cent. formic acid. In an investigation of these products, Croner and Seligmann[3] find that inhibition of moulds, yeasts, and acid-forming organisms begins at 0·15 per cent. formic acid, that sterilization is effected in twenty-four hours by 0·2 per cent., and in ten to thirty minutes by 1 per cent.

Only the free acid is germicidal, although the salts do not favour the growth as do the alkaline acetates. Sodium formate increases the solubility of many antiseptics without lessening their power, and therefore figures as an adjunct in a number of patents.

Acetic acid is one of the most anciently used preservatives; *aromatic vinegar*, and a more or less concentrated acid containing essential oils, had a partially justified reputation against infection. The authors found that *B. coli* is killed by 5 per cent. acetic acid in

[1] *Chem. Zeit.*, 1906, **30**, 1009.
[2] *J. Amer. Chem. Soc.*, 1907, 1236.
[3] *Zeitsch. Hyg.*, 1907, **56**, 387.

five minutes, by 2·5 per cent. in fifteen minutes, while with 0·5 and 0·1 per cent. it is alive after forty minutes.

Pyroligneous acid, or crude wood vinegar, owes its antiseptic power chiefly to the presence of creosote and formaldehyde.

Propionic acid has been tested comparatively by Duggan[1] with the highly resistant *B. subtilis*. He gives as the strengths necessary for killing: Formic acid, 7 per cent.; acetic acid, 9 per cent.; propionic acid, 12 per cent.; numbers proportional to the molecular weights. According to A. C. Jordan,[2] 0·1 per cent. of **butyric acid** in broth-tubes infected with vigorous cultures of *B. typhosus* caused them to remain sterile; *S. pyog. aureus* required 0·2 per cent.

Valeric acid is a feeble antiseptic, but has been introduced, incorporated with a little creosote, as an internal antiseptic called *geosote*.

Oleic acid and the fats, lanoline, etc., have no antiseptic power in themselves, but when applied to the skin may prevent infection by the exclusion of germs. Vicario, however, observed that fatty matter sometimes already contains germs, and Baldas[3] proved that *B. coli* and *typhosus*, *S. aureus* and *albus* retained their virulence in oils for two months; therefore, ointment bases require to be sterilized by heating to 100° or preferably to 120° C., as various bacilli survive in oil far longer than in aqueous solution. In fatty media antiseptics and disinfectants are, as a rule, much less active than in water, hence the ineffectiveness of carbolized oil, as shown by Koch and Breslauer. Lanoline and cold cream contain water, so can enable agents in aqueous solution to come in contact with organisms. Some metallic oleates are parasiticide, as cupric oleate in ringworm and favus,[4] mercuric oleate for pediculi; zinc oleate is said to cure chronic eczema. According to Reichenbach,[5] of the alkaline earth salts of the fatty acids, the palmitates are the strongest in bactericidal action. The potassium salts of the saturated fatty acids are strong bactericides, whilst unsaturated ones, with the exception of elaidic acid, are not (see Chapter VI.).

Oxalic acid is an irritant, corrosive poison, and is said to be antiseptic. Its solutions certainly inhibit the growth of organisms, whilst the oxalates only allow slow growth to proceed. Its toxicity is to be ascribed to the precipitation of calcium oxalate within the micro-organism.

Acids like tartaric, citric, and malic have the general power of inhibiting the growth of bacteria, which prefer a neutral to an acid

[1] *Amer. Chem. J.*, **7**, 62. [2] *Practitioner*, September, 1902, 297.
[3] *Giorn. Roy. Soc. Ital. d'Ig.*, February, 1901.
[4] *Lancet*, 1907, i., 510. [5] *Zeitsch. Hyg. Infekt. Krankh.*, 1908, **59**, 290.

medium, but their effect is much less than that of mineral acids (see Chapter X.), and, as is well known, their solutions quickly become mouldy in warm weather. Several algæ, such as spirogyra, are very sensitive to these acids, a concentration of 0·1 per cent. citric acid proving effective in thirty minutes, 0·05 per cent. maleic or tartaric acid being algicidal within twenty-four hours. According to Löw, even aspartic acid will kill algæ after several days' contact. Citric acid was formerly recommended for sterilizing water. Christmas, in 1892, stated that cholera organisms were killed by 0·08 per cent. and typhoid by 0·10 per cent. Kitasato's figures for tartaric, citric, and maleic acids in nutrient media are, in per cents.: Growth, 0·338; growth restrained, 0·384; no growth, 0·476.

Aceto-acetic acid is slightly germicidal, concentrations of 0·1 per cent. being markedly antiseptic; succinic acid is slightly antiseptic.

The influence of spatial arrangement is to be noted in fumaric and maleic acid; the latter is antiseptic for *Penicillium glaucum*, whilst the former is not.

Acid Peroxides.

Acetyl peroxide and benzoyl-acetyl peroxide are stated by Freer and Novy[1] to be strongly germicidal, as solutions corresponding to 0·005 to 0·01 per cent. of active oxygen (=0·037 to 0·074 per cent. of the former, or 0·056 to 0·112 per cent. of the latter) destroyed all known disease-producing bacteria, and even spores of *B. mesentericus* (which are not killed by 5 per cent. phenol), within a minute, while hydrogen peroxide solution containing 0·05 per cent. of active oxygen was without action on many bacteria, even in sixty minutes. Benzoyl peroxide had no oxidizing action, and was without effect on bacteria. A solution of acetyl peroxide was introduced under the name *acetozone*, but the title is now applied to a more stable and convenient mixture of the benzoyl-acetyl compound with infusorial earth, said to be useful in typhoid, dysentery, and cholera.[2] *Alphogen* or *alphozone*, succinyl peroxide, is said to be a powerful germicide,[3] a solution of 1: 5,000 killing *B. typhosus* in one minute.

Alcohols.

It has long been known that "wood spirit," crude methyl alcohol, in a dilution of as low as about 5 per cent. can kill insects and most micro-organisms, and preserve perishable organic materials, owing to the tar products that it naturally contains. The alcohols themselves are only efficient in a very much higher strength by coagulating albumin and (when absolute) by withdrawing water. Fowler gives the R.W. coefficient of absolute (ethyl) alcohol with

[1] *Amer. Chem. J.*, 1902, **27**, 161.

[2] *Lancet*, 1904, ii., 1160; *Brit. Med. J.*, 1907, i., 634.

[3] *Brit. Med. J.*, 1905, i., 1150; *Lancet*, 1905, i., 367.

B. typhosus as 0·03;[1] Wirgin[2] has tested methyl, ethyl, butyl, and amyl alcohol, with anthrax spores and *S. pyog. aureus*, and concludes that the disinfecting power is low, that it increases with the molecular weight, and that there is scarcely any action on dry spores.

Tsukamoto has compared the various alcohols in their action on infusoria; in this case also their lethal powers increase with the number of carbon atoms.[3] The minimum concentrations required were found to be for methyl and ethyl alcohol 2 to 3 per cent., for propyl alcohol 1 per cent. Normal butyl alcohol was found to be more active than the iso-, and this more than the tertiary alcohol. Amyl alcohol 0·01 per cent. and allyl alcohol 0·005 to 0·01 per cent. were found to be strong disinfectants for these micro-organisms. The tertiary alcohols are very weak germicides; thus propyl alcohol is a stronger disinfectant than tertiary butyl, and butyl stronger than tertiary amyl alcohol.

It has been suggested to add alcohol vapour in steam disinfection, but Siege[4] finds no advantage. Hand disinfection with alcohol is not reliable.[5] Hansen[6] found that epidermal bacteria, especially in suppurating eczema, when moist, are destroyed in one minute by absolute, and in most cases by 50 to 60 per cent. alcohol (see Chapter VI.). In many cases a 55 per cent. alcohol solution exerts the maximum germicidal activity.

Glycerol in strong solutions (25 per cent. and upwards) is antiseptic, but in weaker ones it rather promotes the growth of bacteria.

The esters such as ethyl acetate, ketones such as acetone and pinacone, exert little if any direct germicidal action.

Thio Derivatives.

The replacement of oxygen by sulphur in organic aliphatic compounds brings about a slight enhancement of the antiseptic powers.

According to Löw, methyl sulphide has but little action on algæ and diatoms. Methyl mercaptan in concentrations of 0·1 per cent. will destroy certain organisms such as diatoms, but small infusoria are not affected by it.

Thiodin or **Tiodine,** $C\begin{matrix}\diagup NH.C_3H_5 \\ = S \\ \diagdown NH_2(C_2H_5)I\end{matrix}$ has been claimed as a powerful germicide, but no comparative data are given. It would probably compare unfavourably with the more usual germicides. It is pre-

[1] See Hewlett's "Bacteriology," 1908, p. 341.
[2] *Chem. Zentr.*, 1903, i., 50; *Zeitsch. Hyg.*, 1904, **46**, 149.
[3] See Richardson, *Med. Times Gaz.*, 1899, **2**, 705.
[4] *Chem. Zentr.*, 1902, i., 130.
[5] Goenner, Harrington, *Boston Med. J.*, May 21, 1903.
[6] *Centr. Bakt.*, 1907, 466.

pared from thiosinamine and ethyl iodide, the former being used hypodermically for lupus.

Allyl isothiocyanate, mustard oil, has figured in a number of patents, and is capable of killing many organisms, but not economically.

The xanthogenic acids are stated to be disinfectant and strong preservatives.[1]

Ichthyol and its derivatives are dealt with in a subsequent section (see p. 279).

Aldehydes.

Substances containing the aldehydo grouping $-C\begin{matrix}H\\ \diagup\!\!\diagdown\\ O\end{matrix}$ are germicidal when the grouping is labile or active; in aldehydo sugars no action is to be observed, whilst the simpler aldehydes are by no means indifferent germicides.

Formaldehyde is found in commerce as the 40 per cent. solution, *formalin*, and is antiseptic and germicidal, being official in the British, German, Austrian, Belgian, and Japanese pharmacopœias. Formalin diluted ten times is used for embalming and for preserving bodies for dissection and museum specimens, but for antiseptic work generally a much weaker solution is sufficient. The uses of formaldehyde in food preservation and room sterilization have already been referred to. One of the writers and Dr. Foulerton have proved that 1 in 50,000 of formaldehyde (=1 in 20,000 of formalin) suffices to keep milk sweet for twenty-four hours even in warm weather without injury to health.[2] Apparently because experiments with larger doses showed effects on nutrition, the British Departmental Committee on Preservatives in 1901 recommended "that the use of formaldehyde or formalin or preparations thereof in foods or drinks be absolutely prohibited." And yet its agency in the preservation of foods is as ancient as that of salt. The disinfectant and preservative power of wood smoke is in part due to formaldehyde, which is present on the surface of smoked provisions. H. Will[3] gives formalin a very high place among brewery disinfectants, and notices, like other observers,[4] that it is more powerful against bacteria than against yeasts and mould fungi. Limits recorded as preventing development are: Sarcinæ and bacteria 0·003 to 0·031, yeasts 0·007 to 0·062; moulds 0·031 to 0·125 per cent. In faintly acid solution it appears to be slightly more effective than when neutral.[5]

[1] Lewin, *Virchow's Archiv*, 1878, 78.
[2] *Pub. Health*, May, 1899; *Lancet*, 1899, 1427, 1571.
[3] *Zeitsch. Brau.*, 1905, **28**, 330, 347.
[4] Kinzel, Slater and Rideal, *Lancet*, April 21, 1904.
[5] *Annali di Farm.*, 1899, **8**, 325

Advantages of formaldehyde in disinfection are: (1) That it can be easily applied in the form of gas or vapour for fumigation; in the liquid condition as spray, wash, dipping, or in higher dilutions as an antiseptic; or in the solid form as its polymers or mixtures; (2) that, unlike mercuric chloride and many other agents, it is not thrown out of action by albuminous matter or by other chemicals; (3) that it is effective in strengths that are not irritant or poisonous, and do not injure fabrics or metals. Rosenau states that in quarantine stations large quantities of bulbs, roots, nuts, fruits, etc., coming from plague or cholera infected regions are disinfected by immersion in a 5 per cent. solution of formalin, which does not injure the food value and retards decay. In surgery formaldehyde and its preparations have been of wide service. Salter[1] states that it rapidly kills the fungus of ringworm. As pigment or spray (1 to 2 per cent. formalin) it has been successful in diphtheria; in such strengths it quickly kills other non-sporing organisms, including, according to E. Blake, the *staphylococcus* of eczema. In most cases a ½ per cent. solution is sufficient. Geronzi found that the addition of 5 per cent. of sodium carbonate to the 5 per cent. formalin which he successfully used for obstinate ear disease increased the tolerance and enhanced the germicidal power[2] (*cf.*, however, *ante*).

Bokorny[3] has noted a very interesting case of selective action with formaldehyde: a 0·05 per cent. solution destroys yeast, but not the enzymes; 0·1 per cent. destroys zymase; and 1 per cent. destroys the cell, but not invertase; it is thus possible to prepare an inverting but non-fermenting yeast.

Paraform, paraformaldehyde, trioxymethylene, or *trioxymol*, is a solid polymer, only slightly soluble. Although its germicidal power is rather low, its R.W. carbolic acid coefficient being about 0·7, it is the basis of many internal disinfectants, mostly of German origin. Its antiseptic power, it is stated, is equal to that of β-naphthol. These are so compounded as to liberate formaldehyde slowly, and act rather as an internal antiseptic, preventing the growth of organisms—*e.g.*, staphylococci or coliform organisms—than as a germicide.

Formaldehyde forms a white solid crystalline compound with ammonia, known as **hexamethylenetetramine,** and this forms the active ingredient of a large number of disinfectants. Some of these, together with those containing formaldehyde or its solid polymer, trioxymethylene, may be mentioned:

[1] *Guy's Hospital Gazette*, October, 1896.
[2] *Arch. Ital. d'Otologia*, 1903.
[3] *Allgem. Brau. Hopf. Zeit.*, 1918, **58,** 1093.

Formaldehyde Disinfectants.	Hexamethylenetetramine Disinfectants.

Per se as.

Formol, Formysol, Holzen, Camolin, Methylal, Stersol.	*Aminoform, Cystogen, Cystamine, Formin, Uritine, Urotropin.*

With Inorganic Derivatives.

Formaldehyde in sodium glycerоborate —*Boroform.*	Di-iodide—*Novoiodin.*
	Triborate—*Borovertin.*
Aluminium silicate—*Dreiaform.*	Dichromate—*Chromoform.*
	Acid phosphate—*Hexamitrine.*
	Perchlorate.
	Antimonyl tartrate utilized as a trypanocide.

With Aliphatic Derivatives.

Iodoform—*Ekaiodform.*	Dibromiodo—*Chrysoform.*
Acetamide—*Formicin.*	Hexamethylenetetramine 1 molecule, sodium acetate 2 molecules—*Cystopurin.*
	Iodoform—*Iodoformin.*
	Anhydromethylene citrate—*Helmitol.*
	Aluminium acetocitrate—*Acetoform.*
	Bromethylate—*Bromaline.*
	Sodium citrate—*Forminrol.*

With Aromatic Derivatives.

Phenol—*Phenyloform.*	Resorcinol—*Hetraline.*
Phenol—*Carboformal.*	Guaiacol.
Phenol—*Phenyform.*	Salicylate—*Saliformin.*
Resorcinol—*Polyformin.*	Salicylsulphonate—*Hexal* and *Neohexal.*
Resorcinol—*Resorcinoform.*	
Guaiacol—*Guaiaform, Geoform.*	
Acetylated guaiaform—*Enguform.*	Sulphonate.
Thymol—*Thymoform.*	
Thymol—*Thymoloform.*	Eugenol—*Eugenoform.*
Cresols and potash—*Lysoform.*	
Creosote—*Creoform, Creosoform.*	
Tar—*Empyroform.*	
Pitch—*Pittylene, Pixmethylenate.*	

Carbohydrates.

Lactose—*Steriform* and *Sterisol.*	Milk sugar, sodium sulphate, chloride, and sulphate—*Bonal.*
Dextrin—*Dextroform.*	
Milk sugars—*Formamint.*	
Starch—*Amyloform.*	
Starch and iodine—*Amyloiodoform.*	

Miscellaneous.

Casein—*Proteol.*	Albumin silver—*Argaldin.*
Gelatin—*Collaform, Glutoform, Glutol.*	Camphorate—*Amphotropin.*
Chloromethylmenthyl ether—*Forman.*	Nucleate—*Nucleohexal.*
Menthol and trioxymethylene—*Tholaform.*	
Terpenes and allied substances.	
Condensed with hæmatoxylin—*Lysan, Allmatein.*	
Ichthyol and sulphuric acid—*Ichthoform.*	

FORMALDEHYDE DISINFECTANTS. HEXAMETHYLENETETRAMINE DISINFECTANTS.

Tannins.

Cinchotannic acid—*Chemoform, Quinoform.*
Tannin and phenol—*Tanninphenolmethane.*
Dibromtannin—*Tannobromine.*
Tannin and thymol—*Tannothymolmethane (Tannothymal).*
Gallotannic acid—*Tannoform.*
Tannin creosote—*Tannincreosoform.*
Tannin guaiacol—*Tannoguaiaform.*

The higher aldehydes are by no means so active as formaldehyde, the germicidal activity sinking with an increase in the molecular weight, but many antiseptic solutions have been prepared with acetaldehyde and its polymer $(CH_3CHO)_3$ as the active base. **Acetaldehyde** in sufficiently concentrated solutions is germicidal to anaerobic organisms, whilst it has been stated that algæ are killed after twenty-four hours' contact with a 0·02 per cent. solution. **Amidoacetal,** $CH_2.NH_2.CH<^{O.C_2H_5}_{O.C_2H_5}$ will destroy diatoms and infusoria in a concentration of 0·1 per cent. within fifteen hours.

Acrolein, although toxic, appears to possess no germicidal activity, and is scarcely of any value as an antiseptic.[1]

According to Conradi,[2] **chloral hydrate** is germicidal to *B. typhosus,* and it is exceeded in activity by bromal hydrate. Butyl chloral hydrate is a stronger germicide than bromal or chloral hydrate.

Acetone chloroform, $C(CH_3)_2(CCl_3).OH$, or chloretone, is not only antiseptic, but a good disinfectant.

Amines and Amides.

The methylamines, CH_3NH_2, $(CH_3)_2NH$, $(CH_3)_3N$, are gaseous compounds, very soluble in water at ordinary temperatures, yielding powerfully alkaline solutions of an objectionable fishy odour. Klein found that a 1 per cent. solution is an effective germicide. **Ethylamine,**[3] $C_2H_5NH_2$, possessing similar properties to methylamine, has a carbolic acid coefficient of 1·27.

Amylamine, $(C_5H_{11})NH_2$, produced in the destructive distillation of animal matters, is antiseptic, but seems to possess no special advantage.

Ethylenediamine, $C_2H_4(NH_2)_2$, has been used in combination with mercuric sulphate in *sublamin* as a hand disinfectant. It possesses the advantages of being easily soluble in water, does not coagulate

[1] Lewin, *Arch. exp. Path. Pharm.*, **43,** 301.
[2] *Zeitsch. Bakt.*, **1,** 47, 145.
[3] Morgan and Cooper, *Eighth Int. Cong. Appl. Chem.*, **1912, 8,** 150.

albuminous substances nor precipitate soap, and is much less irritant than mercuric chloride. Its carbolic acid coefficient is low (0·03 to 0·4).

Isoamylamine has a carbolic acid coefficient of 2·8.

Heptylamine, in which the partition coefficient $\frac{\text{lipoid solubility}}{\text{water solubility}}$ is high, was found by Morgan and Cooper to have the remarkably high coefficient of 24·3.

Amides.—Loew and Bokorny[1] investigated the effect of a number of amides and amido compounds on algæ. They showed that algicidal powers were, in general, dependent on the presence of NH_2 groups, although, as we shall have occasion to note, these regularities do not obtain in the aromatic series.

Urethane, $CO<^{NH_2}_{OC_2H_5}$ has no action on algæ; *urea,* $CO<^{NH_2}_{NH_2}$ was algicidal after several days; whilst *guanidine,* $HNC<^{NH_2}_{NH_2}$ destroyed the algæ within a few hours.

Ubaldi[2] noted that $CO<^{NH.C_6H_5}_{NH.C_6H_5}$ was inactive, but states that 1 per cent. $CO<^{NH_2}_{NH.C_6H_5}$ was as antiseptic as sublimate.

Hydantoin, $CO<^{NH—CH_2}_{NH—CO}$ and *creatine,* $HNC<^{NH_2}_{N(CH_3)CH_2COOH}$ on the other hand, exerted no algicidal activity.

Chloroform, $CHCl_3$, in solution is a strong antiseptic, whilst its vapours are actively germicidal; but its action on animals confines its use to preserving medicinal infusions. A 5 per cent. solution in spirit is sold as a preservative.

Bromoform, $CHBr_3$, is a similar, but more expensive, less volatile, equally soluble, and less stable compound.

Iodoform, CHI_3, is a yellow crystalline powder of persistent and disagreeable odour, and is much used in hospitals for dressings, etc., in the form of gauze, or as a fine powder for dusting wounds, and in bougies with cacao butter or in emulsion of 10 to 50 per cent. with glycerine water and gum tragacanth. It owes its germicidal and antiseptic powers to the gradual liberation of iodine by the alkaline wound secretions. Iodoform itself gives rise to iodoform poisoning, owing to the too rapid evolution of iodine. A great number of organic iodine derivatives have accordingly been prepared, which are intended to liberate the iodine contained therein at a slower rate than iodoform.

[1] *J. pr. Chem.*, **36**, 272. [2] *Ann. Chim. Farm.*, **14**, 129.

During the period of the war both pastes and impregnated gauze containing bismuth subnitrate (1 part), iodoform (2 parts), and paraffin wax were used extensively. The germicidal action is due partly to the liberation of iodine by oxidation, and partly to the nitric acid formed by hydrolysis of the bismuth subnitrate.[1] Even when used over large exposed areas, cases of iodine poisoning appear to have been very few in number.

ORGANIC IODINE DERIVATIVES.

Aliphatic Derivatives.

Dibromo-di-iodohexamethylenetetramine—*Chrysoform.*
Ethylene periodide—*Di-iodoform.*
Iodoformin ethyliodide—*Iodoformal.*
Trioxymethylene iodoform—*Eka-iodoform.*
Hexamethylenetetramine iodoform—*Iodoformin.*
α-γ-di-iodopropane-β-ol—*Iothion.*
Iodomono-isovalerylurea—*Iodival.*

Aromatic Derivatives.

Tetraiodopyrrol—*Iodol.*
Di-iodo-*p*-phenolsulphonic acid—*Iodozol.*
Di-iodothymol—*Aristol.*
Iodized thymoloform—*Iodothymoloform.*
Di-iodobutylcresol iodide—*Europhen.*
Tri-iodometacresol—*Iosophan.*
Mono-iodocresol—*Traumatol.*
Methylene disalicylic iodide—*Formidin.*
Di-iodosalicylic methyl ester—*Sanoform.*
o-iodoanisol—*Iodoanisol.*
p-iodoxyanisol—*Isoform.*
Tri-iodophenacetin—*Iodophenin.*
Iodine and guaiacol in sodium iodide—*Iodocol.*
Tetra-iodophenolphthalein—*Iosophen.*
Mono-iododihydroxybenzene formaldehyde—

$$C_6H_3(OH)_2I.HCHO,2H_2O.$$

Tannins and Miscellaneous.

Dihydroxy-iodide methyl gallol—*Iodogallicin.*
Bismuth oxyiodogallate—*Ibit.*
Tetra-iodopyrrol—*Iodol.*
Iodized albumin—*Iodolen, Iodalbacid, Iodalbin, Iodigons.*
Iodized gelatine—*Iodyloform.*
Iodized casein and bismuth—*Iodomenin.*
Iodlecithin.
Iodized gluten—*Iodglidin.*
Iodized peptone—*Beigon.*
Quinine iodine substituted derivatives—*Chiniodine.*

[1] Chambers and Garrat, *Lancet*, March 3, 1917.

Quinoline.

3-iodo-4-hydroxoquinoline-1-sulphonic acid—*Loxetin.*
Quinoline chloromethyl iodochloride—*Iodolin.*
Iodochlorhydroxyquinoline—*Vioform.*

Miscellaneous.

Iodized arachis oil—*Iodin.*
Iodized sesame oil—*Iodipin.*
Calcium monoiodobehenate—*Sajodin.*
Iodine and camphor combined with white clay—*Isapogen.*

A few attempts have been made to prepare other organic iodine derivatives which should liberate iodine slowly in the tissues, be antiseptic, and facilitate granulation. Ethylene tetraiodide or di-iodoform, C_2I_4, which forms the basis of a few iodoform substitutes, liberates iodine even more rapidly than iodoform itself. More successful are alkyl ammonium iodide iodine addition compounds; good results have been obtained with substances such as tetramethyl ammonium periodide, $N(CH_3)_4I.I_2$. The unsaturated fatty acids, their salts and esters, have likewise been used as vehicles of iodine in such compounds as *lipojodin*, $C_{19}H_{37}CI : CI.COOC_2H_5$.[1] *Sajodin*, a derivative of iodobehenic acid, $(C_{22}H_{42}O_2I_2)_2Ca$. Both *iodohion* (di-iodohydroxypropane, $C_3H_5I_2OH$), and *archiodin*, monoiodoisovalerianyl glycocoll urea have been suggested as substitutes for tincture of iodine.

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[1] Loeb and Veldin, *Ther. Mon.*, 1911, 201.

CHAPTER XII

THE CHEMICALS EMPLOYED IN DISINFECTION—*Continued*

ORGANIC SUBSTANCES: AROMATIC DERIVATIVES.

It has long been known that the varieties of tar have antiseptic and preservative properties; hence the use of coal tar for coating wood, and of wood tar for ropes and sacking. Coal tar consists for the most part of a mixture of "aromatic" compounds derived from the hydrocarbon benzene, C_6H_6. They are more or less volatile; many have offensive odours and act as narcotic poisons. This poisonous action may render them disinfectant when used in sufficiently large quantities. Some coagulate albumin, and are caustic like phenol. A few are soluble in water, and these have the most immediate physiological power. As far back as 1573 Bishop Berkeley extolled the virtues of tar-water for nearly every ailment: but its use is now replaced by more definite preparations.

By treatment with acid and alkaline solutions in succession, the tars are separated into three groups of bodies:

1. **Hydrocarbons,** such as benzene, toluene, xylene, naphthalene, anthracene, etc. These are neutral bodies, insoluble in water, alkalies, and acids. Most of them, however, can be emulsified by heating with a solution of ordinary or resin soap, with or without the addition of wood spirit. The more or less clear brown syrup turns milky and white with water, the hydrocarbons being precipitated in minute oily globules, which slowly rise as a scum to the surface, leaving a strongly alkaline solution in the soaps. All these mixtures smell of tar, and are in different degrees antiseptic, but less so than the phenols. They are known in commerce as "neutral tar oils." Specifications for disinfecting powders generally demand their absence, and, in fact, they are looked upon generally as a detriment, or even as an adulteration, if present in any quantity in disinfectants. The hydrocarbon benzene, C_6H_6, and its higher homologues toluene, C_7H_8, etc., have no antiseptic value. Farrel and Howles[1] found that threads infected with *B. typhosus* were not sterilized by six and a half hours' exposure to benzol. Benzene soap has no germicidal power.[2]

[1] *J. Soc. Dyers Col.*, 1908, **24**, 108.

[2] *Ibid.*, 166.

Naphthalene, $C_{10}H_8$, and anthracene, $C_{16}H_{10}$, when pure, are white crystalline solids of greasy feel and tarry odour, slowly volatile, insoluble in water, and feebly antiseptic. Naphthalene is used as an insecticide, and is sometimes employed locally in scabies as a 10 to 20 per cent. solution in oil. It is to be avoided in cases where large surfaces are exposed, but has been used internally[1] and as an antiseptic for wounds.[2] Its derivatives will be further considered (p. 252). Naphthalene has been much used as the basis of cakes or blocks sold very cheaply as "disinfectants" to hang up over sinks and in closets, and to place in the basins of urinals. Some are said to contain "camphor and eucalyptus." The camphor blocks certainly prevent the urinous smell, partly by masking it and partly by retarding the ammoniacal fermentation, but they are of no use as disinfectants.

2. **Phenols,** or so-called "tar acids," carbolic, cresylic, etc. They are hydroxy derivatives of the aromatic hydrocarbons, and combine with caustic alkalies to form carbolates, etc., soluble in water, from which acids again liberate the phenol. The series includes phenols, cresols, and higher homologues; the last are present in the fractions of higher boiling-point, and form unstable compounds with alkalies which are even decomposed by water; hence their solutions turn milky on dilution. They are the basis of a large number of proprietary preparations, and will be described further under phenol, cresol, etc.

3. **Basic substances** are extracted from coal tar by treatment with acids; they contain nitrogen, and are allied to ammonia. They are mostly soluble in water, and comprise pyridine and its homologues, with pyrrole, carbazol, quinoline, acridine, aniline, and other bases in small quantities.

Phenols.

Phenol or carbolic acid, $C_6H_5(OH)$, is the simplest member of the group of phenols or hydroxyl-benzene derivatives, and is commercially known as carbolic acid. The phenols all contain hydroxyl united to the "aromatic" nucleus or benzene ring of carbon atoms, and are more or less antiseptic. Most of them coagulate albumin, and are therefore styptic; they are poisonous in different degrees, and thus, if in sufficient quantity, may be true disinfectants. The carbolates are alkaline, odorous, and somewhat caustic; acids, even carbonic, render their solutions turbid, separating the phenols as an oily layer if the solution is moderately concentrated. Such substances, made with lime or magnesia, constitute a number of

[1] *Amer. J. Pharm.*, 1884, 645. [2] Squire's "Companion," 1890, 289.

the "disinfecting powders," which slowly give off the phenols on exposure to air, leaving behind the inert carbonates of lime and magnesia. The earthy bases then only act as a vehicle, and any undue excess of them must be considered as an adulteration. The pure compounds are not used, as they are deliquescent, caustic, and too rapidly soluble. The powders are usually valued, and sold as containing a stated percentage of the phenol or phenol equivalent. Many so-called disinfecting powders now in the market are supposed to contain 15 per cent. of phenol, when in reality they possess only a trace; moreover, even the best deteriorate on exposure to air, and may become inert, so that their activity should always be controlled by analysis.

Phenol itself is prepared from tar distillates, and in the crude state is a dark oily liquid containing also the higher homologues, cresol, xylenol, cumenol, durenol, besides neutral tar oils of less disinfecting power. "Synthetic" carbolic acid, made from benzene and free from cresol, etc., has been sold, but its price is somewhat prohibitive. Pure phenol forms colourless crystals, with a tendency to turn red in the light. It melts at about 40·5° C. and boils at 181·5° C., and therefore is not easily volatile. It can be volatilized more rapidly by melting and then dropping on to a heated shovel—not too hot, or it is liable to catch fire (Calvert). The vapour is apt to cause severe headache, giddiness, and nausea. Crystals of phenol are very hygroscopic, and may contain up to 8 per cent. of water. Much uncertainty exists as to the exact melting-point of pure phenol, a matter of great importance in the testing of germicides (see Chapter XI.). The most recent determination by Leroux[1] gives 40·85° C. as the melting-point; the presence of 0·2 per cent. of water lowers the melting-point to 40·00° C.

A clear, aqueous solution saturated in the cold contains between 6 and 7 per cent. phenol. It is certainly antiseptic; but as to its disinfecting power, opinions have been diverse. McDougall and Calvert extolled it above all other disinfectants, but the latter observer, although he states that 1 in 200 prevented the putrefaction of meat juice for six days, yet acknowledges that when added in that proportion to already putrid beef juice or egg albumin, it had no effect on the organisms present. The vapour also produced no effect during twenty-four hours on vaccine lymph. Miguel found that the vapour of phenol, "after fifteen or twenty days of action at 20° C., is absolutely incapable of destroying the vitality of bacteria," and that 3·2 grammes of phenol are required to prevent growth in a litre of beef-tea. Delbret[2] states that in comparing phenol with

[1] *J. Pharm. Chem.*, 1919, **20**, [vii.], 88.

[2] *Acad. de Sciences*, March, 1916.

mercuric chloride and hydrogen peroxide by their effect on pus, he found that 2 per cent. phenol in the pus produced sterility in six cases out of fifteen, 2 per cent. mercuric chloride in two cases out of nine, and hydrogen peroxide only in one case out of six. Hypochlorites were found ineffective under these conditions.

Scheurlen was the first to observe that an aqueous solution of phenol is very considerably increased in activity by the addition of salts; alcohol and caustic soda, however, when added to phenol, diminish its activity in conformity with the alteration in the $\frac{\text{lipoid}}{\text{water}}$ partition coefficient. Pasteur and Lister strongly advocated its use in surgery where antiseptic action is mainly aimed at. Phenol was extensively used by Crookes under the sanction of the Cattle Plague Commission. His report estimated its value in destroying the infectious matter as very high (1867).

Koch also remarks that "carbolic acid also kills, if of considerable strength and acting for a long period." He observed that solutions of carbolic acid in oils do not possess the same disinfecting value as solutions in water. This is important in view of the frequent use of carbolized oil in surgery, and will be referred to later. When disinfection is required to be completed in less than twenty-four hours, which is generally the case, Wolffhugel and Von Knorre found carbolic acid useless. In Koch's later experiments silk threads with anthrax spores were placed in carbolic solution of various strengths. A 5 per cent. solution killed the spores in two days, whilst sporeless bacteria, obtained from fresh blood, were killed by 1 per cent. solution, but not by $\frac{1}{2}$ per cent. solution, as proved by inoculation. "As an antiseptic, phenol solution 1 in 850 entirely prevented the development of anthrax spores; 1 in 2,250 caused marked hinderance. Other bacteria are less affected. The vapour at ordinary temperatures, even when allowed to act for six weeks, had no effect on spores, but at 55° C. many were destroyed in half an hour. After three hours there was very little germinating power, after five or six hours all were killed. Other disinfectants act similarly at high temperatures."[1]

Klein observes that phenol (1 in 400 or 500) in nutrient solutions had a decidedly restraining power, but he emphasizes the fact that the spores are only "stunned," not killed, because, if removed and inoculated into an animal, they rapidly recover and cause death. He continues, "as is obvious, according to the nature of the bacillus, the strength of the solution, and the time of action, the result varies. For instance, mature *B. anthracis* is killed by 5 per cent. phenol in five minutes, but is not injured by 1 per cent. in five

[1] *Mitth. Kais. Gesundh.*, December 3, 1882.

minutes." Other observers have found that resistant spores are not killed by 5 per cent. carbolic acid, and in the author's laboratory anthrax spores have germinated in less than twenty-four hours' incubation after four days' immersion in a 5 per cent. solution Crookshank obtained favourable results on the tubercle bacillus by inhalations of carbolic vapour.[1] It is well known that certain organisms, especially those of the coli group, and to a lesser degree *B. typhosus*, are capable of growth in the presence of small quantities of phenol;[2] culture material containing 1 in 2,000 carbolic acid is sometimes employed in bacteriology for the isolation of these organisms. Typhoid and coli organisms are rapidly killed by carbolic acid exceeding 1 per cent.

Solutions of phenol, aniline, or *o*-toluidine, which have been exposed to the air and light, and have consequently become coloured, show a slight elevation in germicidal activity.[3]

The value of phenol for hygienic purposes may be summed up as follows:

1. In a strength of 1 in 400 it is a powerful antiseptic, restraining putrefaction when started, and preventing it for a long time when not commenced, but in this respect it is far inferior to mercuric chloride.

2. To kill bacteria with any certainty, a greater strength than 1 per cent. must be employed. With spores, such as those of *B. anthracis*, phenol is useless, as they are apparently unaffected by a saturated solution.

3. It does not absorb sulphuretted hydrogen nor ammonia, hence it is not a deodorant.

4. Its persistent odour is a decided disadvantage, as the smell remains even when the quantity is utterly insufficient.

5. For treatment of sewage it is a failure, even in proportions practically impossible. Moreover, it renders the material useless for manurial purposes. In Japan, after a cholera outbreak, the Government instituted some experiments to elucidate this point, and clearly showed that "a solution of 0·05 gramme of phenol in 100 c.c. of water weakened the germinating power of the seeds, and with a solution of 0·1 per cent. only one-third of the possible seeds germinated, and in all cases the acid delayed the process of germination."

6. In surgery it is of considerable value. Lister has pointed out that it had a powerful affinity for the epidermis, penetrating deeply into its substance, and mingling with fatty matter in any propor-

[1] *Bacteriology*, 1887, p. 151.

[2] Chantenesse and Widal, *Gaz. Hebdomadaire*, 1887, p. 146; also *Ann. Inst. Pasteur*, October 25, 1890.

[3] Thalhimer and Palmer, *J. Infect. Dis.*, 1911, **9**, 172.

tion, whereas mercuric chloride required a special cleaning of the skin, as it could not penetrate in the slightest degree into anything greasy. Though it avoids the danger of mercurial poisoning, if used too strong it may itself be absorbed and cause dangerous symptoms. For aseptism (prevention), as against antiseptism (cure), in surgery it has, therefore, a distinct field of usefulness.

Polyhydroxybenzenes.

Certain generalizations concerning the influence of the—OH groups entering the benzene ring on the germicidal and antiseptic powers of the compound can be made.

Di- and Tri-hydroxybenzenes.—The antiseptic properties of the polyhydric phenols are less than those of phenol, whilst the toxicity to man increases with the number of —OH groups inserted, although the isomeric compounds show exceptions; thus phloroglucinol is less poisonous than pyrogallol. With the lower fungi, the polyhydroxy derivatives are less poisonous than phenol.[1]

Resorcinol, or "resorcin," meta-dihydroxybenzene, $C_6H_4(OH)_2$, coagulates albumen, forming a white precipitate. It only begins to be toxic in very large doses, 10 to 20 grammes per day internally for an adult, while a 2 per cent. solution is highly antiseptic (Vallin). Andeer,[2] Callias,[3] Dujardin-Beaumetz,[4] Lichtheim of Berne, and others, have experimentally demonstrated that resorcinol is a powerful antiseptic. Callias proved that fermentation was prevented, and many animal liquids preserved, by 1 per cent. of resorcinol, while to keep milk required at least 2 per cent. As to its internal action, Andeer, after a dose of 10 grammes of resorcinol, experienced vertigo, dizziness, loss of smell, and salivation, the symptoms disappearing in five hours with no after-effects. It is, therefore, far less poisonous than phenol. Dr. W. Murrel[5] also reported on its internal use. Morgan and Cooper[6] determined the carbolic acid coefficient against *B. typhosus*, and found it to be 0·29. As an antiseptic the dose is 5 to 20 grains. Weak solutions (1 to 3 per cent.) harden the skin, while stronger ones (10 to 50 per cent.) macerate and destroy it.[7] Internally it has caused untoward effects.[8]

[1] K. Yabe, *Bull. Coll. Agric. Tokyo*, 1894, **2,** 73; Biernacki, *Chem. Soc. Abstr.*, 1893, ii., 32; Loew, *Nat. System J. Giftwirk.*

[2] "Ueber das Resorcin," Wurtzburg, 1880.

[3] "Resorcin en Thérapeutiqne," Paris, 1881.

[4] *Bull. Thérap.*, June and July, 1881.

[5] *Med. Times and Gaz.*, 1881, p. 486.

[6] *Eighth Inter. Cong. App. Chem.*, 1912, **8,** 150.

[7] Helbing's "Modern Materia Medica," 1895, p. 146.

[8] *Lancet*, 1898, ii., 779, 836.

Anusol is a bismuth iodoresorcin sulphonate, having a specific action on the rectal mucosa. It is described as a powerful disinfectant and deodorant for wounds, and, when used in suppositories, is free from unpleasant by-effects.

Catechol, or pyrocatechin, ortho-dihydroxybenzene, $C_6H_4(OH)_2$, like almost all products of destructive distillation, is antiseptic, and a more powerful germicide than resorcinol.

Morgan and Cooper find its carbolic acid coefficent to be 0·48, but a 1 to 2 per cent. solution can be used as a spray in diphtheria and whooping-cough, and a 5 per cent. ointment in skin diseases. It is also used for removing dandruff from the scalp. *Euresol*[1] is the mono-acetyl derivative. It is used in cases of acne, alopecia, and seborrhea, and is said to be milder and more lasting in its antiseptic action than resorcinol.

The third dihydroxybenzene, **hydroquinone** or **quinol,** is the most active. Its internal use in typhoid has been suggested in doses of 3 to 8 grains. The carbolic acid coefficient is stated to be 1·1.

J. R. Duggan[2] investigated the relative amount of the three dihydroxybenzenes required to prevent *Bacillus subtilis* from developing in beef peptone. Taking phenol as 20, he finds the ratio of the three compounds ortho : meta : para = 20 : 25 : 30, whilst pyrogallol is represented by 15. Ratios of action on pathogenic bacilli are different.

Pyrogallol, or "pyrogallic acid," trihydroxybenzene, $C_6H_3(OH)_3$, is inodorous, tastes astringent, and has less corrosive action than allied compounds. Its solution quickly turns brown in air, absorbing oxygen; if an alkali be present, the action is almost instantaneous, the solution becoming dark brown. This property leads it to be destructive to "aerobic" organisms—those which live in presence of oxygen. Bovet, of Neuchâtel, first examined its antiseptic action,[3] and found that a 2 per cent. solution prevented putrefaction, fermentation, and mould for some months, and that 3 per cent. was capable of killing bacteria. Two per cent. solutions have no injurious local action, and disinfect very well; but it cannot be used internally, as it reduces and destroys the blood-corpuscles, causing hæmoglobinuria.

If the hydroxyl hydrogen is esterified, the germicidal and antiseptic actions are lowered, the toxicity is also reduced. Etherification of the hydroxyl group—*e.g.*, anisol phenetate—produces a similar depressing effect.

This is equally true for the polyhydric alcohols.

[1] D.R.P., 103,857; 281,097.
[2] *Amer. Chem. J.*, **7**, 62.
[3] *Rev. d'hyg.*, 1879, 154.

Guaiacol and its Derivatives.—Guaiacol, methoxyphenol or methyl catechol, $C_6H_4(OCH_3)OH$, in odour and taste resembles creosote, of which it constitutes a large portion. Only 0·5 per cent. of it dissolves in water, but it is more easily soluble in alcohol, wood spirit, acetic acid, and in alkalies. Sodium-guaiacol resembles sodium phenol.

As the antiseptic value of wood creosote is due partly to the guaiacol which it contains, it is important to note that this ingredient was usually removed from foreign creosotes.

The largest quantity (60 to 90 per cent.) exists in beech-wood creosote, but it also has been obtained by distillation of guaiacum resin, whence the name.

Its physiological value was first pointed out by Seidel in 1880. It is now made synthetically from ortho-anisidine, a base obtained by the reduction of *o*-nitroanisol, formed by methylating *o*-nitrophenol. It first excites, then paralyses, the nerve centres, and reduces the temperature; therapeutically it is similar to phenol and pyrocatechol, but not so poisonous. Its carbolic acid coefficient (R.W.) is stated to be 0·9 (Martindale). Kenwood and Hewlett[1] find it somewhat stronger than phenol (R.W. 1·2).

To depress the toxicity of the —OH group in guaiacol, but at the same time to permit of slow hydrolysis with the liberation of the active germicide, a very large number of guaiacol derivatives have been prepared for internal treatment. These include ester salts of fatty acids such as *eucol*, guaiacol acetate; guaiacol sebacic ester; and *monotol*, the ester of ethyl glycollic acid. Of the inorganic esters, guaiacol carbonate (*duotal*); phosphate, *phosphatol;* the phosphite, $P{\equiv}\begin{matrix}OC_6H_4OCH_3\\OC_6H_4OCH_3\\OC_6H_4OCH_3\end{matrix}$ and sulphate have been prepared. Einhorn and Heinz[2] introduced a series of water-soluble salts stated to possess many advantages over all other guaiacol preparations, the hydrochlorides of dialkyl-amino-acetyl-guaiacol such as the diethyl derivative, guaiasanol, $C_6H_4{<}\begin{matrix}OCH_3\\O.CO.CH_2.N(C_2H_5)_2HCl\end{matrix}$. Amongst the aromatic preparations may be mentioned the cinnamic ester, *styracol;* tannic ester, *tanosol;* and benzoic ester, *benzosol.*

Guaiacol ethers have likewise been prepared. Of this somewhat smaller group may be mentioned *guaianin*, the glycerine ether, $C_6H_4{<}\begin{matrix}OCH_3\\OC_3H_7O_2\end{matrix}$ a water-soluble germicidal solid. Various preparations of guaiacol leaving the —OH group unprotected have been suggested, but the advantage of such preparations, apart from

[1] *J. Roy. San. Inst.*, 1906, 13. [2] *Arch. Pharm.*, 1902, **240**, 632.

a possible increase in solubility, from a germicidal or toxic standpoint is to be questioned. Thus we find *guaiacyl*, the calcium salt of guaiacol sulphonate, and guaiacol carboxylate or methoxysalicylic acid[1] claimed as antiseptics. The potassium guaiacol sulphonate is known as *thiocol*.[2]

A fourth group of guaiacol derivatives includes derivatives of the $—OCH_3$ group in the guaiacol nucleus, such as the antiseptic guaiacetin, $C_6H_4<^{OH}_{OCH_2.COONa}$ and the calcium salt, *calizibram*. Guaiacol formaldehyde compounds are described under formaldehyde.

The hypodermic solutions known as Picot's, Pignol's, and Morel-Lavallee's contain guaiacol. It has been used for phthisis, administered in cod-liver oil or in weak spirit. J. J. Ridge finds that a solution in olive oil, 1 part in 80, is valuable for anointing the skin in smallpox.[3] *Eugoform* is an antiseptic dusting powder made by the action of formaldehyde on guaiacol and subsequent acetylization.

Creosol, or methyl guaiacol, $C_6H_3(CH_3)(OCH_3)OH$, is the chief ingredient of ordinary wood creosote. It resembles guaiacol, but has a higher boiling-point, is heavier, and less soluble. Its antiseptic and germicidal power is said to be a little higher, as would be expected by nuclear substitution of an alkyl group. A 1 in 150 solution kills *S. pyog. aureus* and *B. typhosus* in three hours (Wescott).

In addition to nuclear alkyl substitution products of guaiacol, derivatives of guathol, $C_6H_4<^{OH}_{OC_2H_5}$ and eugenol, $C_6H_3<^{OH}_{OCH_3}_{OC_3H_5}$ have been prepared, such as *cetiacol* or *palmiacol*, methyl-acetyl guathol; and *duotal*, eugenol-methyl carbonate, $C_6H_3<^{OCOOCH_3}_{OCH_3}_{OC_3H_5}$

These do not appear to possess any advantages over guaiacol preparations, an increase in germicidal activity being most easily obtained by alkyl nuclear substitution, as in creosol.

Cresol or Cresylic Acid and the Higher Phenols.

The higher phenols may be regarded as derivatives of phenol in which one or more of the hydrogen atoms of the "benzene ring" have been replaced by methyl or other fatty radicles. These substitution products form a homologous series of progressively increasing density and boiling-point and diminishing solubility, of which the following are examples:

[1] D.R.P., 287, 960. [2] D.R.P., 132, 645. [3] *Brit. Med. J.*, 1903, No. 2,212.

TABLE OF THE PHENOL SERIES.

Systematic Name.	*Commercial Name.*	*Empirical Formula.*	*Structural Formula.*
Phenol	Carbolic acid	C_6H_6O	$C_6H_5.OH$
o-m- and *p*-methyl-phenol	Cresols or Cresylic acids	C_7H_8O	$C_6H_4(CH_3).OH$
Dimethyl-phenols	Xylenols	$C_8H_{10}O$	$C_6H_3(CH_3)_2.OH$
Trimethyl-phenols	Cumenols	$C_9H_{12}O$	$C_6H_2(CH_3)_3.OH$
Tetramethyl-phenols ..	Durenols	$C_{10}H_{14}O$	$C_6H(CH_3)_4.OH$

Of all, except the first, several isomerides are known. They are all antiseptic; their relative value is not exactly known, but the cresols are decidedly higher than phenol. All dissolve in strong alkalies, giving soapy antiseptic solutions; these compounds in the higher members of the series are decomposed by water, yielding milky emulsions which slowly deposit the oil. The homologues are less poisonous than phenol, and are classed together as phenoloids.

A mixture of these bodies from which phenol had been separated formerly constituted a waste product of the carbolic acid manufacture under the name of "creosote oils," and was used for preserving timber, etc. They are difficult to separate by fractional distillation, and now in various mixtures they are largely used for disinfectants under a great number of fancy names. Some of them contain also the hydrocarbons, or neutral tar oils, and a few contain also the bases.

The waste gases from blast furnaces, formed by the destructive distillation of the upper layers of coal and bituminous iron ore, when cooled, deposit large quantities of empyreumatic products, from which is manufactured on a large scale in Scotland the mixture called "blast-furnace creosote oil" for creosoting timber. It contains 20 to 35 per cent. of phenoloid bodies soluble in caustic soda, the coal-tar creosote oil made in London only containing 5 to 10 per cent. Watson Smith found one sample of the phenoloids obtained from blast-furnace tar to contain only 1·33 per cent. of phenol having a boiling-point of 182° C., while those obtained from Lancashire tar contained 65 per cent. of crystallizable carbolic acid (the phenol may have been previously separated from the former). The fraction that would contain cresol had 4·5 per cent. of phenoloids, and the fraction boiling from 210° to 230° C. consisted of a mixture of the xylenols and cresols. The "creosote oil" is treated with caustic soda, the insoluble hydrocarbon oils separated, and the soda compound decomposed by the waste gases from the furnace. Sodium carbonate is formed, setting free the

phenoloids. The carbonate of soda is treated with lime, giving fresh caustic soda for another quantity of oil. The crude phenoloids are distilled, yielding the "creosote" of commerce. It contains about 1 to 2 per cent. of phenol, a large quantity of cresols, and a smaller quantity of the higher homologues. The hydroxyphenols, similar to those found in wood creosote, are present only in very small quantities.

Schulze has found in coal-tar cresols 40 per cent. meta-cresol, 35 per cent. ortho-cresol, and 25 per cent. para-cresol.

When fresh, creosote is almost as colourless as water, but it gradually darkens on keeping, slowly forming tarry products of less potency. In most forms it is a stronger antiseptic than crude carbolic acid, and has not such a caustic action on the skin.

The Cresols.—*o*-, *m*-, *p*-cresols are soluble in water to the extent of 2·2 to 2·5 per cent. The following table gives the physical properties of these three compounds:

	Boiling-Point.	*Melting-Point.*	*Specific Gravity.*
o-cresol (crystalline)	191°	30°	1·0053
p-cresol (crystalline)	202°	36°	0·996
m-cresol (liquid)	203°	4°	1·05

They are sold under various names (*lysol*, *tricresol*, etc). Mixtures of the cresols are dissolved in fat subsequently saponified with the addition of alcohol. They form brown clear syrups miscible with water to clear saponaceous fluids. With hard waters precipitation of lime and magnesia soaps occurs. Clear solutions are formed in glycerine or alcohol. Morgan and Cooper give the following carbolic acid values against *Staph. pyog. aureus* by the Martin and Chick method of testing:

o-cresol	2·1
p-cresol	2·4
m-cresol	2·0

The Higher Phenols.—The higher boiling-point tar acids (phenols) are practically insoluble in water, and the chemical constitution of fractions of different boiling-points has not been definitely settled. Although higher phenols such as *p*-cumenol are present, and can with difficulty be isolated, yet partly hydrogenated phenoloids are present in the complex which undoubtedly possess germicidal value. The chemical constitution of "tars" derived from various sources such as coke ovens, gas works, etc., varies very decidedly in composition, the chief influence being the temperature of dis-

tillation of the tar. At high temperatures "cracking" occurs, and it is probably during this process that partial hydrogenation of the benzene nuclei takes place, the hydrogen, of course, being derived from other rings which are converted into pitchy matter and carbon.

Owing to their relative insolubility, emulsification has to be resorted to in order to make use of their high germicidal powers. Various manufactured articles of this class are on the market under different names, the preparation of a stable, fine emulsion (the finer the emulsion the greater the germicidal power) being the secret of success or failure provided that the tar acids used are sufficiently active. Emulsification can be brought about in many ways with fats or resin, alkali or soaps, and various oils—*e.g.* castor oil—with or without the addition of stabilizers such as saponins, gelatine, and isinglass. According to Fehrs,[1] the emulsifying oil is not without influence on the germicidal power of the disinfectant, it being claimed that linseed oil is superior to rape oil in this respect. Sulphonation of the phenols and their derivatives yields soluble salts which are also germicidal; acetylization will also bring about the desired solubility.

Homologous Phenols.—The introduction of aliphatic chains into the nucleus of phenols raises the germicidal activity. The superior germicidal activity of the cresols and the "higher boiling-point tar acid fractions" have been already referred to. The *o*- and *p*-positions for the entering groups have a greater influence than *m*-substitution.

Long aliphatic chains introduced into the phenol nucleus do not, however, bring about a corresponding increase in germicidal activity. It is generally stated that the xylenols, of which the *o*- is stronger than the *m*-, are the most effective of the substituted phenols, but evidence is lacking as to the validity of the ordinary methods of comparative testing on account of the rapidly decreasing water solubility of the higher homologues.

When tested against staphylococci, the monosubstituted para-phenols can be arranged in the following order of increasing germicidal activity: amyl, isobutyl, isopropyl, propyl.

There are several exceptions to the general rule on the position of substitution as affecting the germicidal powers—viz., that the ortho compound will be stronger than the meta and the meta than the para. Thus, although the 1 : 2 : 4- normal-propyl cresols follow the rule, the isopropyl derivatives, when tested against staphylococci, exhibit the converse, the order being *p*-, *m*-, *o*-. In the isobutyl cresols the order of activity is *p*-, *o*-, *m*-, whilst in the amyl derivatives the ortho is said to be weakest, the meta and para being equal in activity.

[1] *Centr. Bull. Bakt.*, 1905, **37**, 730.

Trimethol, **trimethyl-methoxy-phenol** (2 : 4 : 5 : 1) has been stated to possess a carbolic acid coefficient of 40 (by the R.W. method) when properly emulsified. It is used in intestinal disinfection.[1]

p-Allyl phenol has been introduced as an antiseptic under the name of *chavosot;* thymol (*iso*-propyl *m*-cresol) and similar derivatives are described under essential oils and perfumes.

Oil of eucalyptus (cineole) combines equimolecularly with *o*-cresol, forming a crystalline body melting at 55·2° C. called cresineol; it has "high germicidal properties."[2]

The Aromatic Acids.

The introduction of —COOH groups or —alkyl COOH groups into the benzene ring yields acids of relatively low antiseptic power, but which increases with the molecular weight of the entering acid.

The introduction of a —COOH group into the nucleus of a phenol likewise generally lowers its germicidal activity. Exceptions, however, are to be found in those cases where the acid thus formed is a relatively strong one, and an enhanced germicidal activity is observed which can be attributed to the hydrogen ion. Ortho substitution likewise occasionally results in the production of an acid stronger than the original phenol.

Benzoic acid, C_6H_5COOH, exists in gum benzoin, balsams of Peru and Tolu, and several aromatic gums that have been used for ages for embalming. It is soluble in about 400 parts of cold water, yielding an acid solution of pungent, disagreeable taste. It is strongly antiseptic both as solid, solution, and vapour, and even in its salts.

Salkowski,[3] in a number of experiments with meat juice inoculated with putrid fluid, showed that benzoic acid, in a dose smaller than salicylic, prevented putrefaction. Buckholz[4] found that 1 in 1,000 stopped the growth of micro-organisms. Haberkorn did not succeed with the bacteria of urine with less than 1 in 400. Jalan de la Croix,[5] in seventy-four experiments with varying quantities, showed that the least quantity that would prevent bacterial growth from being inoculated into a fresh liquid (beef-tea) was 1 in 2,800. To kill bacteria he required 1 in 410, and to sterilize spores 1 in 50. As regards non-organized ferments ("enzymes"), Wernitz[6] declares that pepsin is neutralized by 1 in 200, and others by 1 in 300, of benzoic acid or benzoate of soda.

[1] *Eighth Int. Cong. App. Chem.*, 1912, **8,** 150.

[2] T. T. Cocking, Pharm. Conf., 1920.

[3] "Ueber die antisept. Wirkung d. Salicylsäure und Benzoesäure," *Berlin. Klin. Wochenschr.*, 1875, p. 22.

[4] *Arch. exp. Path.*, 1875, **4.**

[5] *Ibid.*, 1881, **13,** 175.

[6] Dorpat Essay, 1880.

Martindale (Extra Pharmacopœia) gives 0·2 per cent. benzoic and 0·1 per cent. salicylic acid as killing *B. coli communis* in two and a half minutes under laboratory conditions.

Graham Brown[1] stated that sodium benzoate was superior to quinine hydrochloride and sodium salicylate in destroying the virus of diphtheria; he believed even that by saturating the human system with benzoic acid by repeated hypodermic injections it was rendered almost insusceptible of inoculation with diphtheria.

In disorders of the bladder attended by ammoniacal urine, Gosselin and Robin[2] proved that benzoic acid taken internally rendered the urine acid, preventing the precipitation of insoluble phosphates and the formation of carbonate of ammonium and poisonous salts by the urinary bacteria, and also diminished the amount of urea excreted. Therefore, Frerichs introduced it successfully for uræmia. They use 1 to 4 grammes per day dissolved in glycerine and water.

Vallin states[3] that "in most cases, to destroy definitely and without return germs transplanted from a sterilized liquid into the midst of an appropriate culture fluid, the proportion of benzoic acid should be 1 in 77, or even 1 in 50." This would make it rather more potent than phenol, cresol, or other similar compounds. It is not poisonous; Professor Senator, of Berlin, gave as much as 50 grammes of sodium benzoate a day to a patient with acute rheumatism without ill effect. As much as 1 ounce of ammonium benzoate per day can be taken without any noticeable effect, and is excreted as hippuric acid in the urine. Its carbolic acid coefficient is about 5·0 (Rideal, 1910).

In those cases in which the odour and taste are immaterial, a saturated solution of benzoic acid in water delays the putrefaction of animal matters much more effectively than salicylic acid. It has less effect on vegetable effusions. It is also useful for preventing fats from becoming rancid, as in "adeps benzoatus," benzoated lard of many pharmacopœias. Added to milk, a very small quantity prevents coagulation.[4] In a series of experiments by one of the authors in 1899, in which molecular proportions—*i.e.*, sodium benzoate 0·026, potassium benzoate 0·029, benzoic acid 0·022 per cent.—were separately mixed with milk, it was found that all had a marked action in retarding the souring, that the free acid was the most energetic, but that the effect came to an end sooner than with inorganic salts such as fluorides, probably owing to the benzoic acid itself being decomposed by some of the organisms.[5] Following

[1] *Kleb's Archiv*, **8**, p. 140. [2] *Arch. générales de Méd.*, 1874, **24**, 566.
[3] *Désinfectants*, p. 202.
[4] *Chem. News*, 1886, **1**, 130; Horn, *Zeitsch. Chem. Indust.*, 1888, **2**, 392.
[5] Richmond and Miller, *Analyst*, 1907, 32.

a report of the Referee Board of the U.S. Board of Agriculture that doses of benzoates under 0·5 gramme per day were not injurious to health, and that even 4 grammes per day did not act as a poison, the U.S. Board in Pamphlet 104 of 1909 have announced that they will make no objection to the use of sodium benzoate in food provided it is plainly labelled on each package, both as to presence and quantity (see also p. 56).

Benzoic acid and benzoates are ingredients in many antiseptic mixtures. Patented preservative mixtures containing benzoic acid are numerous. With regard to complex formulas it may generally be said that the additions are made for the purposes of solubility or disguise, or to institute a special preparation, and that they very rarely increase, and often seriously diminish, the activity of the central ingredient, which is preferably used only dissolved in water, as pure as possible, and in defined strength.

Dr. Miller states that by using the following mixture he could completely sterilize the mouth and cavities in carious teeth: "Thymol, 4 grains; benzoic acid, 45 grains; tincture of eucalyptus 3½ drachms; water 25 ounces."[1] Benzoic gauze contains 4 per cent. of benzoic acid.

By heating benzoic with boric, tartaric, or citric acid, double compound acids called benzo-boric, etc., are formed, which are, of course, antiseptic, and are mentioned in some of the older patents. Although the benzoic acid is thus rendered much more soluble, and its taste is in a great part disguised, it frequently crystallizes out, and hence these compounds are now seldom heard of. This separation also makes them irritant to wounds and mucous surfaces.

Benzoic aldehyde, or benzaldehyde, $C_6H_5.CHO$, occurs with hydrocyanic acid in oil of bitter almonds. Angus Smith[2] considered it a little below phenol in antiseptic power. It readily oxidizes to benzoic acid, is sparingly soluble (1 in 30), and is of no hygienic use except in ointments, when the crude oil is very effective against eczema, irritation, and parasites, partly on account of the prussic acid it contains. Obviously the skin must not be broken It is official in the U.S. Pharmacopœia.

Sulphobenzoic acids, $C_6H_4(HSO_3)(CO.OH)$, of which there are three isomers, made by the action of oil of vitriol on benzoic acid, are very soluble, and have an acid and bitter taste. They and their salts are antiseptic. The mixture of sodium salts is met with as an antiseptic under the name of *sodium sulphobenzoate.*[3] The derivative *saccharin*, "gluside," or benzoyl sulphonimide, has also

[1] *Chem. and Drug.*, 1887, 83.
[2] *Disinfectants*, Edinburgh, 1869.
[3] *J. Soc. Chem. Ind.*, 1888, 226.

a preservative power, and has been given internally to stop decomposition of urine in chronic cystitis.[1] It has the constitution $C_6H_4<^{SO_2}_{CO}>NH$. The commercial article, used for sweetening, is an impure sodium salt; 0·25 per cent. kills *B. coli* in two and a half minutes (Martindale). Von Heyden proposes as a substitute **amidobenzosulphonimide** $C_6H_3(NH_2)<^{SO_2}_{CO}>NH$, which, "with a sterilizing action equal to that of saccharin, is only half as sweet, without unpleasant after-taste. The sodium salt is not antiseptic."[2]

Benzanilide is a weak antiseptic used as an antifebrile.

Benzosol, or benzoyl guaiacol, $(C_6H_5)CO.O(C_6H_4.OCH_3)$, is a crystalline powder, colourless, almost free from taste and smell, insoluble in water, easily soluble in alcohol, and melts at 50° C. It is said to combine the effects of guaiacol and benzoic acid without any disadvantages, and to be very useful in tuberculosis, facilitating expectoration and rendering the sputum free from bacilli. Professor Sahli, however, remarks that the commercial article is of varying composition, that he found some specimens inert, and that "as the effect of guaiacol and creosote was due to local antiseptic action in the stomach, benzosol could not take their place." It is used largely in diabetes mellitus.

Benzo-paracresol, $C_6H_3(C_6H_5.CO)(CH_3).OH$, is an antiseptic prepared by the action of sodium benzoate on paracresol in presence of oxychloride of phosphorus. It occurs as a crystalline powder almost insoluble in water, but soluble in alcohol (0·15 per cent.). It melts at 71° C.[3]

Benzoyl acetyl peroxide, $C_6H_5CO.O.OCOCH_3$, has been marketed under the name of *acetyozone* as a powerful germicide.

Benzo-naphthol, $C_{10}H_7O.CO(C_6H_5)$, from β-naphthol, melts at 110° C., and has also been proposed for internal antisepsis.

Salicylic Acid.—There are three isomeric hydroxybenzoic acids, $C_6H_4(OH).COOH$, of which only the ortho-compound, called salicylic acid, is of practical importance. It is soluble in about 500 parts of cold and 15 parts of boiling water, in 7 of alcohol, 3 of ether, and 50 of glycerine. When heated quickly it breaks up into phenol, which distils, and carbonic acid. The same decomposition occurs in the human system, as phenol appears in the urine. It is antiseptic and antipyretic.

J. B. Duggan found that it was twice as powerful an antiseptic

[1] *Lancet*, 1888, i., 1195.
[2] Patent 12,743, 1895.
[3] *Rev. Chim. Industr.*, April 15, 1893.

as the corresponding para-hydroxybenzoic acid, whilst the meta acid had intermediate properties.[1]

"Artificial" salicylic acid (from sodium phenate and carbonic acid) is somewhat more toxic in its action than the pure "natural" acid obtained from oil of wintergreen, due to the presence of ortho- and meta-cresotinic acids, $C_6H_3(CH_3)(OH).COOH$, derived from the cresols obtained in the crude phenol from which the salicylic acid had been prepared. It is not corrosive, does not coagulate albumin, and is not volatile at ordinary temperatures.

When the saturated aqueous solution was tested with *B. typhosus*, *S. pyog. aureus* and *anthrax*, Westcott found that in three hours only the former were killed. As a food preservative it is about equal to benzoic acid, their relative activities varying under different circumstances. Its physiological effect is more distinct than that of boric or formic acid or formaldehyde in the small quantities required, but there is no clear evidence that it causes injury to adults if the amount is limited. The British Departmental Committee on Preservatives recommended restriction in that "it be not used in a greater proportion than 1 grain per pint in liquid foods and 1 grain per pound in solid food," or 0·0114 and 0·014 per cent. respectively, which practically would amount to a prohibition, since moulds and ferments are only reliably inhibited by 0·1 per cent., the amount commonly employed, though often exceeded. Addition of the acids to foods is forbidden in France, Austria, and some other countries. Traces are present in a large number of fruits.[2]

Among special salicylic acid preparations the following may be noticed:

Solution for Local Antisepsis.[3]—Water, 1,000; boric acid, 12; salicylic acid, 2.

Antiseptic Tablets.—(1) For Thiersch's solution: 14 grains of resublimed salicylic acid and 84 grains of pure boric acid, compressed into a tablet, are dissolved when required in 16 ounces of hot distilled water.[4] (2) Pastilles of sodium bicarbonate, biborate, benzoate, and salicylate, with menthol, eucalyptol, and oil of wintergreen. One of the pastilles gives 2 ounces of a solution to be supplied as spray in nasal catarrh. "Strongly deodorant as well as antiseptic."[5]

Salicylated Gauze.—Gauze is washed with soda to remove grease, then in succession with water and acidulated water, then bleached with chloride of lime and weak acid, and finally well washed with

[1] *Amer. Chem. J.*, **7**, 62.
[2] *Analyst*, 1903, 149.
[3] Carcano and Cesares, *Rev. Chim. Indust.*, April 15, 1893.
[4] *Chem. and Drug.*, 1891, **38**.
[5] *Lancet*, 1890, ii.; 1889, ii., 174.

water and dried. Next it is soaked in a solution of salicylic acid, 5·6 parts; glycerine, 15; rectified spirit, 50; distilled water up to 100 parts; drained, nearly dried by a current of sterilized warm air, and rolled or folded by machines previously made aseptic. The finished gauze is packed in cylinders freshly lined with melted paraffin sterilized by heat. The gauze is thus kept permanently slightly moist.[1] Contact with iron must be avoided, or purple stains result.

The Salicylates.—Owing to the powerful antiseptic and antipyretic properties of salicylic acid, a very great variety of derivatives, both organic and inorganic, of this acid have been prepared.

Amongst the inorganic compounds are found the metallic salts, of which the sodium salt is most generally employed.

Recently boro-disalicylic acid, $BHO<^{OC_6H_4COOH}_{OC_6H_4COOH}$, has been claimed as a strong bactericide.[2]

Amongst the organic derivatives those of the salol class are most frequent; these include oil of wintergreen and salol, phenyl salicylate, as the older and more well-known derivatives, and are largely employed as wound antiseptics. The esterification of the carboxyl group ensures the production of an ester of low toxicity, which on hydrolysis will liberate the active acid and alcohol or phenol.

Oil of wintergreen (*Gaultheria procumbens*) and **oil of sweet birch** (*Betula lenta*) consist almost entirely of methyl salicylate, $C_6H_4(OH)COOCH_3$. It is a colourless fragrant liquid, sparingly soluble in water, but easily in alcohol, and also in alkalies. Specific gravity, 1·18; boiling-point, 222° C.

Perier, of the hospital of St. Antoine, Paris, substituted the former oil for phenol in surgery, using a mixture which was perfectly miscible with water: Oil of wintergreen, 30 grammes; tincture of quillaia, 6 grammes; water, 1 litre. Gosselin and Bergeron[3] found that this oil, both as a solution and as a vapour, hindered the putrefaction of blood, and that its odour was inoffensive. It is still used in France as dressings, but is inferior to phenol and other agents in power. It does not coagulate albumin, and is comparatively non-poisonous, but it is found that the natural oil is somewhat irritant, whereas pure methyl salicylate is not so.[4]

Salol, phenyl salicylate, $C_6H_4(OH).COOC_6H_5$, is insoluble in cold water, soluble in 15 parts of rectified spirit, in 3 of ether, and very soluble in chloroform and in oils. Antipyretic and anti-

[1] Seward Williams, *Chem. and Drug.*, May 27, 1893.
[2] D.R.P., 230, 725.
[3] *Arch. général. de Méd.*, 1881, p. 16.
[4] *Lancet*, 1898, i., 52.

septic, rather stronger than methyl salicylate,[1] it passes through the stomach unchanged, to be decomposed in the duodenum into phenol and salicylic acid.[2] It is used in diarrhœa, dysentery, cholera, etc., as an internal antiseptic, also as an injection in gonorrhœa and cystitis. It has been employed externally as a substitute for iodoform in skin and nasal diseases. Lowenthal[3] has shown that salol will kill cholera bacilli in a paste containing pancreatic juice. Spirituous solutions (5 per cent.) are employed with various flavouring agents for mouth washes and dentifrices, toilet powders and soaps. When melted with camphor, salol, like many other substances, forms a permanent liquid which has also been used to replace iodoform.[4]

Salophen, $C_6H_4(OH)(COO.C_6H_4.NH.CO.CH_3)$, the salicylic ester of acetyl-*p*-amidophenol, resembles the preceding in properties, but is said to have rather stronger antiseptic power. Melting-point, 188° C. It has not been much used, and is expensive.

Cresyl Salicylates.—The three cresols form corresponding salicylates, and have been proposed as internal antiseptics. *Betol*, salinaphthol, or naphthosalol, is β-naphthyl salicylate. *Salbromanilide* is said to be a mixture of bromacetanilide and salicylanilide. *Salipyrin* is a compound of antipyrin and salicylic acid.

Amongst other salol type compounds which have been prepared and had limited application from time to time may be mentioned *salacetol*, $C_6H_4{<}^{OH}_{COOCH_2.COCH_3}$ *glycosal*, the monoglyceride and its derivatives, $C_6H_4{<}^{OH}_{COOCH}{<}^{CH_2Cl}_{CH_2Cl}$ and *protosal*—

$$C_6H_4{<}^{OH}_{COOCH_2}{>}^{CH_2}_{CHO}{>}CH_2.$$

Other aliphatic derivatives, including

$$C_6H_4{<}^{OH}_{COOC_3H_5(OH)_2}$$

spirosal, $C_6H_4{<}^{OH}_{COOCH_2CH_2OH}$ and glycol disalicylate, have recently been introduced.[5]

In benzoyl guaiacol ester, $C_6H_4{<}^{OCH_3}_{COOC_6H_5}$; *analutos*, calcium acetyl salicylate; and *vesipyrin*,[6] $C_6H_4{<}^{OCOCH_3}_{COOC_6H_5}$; we find attempts

[1] *Practitioner*, March, 1907.
[2] *Brit. Med. J.*, 1887, ii., 1438.
[3] *Compt. rend.*, **107**, 1169.
[4] *Répertoire*, 1889, p. 185.
[5] D.R.P., 218,466, and 227,999.
[6] *Therapie der Gegenwart*, 1906, **8**, 92.

to reduce the toxicity of the compound still further by the protection of the phenol —OH group.

In the aromatic derivatives we find naphthol, resorcinol, and other homologous phenols substituted for phenol in the carboxyl group.

Phenosalyl is a mixture of phenol, salicylic, benzoic, and lactic acids, made by heating them together at 140° C., adding menthol and eucalyptol, and, after cooling, adding four times the volume of glycerine. According to Sibut, it is composed of phenol 80, salicylic acid 10, lactic acid 20, menthol 1, melted together.[1] It is a clear, syrupy liquid, of sweetish taste, easily miscible with water or alcohol, is not poisonous, and has a pleasant and non-persistent odour, which does not cling about the hands and clothes. The solutions have no corrosive action on the skin, the mucous surfaces remain smooth and slippery, and do not become dried up, as is the case after washing with carbolic acid or corrosive sublimate. Of course, this latter advantage belongs to the glycerine, and would equally pertain to phenol or mercuric chloride in the same medium.

Professor Fränkel,[2] in a series of bacteriological trials, found that phenosalyl possessed an antiseptic power superior to phenol in dealing with the micro-organisms of cholera, anthrax, pneumonia, typhus, diphtheria, tuberculosis, *Bacillus pyocyaneus*, and *Staphylococcus pyogenes aureus*. It has been used by Duloroy in the sterilization of instruments, of gauze, and of different organic substances like blood, as well as decomposing urine and the saliva of consumptives, with most encouraging results. It does not corrode nor discolour metals under ordinary circumstances of contact.

A very large number of derivatives of salicylic acid have been introduced, and many of them patented, as antiseptics in medicine, as, for instance, F. Hoffmann's sodium ethylsalicylcarboxylate;[3] Eichengrün's *resaldol*, an acetyl condensation product with resorcinol, said to be toxic to bacteria, not only in neutral but in alkaline menstrua (he also recommends the similar product from thymol).

Phenoxyacetic acid, $C_6H_5O.CH_2COOH$, is stated to have a mild antiseptic action, due probably to hydrolysis with the liberation of phenol and acetic acid.

Phenyl acetic acid, $C_6H_5.CH_2.COOH$, is antiseptic, and was regarded very favourably by Klein as a strong disinfectant exceeding phenol in strength. A derivative of this acid, *p*-bromophenyl acetamide, has been introduced as a powerful antiseptic under the name of *antisepsin*.

[1] *Year Book Pharmacy*, 1899, 234. [2] *Bacterien Kunde*, Berlin, 1890.
[3] *Chem. Zeit.*, 1901, **35**, 1045.

Anisic acid, or *p*-methoxybenzoic acid, $C_6H_4(OCH_3)COOH$, occurs in colourless prisms, melting at 175°, and distilling at 280° C. The sodium salt was recommended by Curci in 1887 as antiseptic and antipyretic in doses of 15 grains. It was said to be analogous in action to sodium salicylate, but without disturbing influence on digestion.

Cresotinic acid, $C_6H_3\begin{cases}CH_3\\OH\\COOH\end{cases}$ has been introduced as a germicide in the form of its water-soluble sodium salt and the phenyl ester *solveol*. Glyceryl tri-*p*-cresotinate has been suggested as a powerful germicide and antiseptic for internal use.

Cinnamic acid, $C_6H_5.CH:CH.COOH$, melts at 133°, boils at 290° C. It is somewhat strongly antiseptic. Balsam of Peru contains cinnamic and benzoic acids. Piorkowski[1] finds that proportions of the balsam up to 20 per cent. have only a slight retarding action on the growth of bacteria. A culture of *B. pyocyaneus* after contact with it for twenty-four hours still showed some growth when transferred to a nutritive medium. Cinnamein (benzyl-cinnamic ester, of which the balsam contains about 62 per cent.) does not destroy bacteria at a concentration of 1·5 per cent., nor does styracin at 4 per cent. Cinnamic acid at 2 per cent. prevents the growth of bacteria, and at 4 per cent. destroys them. Peru and storax balsams are parasiticide in skin diseases.

French patent 371,091 preserves butter by enclosing it in a wrapper impregnated with cinnamic acid, which "prevents butyric fermentation."

Hetocresol, cinnamyl-*m*-cresol, is weakly germicidal, but a powerful antiseptic, and has been utilized for tubercular infections. The *o*- and *p*-cresol esters are less active. The introduction of other alkyl groups into the esterifying phenol elevates the activity of the ester.

Styracol, or cinnamyl-guaiacol, $C_6H_5.CH:CH.COO.C_6H_4.OCH_3$, occurs in needle crystals; is said to be a strong antiseptic in catarrh of the bladder and intestines, and in phthisis; soluble in alcohol.[2]

Styrone, cinnamic alcohol, forms silky white crystals of a sweet taste, and having an odour like hyacinths. It is soluble in 12 parts of water, and easily in alcohol. The saturated aqueous solution has been recently used in America for the deodorization of foul ulcerated surfaces, and it does not cause irritation. As an antiseptic it is said to exceed thymol. This explains the healing properties long attributed to tincture of benzoin, of which liquid storax is a constituent.

[1] *Chem. Zentr.*, 1903, i., 414. [2] A. Haas, *Sudd. Apoth. Zeit.*, 1895, 55.

β-Phenyl-propionic acid, or hydrocinnamic acid,

$$C_6H_5.CH_2.CH_2.COOH,$$

is formed in the decay of albuminous matter, and, like other similar products, is a bactericide.

Acetyl-*o*-coumaric acid, *tylmarin*, is another internal antiseptic, said to have a R.W. coefficient of 4·5.

Gallic acid, trihydroxybenzoic acid, $C_6H_2(OH)_3,COOH$, is astrigent and feebly antiseptic.

Tannin, gallotannic acid, $C_{14}H_{10}O_9,2H_2O$, is an amorphous powder, usually brownish, very soluble, and strongly astringent. It is well known to precipitate gelatine, and to form a compound with skins which is imputrescible (leather). It also coagulates albumin. Therefore it is, in some sense, antiseptic, but Gosselin and Bergeron,[1] having added to 2 grammes of fresh blood 8 drops of a 10 per cent. aqueous solution of tannin, saw vibrios appear in the mixture on the fourth or fifth day—that is to say, almost as soon as they would without any antiseptic. Gubler and Bordier[2] state that a horse which for many days had received doses of 20 grammes of tannin remained with its blood unputrefied till the fifth day after death.

None of the extracts of the many varieties of tannins from different plants have even the power to preserve their own solutions.

Sodium dithiosalicylate "No. 1," $\begin{matrix} S.C_6H_3(OH).COONa \\ | \\ S.C_6H_3(OH).COONa \end{matrix}$ is said to be a powerful antiseptic. According to Hueppe, in a 15 per cent. solution the most resistant bacilli are easily destroyed in from twelve to fifteen minutes. In a severe case of ozæma it effected a complete cure in a relatively short time. In 2½ per cent. solution, this preparation is reported to have yielded most strikingly beneficial results in the treatment of foot-and-mouth disease.

Sulphonic Acids.

According to Schneider[3] the sulphonated phenols and cresols, especially the *o*- and *m*- substituted products, are stronger disinfectants than the corresponding phenols. Since the water solubility is increased by sulphonation, it would appear probable that the germicidal activity of these compounds is due in part to the undissociated acid, but also to the hydrogen ions resulting from dissociation, the acids being relatively strongly dissociated. It is thus to be expected that the sodium salts of the acids would be weaker germicides than the corresponding phenols. Schneider states that

[1] *Arch. Méd.*, 1881, 16.
[2] *Bull. Thérapeut.*, 1873, **84**, 265.
[3] *Zeitsch. Hyg.*, 1906, **53**, 116.

the sulphonic acid esters produced by the prolonged action of cold concentrated sulphuric acid on the phenol are even more powerful in germicidal activity.

Cresol disinfectants are more germicidal in weakly acid than alkaline solutions, which is due to the decreased water solubility caused by the salting-out effect and the decomposition of the soluble sodium phenolate.

Aseptol, which originally consisted of *p*-hydroxybenzene sulphonic acid,[1] has been employed both as an antiseptic and a germicide; the commercial article usually contains both the *o*-acid, the ethyl esters of both acids, and ethyl sulphate in addition.

Esters.

A few preparations have been introduced containing the phenyl esters of aliphatic acids, such as thymol palmitate and sodium cresylacetate, which, containing 25 per cent. of free cresols, is known under the name of *cresin*. *Cresosteril*[2] is *m*-cresol oxalic acid.

HALOGEN AND NITRO-SUBSTITUTED BENZENE DERIVATIVES.

The replacement of hydrogen by a halogen in the nucleus brings about a marked elevation in germicidal activity; unfortunately the toxicity of the phenol is raised by such replacement, although the introduction of but one halogen group causes a slight decrease. The toxicity can be compensated for by the simultaneous introduction of an aliphatic group in the nucleus. Accompanying an increase in germicidal activity there is a decrease in solubility, and the substance acquires an unpleasant odour and irritating property. Substitution in the *p*-position is more effective than in the *m*-, whilst ortho-substitution produces but little effect.

p-Chlorophenol, $C_6H_4(OH)Cl$, is soluble in spirit, ether, and fixed oils, and practically insoluble in water. It has been used as an ointment (2 to 3 per cent. with vaseline) in the treatment of erysipelas and lupus.

Trichlorophenol, $C_6H_2Cl_3(OH)$, has been used as a disinfectant, and claimed to be "twenty-five times stronger than carbolic acid" (Martindale). It occurs in white needles of unpleasant odour and pungent taste, volatile with steam. It is nearly insoluble in water, but dissolves in dilute alkalies, and is again liberated by carbonic or other acids. The calcium and magnesium salts have been used medically, and are not irritating.

Laubenheimer[3] and Conrad[4] suggest the use of trichloro-*m*-cresol, *lysocresol*, as a powerful non-toxic hand disinfectant, and this substance has been incorporated in a soap or sulphonated fat or fatty

[1] Obermuller, *Ber.*, 1897, **40**, 3623.
[2] D.R.P., 226,231.
[3] *Deutsch. Med. Wochensch.*, 1910, **4**, 199.
[4] *Arch. Gynäkol.*, 1910, **91**.

acid.[1] *p*-Chloro-*m*-cresol, which is stronger than *p*-chloro-*p*-cresol or *p*-chloro-*o*-cresol, when tested against staphylococci and chlorinated xylenols, has also been the subject-matter of patents.[2] Mixed chlorophenols prepared by the action of chlorine and hypochlorites on crude phenol incorporated with absorbents form the basis of some disinfectants.

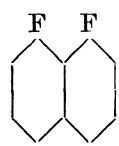
Tribromophenol, $C_6H_2Br_3(OH)$, is a white or brownish crystalline volatile substance, very insoluble in water, obtained by adding bromine water to phenol solution, when it falls as a white precipitate. It is interesting as a delicate test for phenol and as a way of separating it from cresol, since tribromocresol is liquid. Both compounds have disagreeable odours, and are antiseptic, but too insoluble to be of much use. *Xeroform* is tribromophenol bismuth.[3]

The investigations of Bechhold and Ehrlich[4] have shown that tribromophenol, *bromol*, is some twenty-five times and pentabromophenol some 500 times stronger as antiseptics than phenol, whilst tetrabromophenol is 250 times stronger, possessing, at the same time, only one-half of the toxicity.

The germicidal activity of the halogen substituted phenols can, as has already been pointed out, be still further enhanced by alkyl nuclear substitution in addition to halogenation; thus tribromo-*m*-xylenol is twenty times as powerful and antiseptic as tribromophenol, and tetrabromocresol exceeds the powerful tetrachlorophenol some sixteen times in activity. Somewhat singularly the bromo-*p*-cresol is weaker than the ortho- or meta- derivative when tested against staphylococci.

The use of halogen hydroxy-aromatic acids—*e.g.*, 6-chloro-3-hydroxy-*p*-toluic acid—as disinfectants has been suggested by S. Priedel.[5]

The effect of fluorine substitution on germicidal activity has not been investigated.



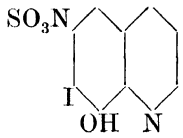
however, is stated to be non-germicidal.

Aromatic Iodine Derivatives.

Nuclear substitution by iodine does not appear to produce any marked increase in germicidal activity; the iodophenols are light, sensitive, and unstable. *Traumatol*, iodocresol, has been employed

[1] D.R.P., 244,827, 1908.
[2] D.R.P., 300,321; 302,013.
[3] *Therap. Monatsh.*, 1899, **12**, 64.
[4] Hoppe Seyler, *Zeitsch. Physiol. Chem.*, 1906, **47**, 182.
[5] *J. Soc. Chem. Ind.*, 1914, 807.

for surgical purposes.[1] Tri-iodocresol, or *sorapure*, appears, however, to be an active germicide.[2] *Losophan*, trichloracetyl diphenyl dioxide, is a powerful antiseptic, but weak germicide. A feeble activity is likewise found to be present in *p*-iodoanisol; the methyl ester of di-iodosalicylic acid, or *sanoform*; and *sozoiodol*, $C_6H_2I_2<^{SO_3H}_{OH}$. *Pikrol*, the potassium salt of di-iodoresorcin sulphonate; *loretin*,

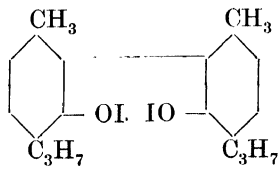


and *nosophen*, tetra-iodophenolphthalein, are weak antiseptics.

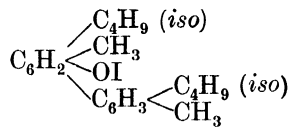
Iodocatechin and iodoterpin, $C_{10}H_{10}I$, *neosiode*, represent other attempts to produce efficient germicides and antiseptics by nuclear substitution in the benzene ring. It cannot, however, be said that these results in the light of effectiveness of the bromo and chloro substituted products are in any way successful. Attempts to improve matters by the introduction of iodine oxygen compounds or substitution of nitrogen ring compounds for the benzene ring have been made, such as in



p-iodoguaiacol, and *aristol*, dithymol di-iodide,[3]



and *europhen*,[4]



and *isoform*, $C_6H_4<^{OCH_3}_{IO_2}$, among the former; and *iodol*, tetra-iodopyrrol,[5] pyrroldiazol iodide, and N-$\alpha\beta\gamma$- tetra-iodoimidoazol amongst the latter. These appear to be antiseptic, and to have some slight

[1] Robin, *Répertoire*, **7**, 11. [2] *Med. Press*, 1916, **153**, 377.
[3] Neiszer, *Ber. Klin. Wochenschr.*, 1890, 19.
[4] *Therap. Monatsh.*, 1891, 373, 379, 536.
[5] Pick, *Vierteljahrschrift f. Derm. u. Syph.*, 1880, 583.

effect in treatment of tuberculosis and syphilis, owing to the fact that the iodine is not so firmly attached to the nucleus.

Aromatic nitro compounds, such as nitrobenzene, have often been proposed as disinfectants, but are precluded by their odour, poisonous action, and sparing solubility. Trinitrophenol is rapidly fatal in a saturated solution (about 1 per cent.) to bacteria and spores, but it causes yellow stains, is irritant, and very poisonous. Its R.W. coefficient is about 6. Cotton-wool soaked in the solution is used very successfully in the aseptic treatment of burns, hence it is recommended by H.M. Inspector of Explosives to keep handy for this purpose. Potassium dinitro-*o*-cresol, *antinonnin*, 1 in 400, is destructive to all common injurious parasites, and does not injure plants. The nitro-naphthols, such as Martin's yellow, are described under the dyestuffs.

Amido-Benzene Derivatives.

The introduction of an $—NH_2$ group into the benzene ring produces substances of low germicidal activity. The disinfectant strength can, however, be elevated in the usual way by nuclear alkyl substitution.

Aniline, $C_6H_5.NH_2$, has a carbolic acid coefficient of 0·57.[1]

Euphorin, $C_6H_5.NH.COO.C_2H_5$, or phenyl urethane, has found application as a strong antiseptic.

Nuclear substitution with a second $—NH_2$ group lowers the germicidal activity, contrary to Loew's hypothesis of active groups, as is noted by the following carbolic acid coefficients:

m.-phenylenediamine	0·2
o-phenylenediamine	0·4
p-phenylenediamine	0·3

Alkyl or aryl nuclear substitution results in an elevation of the germicidal powers. Thus the carbolic acid coefficients of the toluidines are given by Morgan and Cooper[2] as follows:

o-toluidine	1·00
m-toluidine	1·30
p-toluidine	1·25

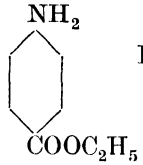
Toluene-1 : 4-diamine has a coefficient of less than 0·2. The effect of aryl substitution is noted in ac.-tetrahydronaphthylamine, which has a coefficient as high as 5·3.

The specific action of the $—NH_2$ group as germicide and antiseptic in the benzene ring is doubtless also present, although masked

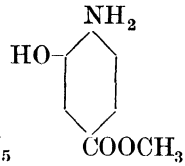
[1] Morgan and Cooper, Eighth Inter. Cong. App. Chem., 1912.
[2] *Loc. cit.*

in those aryl derivatives containing other groups, such as in *phenacetin* and aminophenacetin, $C_6H_4<^{O.C_2H_5}_{NH.CO.CH_2NH_2}$ which was shown by Mosso[1] to be a good antiseptic. The various *p*-aminobenzoic acid esters which have lately come into prominence as anæsthetics and the *orthoforms* of Einhorn and Heinz[2] are antiseptic as well as anæsthetic in action.

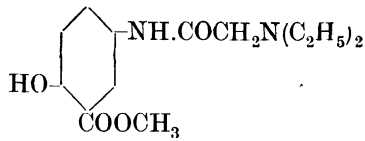
As derivatives of these types may be mentioned:



Anæsthesin.



Orthoform.



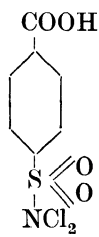
Nervanin.

The $—NH_2$ group has likewise been introduced into a great variety of other phenols and phenolic derivatives in order to increase the solubility of the substance in the form of a salt.

The Organic Chloramines.

Chloramine, NH_2Cl, was found by one of us to be an exceedingly strong disinfectant, but owing to its instability its utilization as a disinfectant, except when specially prepared, is somewhat limited. A search for more stable chloramine derivatives resulted in the discovery by Dakin,[3] and by Dakin, Cohen and Dufresne[4] of a series of stable organic chloramines of great activity. Derivatives of the type $\frac{R}{R'}>NCl$ are all germicidal.

Halazone, p-dichlorsulphonaminobenzoic acid,[5]



a white powder soluble in dilute alkali and sodium carbonate solutions containing about 26 per cent. of available chlorine, has found extended application for field water sterilization. Tablets contain-

[1] *Arch. Exp. Path. Pharm.*, **32,** 401.
[2] *München. Med. Wochensch.*, 1897, **34,** 931.
[3] *Brit. Med. J.*, 1915, i., 318; 1916, **87,** 335. [4] *Proc. Roy. Soc.*, 1916, **89**B, 232.
[5] Dakin and Dunham, *Brit. Med. J.*, May, 1917.

ing halazone and borax or sodium carbonate sufficient to give a dilution of 1 in 300,000 effectively sterilize polluted water in half an hour.

Of the more important chloramines which are now widely used for disinfectant purposes may be mentioned *chloramine-T*, sodium toluene-*p*-sulphonchloramine,[1] *dichloramine-T*, toluene-*p*-sulphondichloramine,[2] and *chlorazine* or *tochlorin*, the sodium salt of *p*-toluene-monochlor-sulphamide.

For medical purposes dichloramine-T dissolved in chlorinated eucalyptus (*chlorcasane*),[3] or chlorinated paraffin wax, is finding extended applications.

Dakin and his workers have shown that the introduction of a second NCl group into the nucleus does not appreciably raise the germicidal power. Nuclear substitution by halogens, alkyl, or $-NO_2$ groups usually produces a slight lowering effect. Molecule for molecule the chloramines are stronger than sodium hypochlorite; similarly the bromamines are more effective than sodium hypobromite. Naphthalene chloramines and sulphochloramines are stated to be similar to the benzene derivatives.

Benzene sodium sulphochloramine is germicidal to staphylococci in concentrations of 1 : 500,000 with two hours' contact; the toluene derivative is about twice as strong. In the presence of serum the necessary concentrations are stated to be 1 : 1,500 for the benzene and 1 : 2,500 for the toluene derivative, this latter being only one-fifth of the molar concentration of sodium hypochlorite necessary to achieve the same results.

B. pyocyaneus, *B. typhosus*, and *B. coli* are, however, somewhat more resistant than the staphylococci.

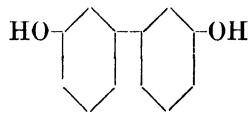
The chloramines of the proteins have been investigated, but are relatively unstable, the simplest being chloramino-acetic acid, the sodium salt, $CH_2.NHCl.CO_2Na$, of which is prepared by the interaction of sodium toluene-*p*-sulphochloramine, and glycerine. It is possible that the germicidal power of all the aromatic chloramines may be due to the intermediary formation of an aliphatic derivative of this type.

Linked Benzene Derivatives.

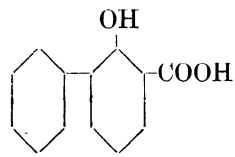
Nuclear substitution by a phenyl group, as we have seen, augments the germicidal activity to a very considerable degree, the nuclear substitution of the $C_4H_4<$ group producing naphthalene, and its derivatives likewise result in the formation of useful germicides.

[1] Inglis, *J. Soc. Chem. Ind.*, 1918, **37**, 288.
[2] Chattaway, *Chem. Soc. Trans.*, 1905, **87**, 145.
[3] *Brit. Med. J.*, January, 1918.

The direct linkage of two phenols—*e.g.*,

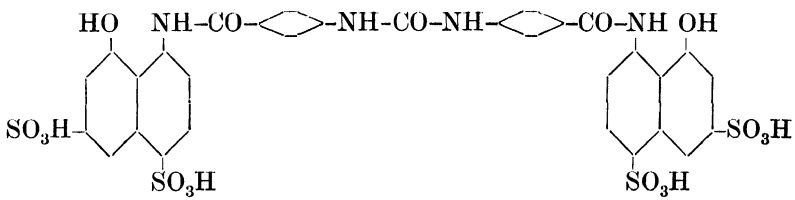


or linkage through the groupings —CH_2—, —CHOH—, —CHOR—, where R is an alkyl group, increases the antiseptic power of the phenol, which can still further be enhanced by nuclear substitution in the usual way. Linkage through the groupings —CO— or —SO_2— results in the formation of relatively weak germicides, the activity of which, however, can be augmented by nuclear substitution. Bechold[1] found that the halogen substituted biphenols were strong germicides when used against anthrax and staphylococci, but states that they were weaker than lysol. Bock[2] finds *o*-hydroxydiphenylcarboxylate,



a good disinfectant.

Amino- linkage through the —CO— group by means of phosgene has resulted in the formation of many complex derivatives, the germicidal activities of which, however, have not been investigated. According to Bayer[3] the compound,



is both trypanocidal and spirillocidal.

Naphthalene Derivatives.

β-Naphthol is official in the British (1898), Belgian, and German Pharmacopœias, the dose in the former being 3 to 10 grains in a cachet for internal antisepsis, especially in typhoid and in cholera as a preventive. Its solubility in water is increased by

[1] Hoppe Seyler, *Zeitsch. Physiol. Chem.*, 1906, **46**, 173.
[2] *Diss.*, Berlin, 1912. [3] D.R.P., 278,122.

boric acid. Schneider observes that naphthols dissolved in alkaline carbonates have greater disinfectant powers than alkaline naphtholates; the former solutions contain naphthol in the free state. He states that staphylococci and typhoid are killed in a short time by 0·5 to 1 per cent. of β-naphthol alkaline carbonate solution.[1]

Ointments containing 10 to 15 per cent. are sufficient in scabies and psoriasis. It is also prescribed for typhoid and intestinal dyspepsia, and in summer diarrhœa of children. *Betol* or β-naphthol salicylate is less soluble than naphthol, and is seldom used. A number of easily soluble beta-compounds have been introduced, such as β-naphthol sulphonates, *aspaprol* or *atrastol* (the calcium salt), and *aluminol* (the aluminium salt). Helbing states that an aqueous solution of the latter 1 : 250 prevents all growth of *gonococci*, pus *cocci*, and allied bacteria.

The sodium β-naphtholate, *microcidin*, has found application as a germicide. *Epicarin*, or β-hydroxynaphthol-*o*-hydroxy-*m*-toluylic acid, and its salts have been introduced by Eichengrün[2] as soluble powerful disinfectants for dermatological purposes. Schering[3] suggests the use of cerium hydroxide and phenol or β-naphthol as germicides.

α-Naphthol is stated to be three times as powerful an antiseptic as the β- derivative; the salicylate appeared contemporaneously with *betol* as *alphol*.

The hydronaphthols, such as tetrahydronaphthol, or *tetralin*, are stated to be more powerful germicides than the naphthols,[4] and equivalent to the xylenols in germicidal activity.

Halogen Substituted Naphthols.

Bechhold[5] finds the odourless and non-poisonous halogen substitution naphthols more powerful than any disinfectant except mercuric chloride. These compounds appear to exert a markedly selective action on various organisms; thus tribromonaphthol, *providoform*, which has exceedingly little action on *B. pyocyaneus*, *B. paratyphosus*, or *B. tuberculosis* (dilutions of 1 : 1,000 being required), has a high germicidal value against diphtheria bacilli, streptococci and staphylococci, killing the latter in concentrations of 1 : 250,000. The dibromo-β-naphthol, on the other hand, is selective for *B. coli*. Against *B. paratyphosus* it is stated that the introduction of one or two halogens, either chlorine or bromine, produces but little effect, the germicidal power actually sinking on further halogenation. Monochlornaphthol exerts but little selective action, its action being uniform for all organisms,

[1] *Zeitsch. Hyg.*, 1906, **52**, 534.
[2] *Pharm. Zentr.*, **41**, 87.
[3] D.R.P., 219,782.
[4] D.R.P., 302,003.
[5] *Zeitsch. Anorg. Chem.*, 1909, **22**, 2033; *Zeitsch. Hyg.*, 1919, 841.

including tubercle. A dilution of 1 : 2,000 was found to be the antiseptic concentration for *B. pyocyaneus;* for other organisms it was found weaker than the tribrom derivative. The introduction of a carboxyl group in the naphthol nucleus results in the formation of strongly antiseptic acids. The *o*-carboxylate is stated to be stronger than salicylic acid.

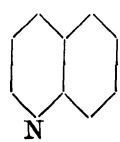
Dihydroxynaphthalenes.—The 2:3- substituted compound has a relatively high germicidal activity. Morgan and Cooper state the carbolic acid coefficient to be 4·4.

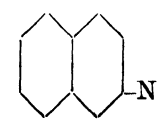
The 2 : 7- derivative has a coefficient of 2·8.

Nitrogen Ring Compounds.

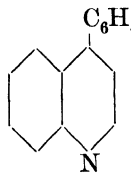
Pyridine and *quinoline* contain nitrogen in the benzene ring. The former is volatile, mixes freely with water, and is strongly insecticide, but has a very unpleasant odour, which has militated against its use in horticulture. Tobacco smoke, indeed, owes its powers, not to nicotine, which is almost entirely decomposed by the heat, but to the products, pyridine and its homologues, which are formed. Tessarini destroyed the bacilli of cholera and pneumonia by tobacco smoke passed from ten to thirty minutes through a tube containing infected gelatine. Wynter Blyth killed the bacillus of nasal catarrh by 1 per cent. solution of pyridine and its homologues (from bone oil), or by tobacco smoke. There is proof that smokers and workers in tobacco enjoy comparative immunity from epidemics, but pyridine inhalations (*e.g.*, in whooping-cough and asthma) require care, as it is a cardiac depressant. The above experiments confirm the general view that disinfectant preparations containing the basic constituents of coal tar are to be preferred to those only including the phenols.

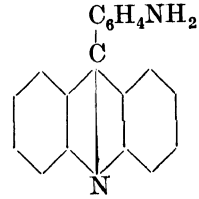
Tobacco juice, of course, contains nicotine, and in France is sold as an insecticide under an official guarantee as to its nicotine strength. In England a solution of the pure base in water is sometimes used as more definite. Richards' cakes for fumigation are nicotine and camphor; one of the writers found a sample in 1909 to contain 1·17 per cent. of nicotine, and to be completely volatile at a gentle heat. Solutions of nicotine containing from 0·01 per cent. and 0·5 per cent. are insecticidal.

Both quinoline, 

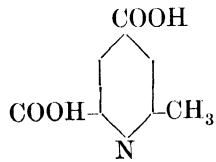
and isoquinoline, 

are mildly antiseptic,[1] the activity of which can be raised by the introduction of further aromatic groupings such as

γ-phenyl quinoline, 

and chrysaniline, 

The introduction of the alkyl groups into the pyridine ring, as in the case of phenols, also increases the antiseptic and germicidal powers; thus dicarboxypicoline,



is stated to be a more powerful germicide than salicylic acid.

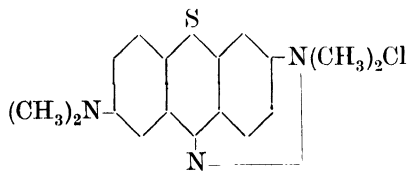
Chinosol is potassium oxyquinoline sulphate, $C_9H_6NO.SO_3K$, a yellow powder easily soluble in water to an acid yellow solution, which does not stain, has only a slight aromatic odour, is permanent on keeping, is non-poisonous, and does not coagulate albumin. It has been patented as a disinfectant, and more especially as an antiseptic. Klein compared its action on *S. pyog. aureus*, *B. coli*, and *B. anthracis* with that of carbolic acid, and reports that a solution of the latter of 1 in 20 strength is required to kill *S. aureus* or *B. coli* in five minutes with certainty, whereas chinosol does this in a strength of 1 in 150. Anthrax spores are not appreciably affected in forty-eight hours by 5 to 6 per cent. carbolic, whereas chinosol of 1 per cent. acts germicidally on them in five minutes. Bechhold[2] found that it exceeded lysol in strength. In the writers' laboratory, *B. coli* was not sensibly affected after four hours in 1 in 1,000 chinosol, while 1 in 2,000 of mercuric chloride produced sterility under the same conditions in fifteen minutes, so that it is difficult to explain the much higher powers that some observers have found for chinosol. Thresh and Sowden state that chinosol spray of not less than 1 per cent. is a reliable disinfectant.[3] Mouston did not succeed in killing *B. coli* in excreta by 1 in 75, and on linen by 1 in 62.[4] On account of its acidity it acts on iron and steel.

[1] Donath, *Ber.*, 1881, **14**, 178, 1769; Stockenam, *J. Physiol.*, **15**, 295.
[2] *J. San Inst.*, January, 1903.
[3] Hoppe Seyler, *Zeitsch. Physiol. Chem.*, 1906, **46**, 173.
[4] *Practitioner*, 1902, 331.

Organic Dyestuffs and their Derivatives.

We have already referred to the use of dyes in the staining of micro-organisms, to the development of the principle by Ehrlich in the preparation of synthetic spirillocides, and have noted that water-soluble sulphonated dyes are, as a rule, not so germicidal as the basic dyes, and those which will exist in colloidal solution in water. Selective action of a particular type of dyestuff for a certain organism is especially evident, and much attention has been paid to this feature in the development of methods of selective staining, although the penetration of the coloured dye is not due in all cases to the chromophoric or auxochromic grouping, the former being frequently reduced by the micro-organism with the formation of leuco bases.

One of the oldest dyestuffs employed as a germicide is **methylene blue,**



which is specific in its action against malaria; the parasites, however, are not coloured by the dye, and it is, contrary to the expectations of Ehrlich, less effective than quinine. Lilian[1] has found it remarkably effective against bilharzia. Michailow[2] has made the significant observation that living protoplasm is not stained by methylene blue, but once the protoplasm begins to die, staining rapidly ensues. Tubercle bacilli absorb the dye, and their activity is impaired but not destroyed. Binger[3] finds it to have a powerful inhibiting action on meningococci, being only slightly less active than mercuric chloride.

The diphenyl- and triphenyl-methane dyes have long been used as antiseptics and disinfectants.[4] *Malachite green* and *brilliant green* (tetramethyl- and tetraethyl-diaminodiphenylcarbinol), when injected into the blood, are effective agents against trypanosomes,[5] killing them within forty-eight hours.[6] Brilliant green will destroy pneumococci in a dilution of 1 : 30,000; phagocytes are not inhibited until a dilution of 1 : 2,000 is reached. A definite

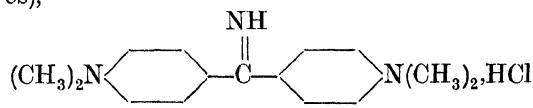
[1] *Lancet*, May, 1902.
[2] *Petersburger Med. Wochenschr.*, 1899, 23.
[3] *J. Infect. Dis.*, 1919, **25**, 277.
[4] Stilling, *Lancet*, 1871, 272.
[5] Wendelsladt, *Zeitsch. Hyg.*, 1906, 52.
[6] *Brit. Med. J.*, 1904, ii., 1449, 1648; *Deut. Med. Woch.*, 1906, **21**, 463.

bactericidal action of this dye can be noted in a dilution as great as 1 : 5,000,000,[1] although to destroy organisms such as *B. subtilis* or *B. mycoides* a dilution of 1 : 100,000 is required.[2]

Rosanilines.—*Methyl violet* and *gentian violet*, the methylated *p*-rosanilines, are slightly more effective than rosaniline as germicides; thus gentian violet requires a dilution of 1 : 300,000 to kill *B. mycoides*, whilst the same result can only be obtained with a dilution of 1:200,000 of rosaniline.[3] Jacobi[4] reports favourably on the use of these dyestuffs in sarcoma.

Aniline blue (triphenylrosaniline) and *toluidine blue* are strong bactericides, and the former appears to have a slight selective action on malaria, as in the case of methylene blue. The parasites are not coloured with the dye.[5]

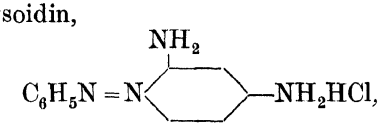
Pyoletannin and *ethylpyletotannin* (auramine hydrochloride and its derivatives),



were originally suggested by Stilling[6] as antiseptics. The substitution of the methyl by ethyl groups increases the antiseptic power, but they appear to be less effective than methylene blue, brilliant green, or methyl violet in germicidal activity. The fugitive colours *dahlia blue* and *cyanin* are stated to be extremely effective germicides.

The introduction of the chromophoric $-NO_2$ grouping in phenols has, as we have already noted, a marked effect on the germicidal activity, but the toxicity is likewise raised. Martin's yellow (dinitro-α-naphthol) is germicidal, but naphthol yellow S (dinitro-α-naphthol sulphonic acid) is not, owing to the introduction of the $-SO_3H$ group causing an increase in the water solubility.

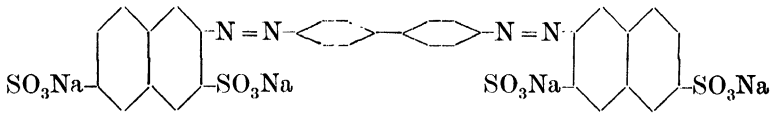
Diazo dyes are weakly germicidal, and the diazo grouping is not toxic. Chrysoidin,



exhibits the peculiar characteristic of agglutinating cholera and allied vibrios.

[1] Leitch, *Brit. Med. J.*, 1919, i., 236.
[2] Crossley, *J. Amer. Chem. Soc.*, 1918, **41**, 2083.
[3] Crossley, *loc. cit.*
[4] *J. Amer. Med. Assoc.*, **47**.
[5] *Philadelphia Med. J.*, 1898, 13.
[6] *Loc. cit.*

Tetrazo colours derived from naphthalene disulphonic acid (3 : 6-) are strongly parasitotropic. Ehrlich showed that trypan red,



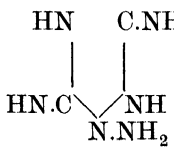
and its various derivatives were effective trypanocides.[1]

Trypansosan (a derivative of parafuchsin) is not only selective for trypanosomes, but is likewise effective against tubercle.[2]

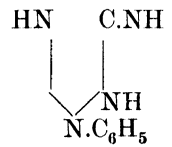
Flavine, or *trypoflavine* (diamino-3 : 6-methyl-2-acridine chloride), prepared by Bendon, was shown by Browning and Gilmoor to have a marked action on trypanosomes; infections have been investigated in detail at the Middlesex Hospital. It kills *B. coli* and cocci at a dilution of 1 : 100,000, but only inhibits phagocytes at a concentration of 1 : 500, and therefore appears superior to brilliant green for internal use. It is approximately ten times as germicidal as mercuric chloride towards *B. coli* in serum.[3] It is three times as powerful as acridinium yellow. *Safranin, eurodin,* and *chrysaniline* are stated to be extremely powerful trypanocides.

A. Raal[4] asserts that strongly fluorescent bodies much increase the action of sunlight on organisms, whilst they are almost inert in the dark. A 1 in 20,000 solution of acridine killed infusoria exposed to sunshine in six minutes; in the dark they survived for twenty-four hours. Similar results were noted with quinine sulphate and with eosine. The inference is that the effect is caused by the fluorescent rays. Fluorescin has been patented as an antiseptic by Turpin, chiefly for toilet preparations.[5] The bromofluorescins, particularly eosin, are found to have greater power He claims a large number of other phthalein compounds as disinfectants.

The more complex azo ring compounds, such as aminoguanazol,



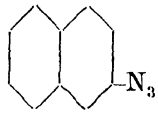
and phenylguanazol,

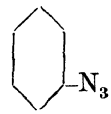


are stated to be weak bactericides.

[1] *Ber. Klin. Wochenschr.*, 1907, 9-12.
[2] Roehl, *Zeitsch. Hyg. exp. Therap.*, 1909, **1,** 70.
[3] *Brit. Med. J.*, 1917, i., 73.
[4] *Pharm. Zeit.*, 1900, **45,** 569.
[5] *Centr. Bakt. Par.*, 1914, **73,** 413.

Azoic acid, N_3H, is a strong antiseptic, and its organic derivatives, such as



and


also possess antiseptic powers.

Sulphur Ring Compounds.

Cyclic thio- compounds are feebly antiseptic, and generally antiparasitic in their action; thus thiophene has a marked antiseptic action, but the germicidal action is negligible. Nuclear substitution by iodine slightly increases the germicidal activity.[1]

Ichthyol and its derivatives which are powerful antiparasitics in their action have already been referred to.

Quinine, Hydrocuprein, and Cuprein.

Quinine has long been a recognized specific for malarial infections, and is chiefly utilized in its more soluble forms, such as ammoniated tincture of quinine, bromoquinine, *euchinin*—quinine carbonic ethyl ester—or β-naphthol and monosulphonate of quinine.[2]

Quinine has but little action on pneumococci, although quinine hydrochloride appears to be distinctly germicidal to these organisms.[3] Quinine itself is antiseptic to anthrax in dilutions of 1 in 625, whilst a mild restraining action on *B. paratyphosus* is to be noted with concentrations of 1 in 19,000.

The germicidal activity of quinine can, according to Schroeder,[4] be sensibly increased by halogenation of the vinyl group.

The aliphatic derivatives of hydrocuprein, on the other hand, exert a marked selective action on pneumococci, as do other cinchona derivatives.[5] The pneumococci germicidal power of ethyl hydrocuprein (*optochin*) is extremely high, a dilution of 2 in 3,000,000 being effective,[6] and its activity is not lowered by the presence of blood-serum.[7] Although optochin has but a feeble germicidal action on streptococci and staphylococci, yet substitution of the methyl group by longer aliphatic groups increases its activity until octylhydrocupreine is reached, the activity then falling again.

[1] Spiegler, *Therap. Mon.*, 1897, 67. [2] *Weiner Med. Blatt.*, 1896, 47.
[3] Aufrecht, *Berlin Klin. Wochensch.*, 1915, **52**, 104.
[4] *Arch. Exp. Path. Pharm.*, 1913, **72**, 361.
[5] Cohen and Kolmer, *J. Infect. Dis.*, 1917, **20**, 273.
[6] Morgenroth and Halberstädter, *Sitzungsber. Kon. Preus. Akad. Wiss.*, 1910, 723; 1911, 30.
[7] Wright, *Lancet*, December, 1912.

When tested against staphylococci, *iso*-propylhydroquinine is twice as powerful as optochin, *iso*-butyl eight times, *iso*-amyl, which is antiseptic to *B. diphtheriæ* in dilutions of 1 in 50,000 to 1 in 100,000, and *iso*-hexyl some ten times to twelve times, and *iso*-heptyl some forty times; the *iso*-octylhydrocupreine being germicidal to staphylococci in concentrations at 1 : 80,000. With staphylococci a slight decrease is noted in the decyl, with a subsequent increase in the dodecyl derivative.[1]

Salts of cuprein, $C_{19}H_{20}N_2(OH)_2$, possess a similar germicidal activity to hydrocuprein.[2]

Alkaline solutions interfere with its power; one of the writers showed that a soap containing 5 per cent. chinosol was inferior to a 0·5 per cent. mercuric iodide soap. F. G. Muller reports encouraging results, as with chinosol in leprosy.[3] *Cresochin*[4] is said to be a neutral sulphonate of quinoline and tricresol, which is recommended for washing instruments, as it does not darken the steel.

The sulphocyanide of quinoline is stated to be a powerful antiseptic.[5]

Diquinoline-*o*-hydroxyphenyl sulphonate, *diaptherin*, and hydroxyquinaseptol have been introduced as non-poisonous water-soluble disinfectants.

Emetine hydrochloride, which is much used in cases of dysentery, has powerful amœbicidal properties, but is a comparatively weak germicide; a 5 per cent. solution does not destroy *B. typhosus* in fifteen minutes.[6]

Essential Oils and Camphors.

Perfumes, composed chiefly of terpenes and their oxidized products, such as thymol, menthol, and eucalyptol, have a limited sanitary value. All of them are very sparingly soluble in water, but impart to it a more or less antiseptic effect. Early estimates of their power have not been concordant, chiefly owing to their having been tried variously in aqueous or alcoholic solution, or in emulsified form. A saturated solution of thymol, $C_6H_3\begin{cases}OH\\CH_3\\C_3H_7\end{cases}$ in water (0·3 per cent.) arrests fermentation and putrefaction (the *o*-, *m*-, *p*- derivatives are stated to be equally germicidal, but in toxicity the ortho- exceeds the meta- and para-). Peppermint (containing menthol and menthene) has had a high reputation, and a

[1] Morgenroth, *Biochem. Zeit.*, 1917, **79,** 257.
[2] Brunn and Schaeffer, *Berlin Klin. Wochenschr.*, 1917, **54,** 885.
[3] *Pharm. Centr.*, **37,** 247. [4] *Zeitsch. oest. Apoth. Ver.*, **35,** 858.
[5] *J. pr. Chem.*, [ii.], **54,** 340; [ii.], **66,** 209.
[6] J. Kolmer, *J. Infect. Dis.*, March, 1915.

number of recipes for "plague-water" have it as a basis. The use of hops in brewing partly rests on the power of the essential oil to check fermentation. "Terbene," made from turpentine by the action of sulphuric acid, was once reputed as a disinfectant, but now hardly figures except in terbene soap. Among other artificial products from turpentine are terpin hydrate (said by Colpi to arrest the growth of tubercle bacilli in 0·25 per cent. strength) and terpineol (stated to kill anthrax in 1 per cent. and staphylococci in 10 per cent. solutions in sixty minutes at ordinary temperatures).[1] Camphor is much spoken of as a personal prophylactic, but there cannot be sufficient of the vapour to disinfect the air. Above 45° C., however, its antiseptic action is quite marked. It is an ingredient in many remedies for cholera and diarrhœa, and in several "block disinfectants," such as *sanocent*, *camphortar*, etc. *Eucalyptus globulus* and other species, which have long been famous as antimalarial, are largely planted on the Continent in marshy districts. The essential oil is decidedly germicidal, and has been given with some success in typhoid, and also against tapeworm and threadworm.

Greig Smith[2] has investigated the germicidal powers of eucalyptus oils in great detail. It was found that the average coefficient of *E. australiana*, the cheapest oil, was 5·8, and of *E. conerifolia* 4·8, the values of which would be augmented by the addition of acid to the aqueous emulsion. The coefficient was found to vary with the time; thus no action was noticeable until a contact period of 1·5 minutes had elapsed, the 20° C. carbolic acid coefficient was 3·1 with fifteen minutes, 3·4 with thirty minutes, and 2·8 with four hours' contact. Of the constituents of cineole, aromadendral was most active, having a coefficient of 21·1, piperitone a coefficient of 4·1, and the residual pinene and sesquiterpene the usual values of 0·8 and 0·5 respectively.

It is interesting to note that Greig Smith found that the germicidal activity was proportional to the amount of iodine liberated from potassium iodide (see below).

Pinol is a liquid of similar character from *Pinus punilis*. H. Marx[3] has investigated the action of various perfumes on anthrax and *S. pyog. aureus*. Kobert[4] finds that the terpenes by themselves have in general only a weak antiseptic action. The proportions needed for sterilizing exceed the solubility in water, and can only be reached by a spirituous solution or an emulsion.

But it has been recognized since Schönbein pointed out the fact

[1] H. Marks, *v. infra*; also Ger. pat. 207,576 of 1906.

[2] *Proc. Linn. Soc. N.S. Wales*, 1917, **47**, 321.

[3] *Centr. Bakt.*, 1903, [i.], **33**, 74.

[4] *Chem. Zentr.*, 1907, i., 419.

about 1840 that essential oils have a disinfectant power conferred on them by their slow oxidation in the presence of air and moisture, whereby ozone or hydrogen peroxide is produced; that as long as air and oil are present, the ozone or hydrogen peroxide is continually regenerated and absorbed, forming oxidizing and antiseptic products which dissolve in the water along with peroxide of hydrogen. This is the principle of Kingzett's *sanitas*. In his first patent (274 of 1876), 9 parts of turpentine oil and 1 ounce of water kept constantly at 60° F. were treated with a current of warm air or oxygen for seven to ten days, when the aqueous liquid, "Sanitas Fluid," contains H_2O_2. Both these average an equality with a 10 per cent. solution of hydrogen peroxide.[1] They are recommended as non-poisonous and non-corrosive oxidizers and antiseptics, suitable for household disinfection and for surgical operations. The antiseptic concentrations of various essential oils are cited by Heinz[2] as follows:

Oil.	*Organism.*	*Antiseptic Dilution.*
Menthol ..	B. diphtheriæ ..	.. 1 : 16,000
	Staphylococcus ..	.. 1 : 6,000
	B. typhosus	.. 1 : 8,000
Camphor ..	Staphylococcus ..	.. 1 : 600
	B. diphtheriæ ..	.. 1 : 30,000
Turpentine ..	Staphylococcus ..	.. 1 : 15,000

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[1] *Lancet*, 1890, i., 809.

[2] "Handbuch der Pathologie."

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CHAPTER XIII

THE CHEMICALS EMPLOYED IN DISINFECTION—*Continued*

THE ORGANO-METALLIC DERIVATIVES.

A GREAT number of organo-metallic derivatives have recently been introduced for disinfectant purposes. They are chiefly intended for internal use, and are consequently prepared to exhibit the minimum of toxicity to the human organism. Some are germicidal *per se*, but the great majority of substances of this class owe their property to the fact that by hydrolysis in the system the active constituent is liberated at a rate sufficiently slow to avoid the accumulation of a lethal or toxic dose in the human organism, but at the same time to ensure a germicidal concentration being present. Attempts have also been made to prepare substances which shall be selectively adsorbed by the micro-organism, and thus ensure a local lethal concentration.

Of the organo-metallic compounds, those of arsenic and mercury are by far the most important, but recent research has drawn attention to the desirability of investigating the germicidal activity of the ever-growing number of other organic-inorganic derivatives.

Arsenic.

The organo-metallic derivatives of this element have achieved an especial prominence owing to the researches of Ehrlich, culminating in the successful synthesis of the trypanocide salvarsan. Ehrlich, following Loew, assumed that in the protoplasm of the parasite there existed certain groupings which reacted with the others in the disinfectant, the chemoceptors of the organism combining with the parasitotropic groupings of the disinfectant; these are very specific in their reactivity, since certain strains of trypanosomes which react with orthoquinone colours and with arsenic derivatives, do not react with paraquinones, whilst strains which do react with paraquinones and not with orthoquinones have also been isolated; these, however, react normally with arsenicals. The conclusion must be inferred from these experiments that there may be several such chemoceptors in an organism requiring the corresponding parasitotropic grouping in the disinfectant.

Levaditti and Lenz[1] consider the chemoceptors to be albuminoid in character. As has been previously noted, unsaturated compounds are usually more germicidal than saturated ones, and trivalent arsenic is found to be a strong germicide, pentavalent arsenic being relatively weak; thus Joachimoglu[2] showed that for isolated organisms, arsenious acid, $As(OH)_3$, was some three hundred times more germicidal than arsenic acid, $AsO(OH)_3$, whilst trypanosomes were destroyed by the respective concentrations 1 : 20,000 and 1 : 100. These conclusions have been confirmed by Führer on the destruction of infusoria,[3] and by Friedberger and Joachimoglu's experiments on the relative antiseptic powers of the arsenites and arsenates for yeast cells[4] (see *ante*).

Of the early organo-arsenicals, derivatives of cacodyl were first employed, but their great toxicity limited their application.

Arsenic Derivatives.—Of the pentavalent aliphatic arsenic derivatives possessing distinct germicidal or spirillocidal powers, resulting in all probability from a slow hydrolysis and reduction of the pentavalent to the trivalent arsenic may be mentioned:

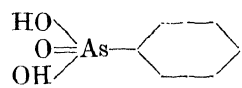
Arrhenal,[5] $O=As\begin{matrix}ONa\\CH_3\\ONa\end{matrix}$ and *solarson*, $O=As\begin{matrix}ONH_4\\CH:CCl(C_2H_4)_4CH_3\\OH\end{matrix}$.

Pentavalent arsenic derivatives containing an aromatic nucleus are much more common; these may be divided into the two divisions in which the aromatic nucleus is linked to the arsenic directly, and those where linkage occurs through oxygen. Of these latter may be mentioned such substances as guaiacol cacodylate,

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>As\!\!<\!\!\begin{matrix}O\\O{-}C_6H_4OCH_3\end{matrix}$$

and cacodyl cinnamic acid employed by Astruc and Marco[6] in cases of tuberculosis.

Among the former and more important derivatives we find the various derivatives of benzene arsonic acid,

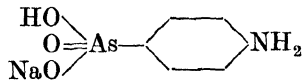


such as arsanilic acid (sodium arsanilate is known under the name of *soamin*) and *p*-hydroxyphenyl arsonic acid, their salts and esters. The *p*-hydroxy- compound is, however, less spirillocidal

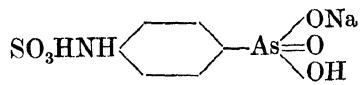
[1] *Zeitsch. Immunitäts Forschung*, **2**, 545.
[2] *Biochem. Zeit.*, 1915, **70**, 144.
[3] *Arch. Exp. Path. Pharm.*, 1917, **87**, 44.
[4] *Biochem. Zeit.*, 1917, **79**, 136.
[5] Gautier, *Presse Médical*, 1902, 791, 824.
[6] *J. Pharm. Chim.*, **12**, 533.

than the *p*-amino- derivative, being some two and a half times less potent, the introduction of one $-NH_2$ grouping into the nucleus lowering the toxicity, but increasing the parasiticidal powers.

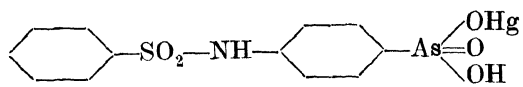
In this group is included *atoxyl*,[1]



and its many derivatives. Atoxyl has achieved a marked success in trypanosome infections, but is much inferior in germicidal activity to the trivalent arsenious derivatives such as salvarsan. Amongst the more important derivatives of atoxyl may be mentioned the acetyl, phenoxyacetyl, and phthalyl derivatives, which are as active or more trypanocidal than atoxyl, and much less toxic.[2] The proprietary articles *Hiktin* and *Hektargyr* have the following constitutions:[3]



Hiktin.



Hektargyr.

These appear, however, to be relatively weak trypanosomicides.

Kharsin, or *o*-toluidinarsonic acid, is a strong trypanosomicide.[4] By reduction of benzene arsonic acid, derivatives of the type  —As=O can be obtained. These trivalent arsenious compounds are much stronger than the derivatives of the pentavalent acid; thus the *p*-amino- derivative is some seventy-five times stronger than arsanilic acid,[5] destroying trypanosomes *in vitreo* in a dilution of 1 in 3,000,000. A restraining action can easily be observed in dilutions as great as 1 in 24,000,000.

The *p*-hydroxy- derivative is some 173 times as germicidal as *p*-hydroxyphenyl arsonic acid.

[1] Ehrlich and Bertheim, *Ber.*, 1907, **40**, 3292.

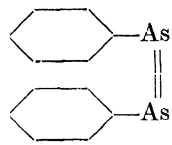
[2] Neiszer, *Deut. Med. Wochenschr.*, **34**, 1500.

[3] *Biochem. Zeit.*, 1916, **78**, 191.

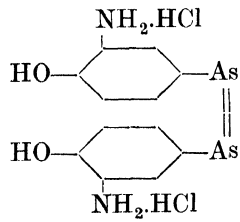
[4] For more complex derivatives of arsenic acid and their trypanocidal activity see Plimmer and Thomson, *Proc. Roy. Soc.*, 1907, **79B**, 50; and Morgan, *Chem. Soc. Trans.*, 1908, **93**, 2144.

[5] Ehrlich, *Ber.*, 1911, **44**, 1207.

Arsenious Derivatives.—A few substituted arsenious acids have been investigated, notably by Joachimoglu,[1] such as arseno-phenyl-acetic, -glycollic and -propiolic acids, and *elarson*, a strontium salt of chlorarsenobehenolic acid. Data as to their germicidal activities appear to be lacking. More important are the derivatives of arsenobenzene,

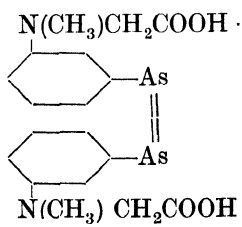


to which class belongs *salvarsan*,



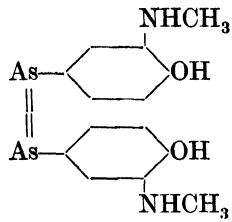
Salvarsan is a strong antiseptic in minute concentrations, whilst in dilutions from 1:1,000,000 to 1:500,000 it is a powerful germicide. The substance exerts a peculiar selective action both as a spirillocide and on anthrax, erysipelas, and glanders, having but little action on pneumococci. The selective action is even more pronounced in serum.[2] The isomeric 22′-dihydroxy-44′-diamino derivative is less effective than salvarsan.[3] Salvarsan, unfortunately, somewhat readily undergoes atmospheric oxidation to the very toxic oxide, and much ingenuity has been exercised on the production of similar derivatives less subject to oxidation. *Neosalvarsan* is sodium-3:3-diamino-4:4′-dihydroxy-arsenobenzene-methanal-sulphoxylate. *Arsalyt* is methylamino-tetramino-arseno-benzene.[4]

Laveran,[5]



[1] *Arch. Exp. Pharm. Path.*, 1915, **78**, 1. [2] *Zeitsch. Hyg. Infect.*, 1914, **77**.
[3] Bauer, *Ber.*, 1915, **48**, 1579.
[4] Leichmann, *Biochem. Zeit.*, 1907, **81**, 284.
[5] Dechsler, *Annalen.*, 1907, **234**, 1.

is stated to be a powerful trypanocide. According to Berthein,[1]

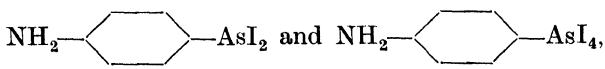


is much more toxic than salvarsan and less germicidal.

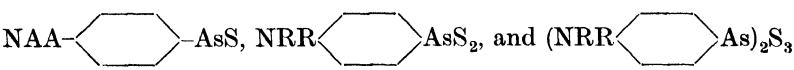
More complex derivatives, such as bis-methyl hydrazinetetra-aminoarsenobenzene, are to be found in the patent literature. They are all trypanosome reactive, but quantitative comparisons with salvarsan are not forthcoming. *Arsenophenyl* has long been used as a therapeutic.[2]

A few substituted arsines have been prepared, but appear to be relatively unstable, such as $H_2As—C_6H_5—NHCH_2COOH$ and $H_2As—C_6H_3<^{OH}_{NH_2}$.

The introduction of the halogens, either in the nucleus or the side chain, such as



results in the production of trypanocidal, but highly toxic substances. These compounds appear to possess marked spirillocidal properties. The sulphides have a very definite action on parasites, but do not appear to possess any marked advantages over other substances more readily prepared. Derivatives of the types



have been prepared.

A greater measure of success has been attained with the metallic salts of the arsenicals, especially those of mercury; those of *atoxyl* are found under the names of *atyrosyl* and *asiphyl*.[3] A double salt of methyl benzene arsonate and mercuric salicylate is the active constituent of *enesol*. Danysz[4] has noticed the interesting fact that the addition of silver bromide or iodide to salvarsan considerably augments the antiseptic action to a value exceedingly greater than that obtained by either constituent singly.

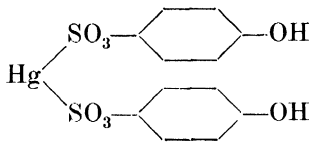
[1] *Ber.*, 1915, 350. [2] R. Kahn, *Zeitsch. Angew. Chem.*, 1895, 25.
[3] Blumenthal, *Biochem. Zeit.*, 1910, **28**, 91.
[4] *Ann. Inst. Past.*, 1914, **28**, 238.

Mercury.

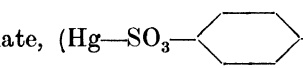
The number of organic mercurials which have actually been prepared and suggested for disinfectant or therapeutic purposes exceeds those of arsenic. A comprehensive bibliography of the compounds which have been synthesized is given by F. C. Whitmore,[1] to which the reader is referred for chemical references.

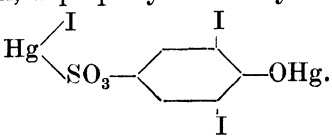
Calomel and highly ionized mercury salts rapidly precipitate albumin, thus entailing both a waste of disinfectant on inert organic matter, and ineffective penetration into the material to be disinfected. A minor objection is the action on surgical instruments. A search for organic mercurials was accordingly conducted with the object of obtaining a mercury-containing compound which would rapidly diffuse and slowly liberate an ionized mercury salt on hydrolysis, a result partially achieved with colloidal mercury (see p. 206). The precipitated albumin mercury complex has, however, a germicidal activity *per se*, and Schrauth and Schöller[2] incline to the view that the complex itself is the active germicide.

Acid Salts.—The mercuric salts of the acids, such as mercuric dipropionate, glycocollate, or dibenzoate,[3] are but feeble germicides. Mercuric-*p*-phenylsulphonate,



known in the form of a double salt of ammonium tartrate as *asterol*. is somewhat weaker than mercuric chloride, and is sufficiently ionized in solution to attack metals and precipitate albumin.

The mercurous sulphonate,  , or *hydrargyrol*, is stated not to possess these defects, but is somewhat easily hydrolysed in aqueous solution.

Hermophenyl,[4] or mercuric phenyl disulphonate, does not precipitate albumin, a property shared by *meriodin*, mercuric phenyl iodisulphonate,  .

[1] *J. Ind. Eng. Chem.*, 1919, **11**, 1083. [2] *Ber.*, 1908, **41**, 2087.

[3] Blumenthal, *Biochem. Zeit.*, 1912, **39**, 58; *Zeitsch. Immun. Exp. Ther.*, 1915, **41**, 47.

[4] Lumière and Chevrother, *Compt. rend.*, **132**, 145.

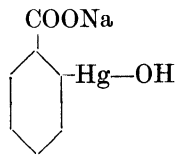
Salts of the type $Hg<^{OH}_{CHR.COOR'}$ and their anhydrides, $Hg<^{O}_{CHR}>CO$ have been investigated by Schöller and Schrauth, and shown to possess a high germicidal activity.[1]

Derivatives of the Phenols.—A great number of derivatives of the type  —OHg—OH have been prepared, as well as those of the halogenated phenols, and have been investigated for germicidal activity by Schrauth and Schöller.[2]

Those of phenol, resorcin, and naphthol are readily soluble in dilute acids, but somewhat easily hydrolysed. Of the cresol derivatives, the meta- is stronger than the ortho- or para-compound. *Upsalan* and *providal* consist of hydroxymercury-sodium-*o*-chlorphenolate, and the dihydroxymercury derivative. The introduction into the nucleus of a second —OHg—OH grouping has but a slight effect on the germicidal activity.

Similar derivatives of *p*-xylenol, and thymol, which are not readily soluble, have likewise been prepared.

Carbon Mercury-linked Compounds.—The aliphatic derivatives of the type $CH_3>Hg$ are exceedingly poisonous;[3] those of the aromatic series have been found to be extremely effective spirillocides, although the hydrocarbon compounds—*e.g.*, $Hg<^{C_6H_5}_{C_6H_5}$ are too toxic for practical utilization. Compounds of the type $R=C=Hg$ appear to possess little germicidal activity. Schöller and Schrauth[4] have carried out an extensive series of investigations on the effect of substitution on sodium hydroxymercuric benzoate,



It itself is a powerful germicide, but can be further augmented in activity by nuclear substitution with halogens, aliphatic or methoxy groupings as in *aphidol*, the sodium salt of hydroxymercuric *o*-methyl benzoate. A similar elevation is produced by the introduction of a second —Hg—OH group, or by the elimination of the carboxyl from the nucleus.

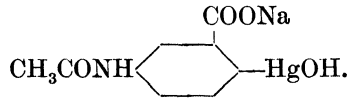
Sulphonation, as in *hermophenyl*, $C_6H_3(HgOH)(SO_3Na)_2$, or the

[1] *Loc. cit.* [2] *Zeitsch. Hyg Infekt.*, 1916, **82**, 279.

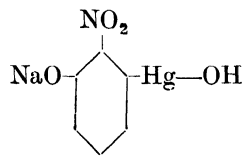
[3] Hoppe-Seyler, *Arch. Exp. Path.*, 1887, **23**, 91.

[4] *Zeitsch. Hyg. Infekt.*, 1910, 1911, **66**, 417.

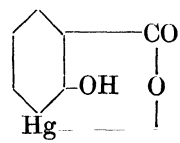
introduction of a salt-forming hydroxy into the nucleus as in *asurol*, hydroxymercuric sodium salicylate, or substitution with an amino grouping, depresses the activity, as would be expected from the effect on the water solubility. Replacement of a hydrogen in the amino group by an alkyl or aryl group elevates, and by an acetyl group depresses the germicidal activity as in *toxyncn*,



The introduction of an $—NO_2$ group into the nucleus elevates its toxicity somewhat, but mercurophen,

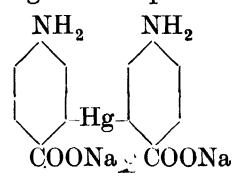


is still less toxic than mercuric chloride. According to Schamburg, Kolmer, and Raizen,[1] it is some fifty times as germicidal towards staphylococcus as mercuric chloride, the organism being destroyed in bouillon by a dilution of 1 in 10,000,000, whilst by the R.W. method (see Chapter XI.) it is stated to be 10,000 times as active as mercuric chloride, and has only one-fifth the serum protein precipitating effect of this salt. In dilutions of 40,000 to 10,000 to 1 it is employed as a hand disinfectant. Similar derivatives are found under the proprietary names of *phenegol*, *thymegol*, and *cresegal*. Nuclear substitution of —HgI, —HgBr, —HgCl, —HgS likewise produce substances of great germicidal activity. Internal linkages are suggested by anhydrides of the type



but their germicidal activity would not be greater than that of the corresponding acids or salts.

Blumenthal[2] has investigated compounds of the type



[1] *J. Amer. Med. Assoc.*, 1917. [2] *Biochem. Zeit.*, 1911, **32**, 59.

with *pp'*-NH_2 groupings. The *oo,'* and *mm,'* compounds have likewise been prepared. They are strong spirillocides, and their activity can be augmented by the nuclear introduction of an —NO_2, —OH, or NH_2 grouping.

Mercury Nitrogen Linkages. — Intermediate in spirillocidal activity between the compounds of the type R—O—Hg—OH and the more potent R—Hg—OH and R—Hg—R' derivatives are found a few compounds of the type =N—Hg—N=, derivatives of amides such as $Hg<^{NHCHO}_{NHCHO}$ the formamide of Liebreich, and Vollert's succinamide derivative, $C_2H_4<^{CO}_{CO}>N—Hg—N<^{CO}_{CO}>C_2H_4$.

Comparative data on the germicidal activity of compounds of this type are, however, lacking. Schöller and Schrauth[1] have also reported favourably on —S—Hg linked derivatives such as

$NaO_3S—S—Hg—CH_2COONa$ and $NaSO_3—S—Hg—C_6H_4COONa$.

Silver.

For eye infections, as well as for the treatment of infection by micrococci, a number of organo-argentic derivatives have been introduced. These include silver salts of the fatty and aromatic acids, such as silver citrate, *itrol;* lactate, *actol;* the glycollate; phenyl sulphonate, *silberol;* the picrate; the nitro-picrate, *picratol;* the silver salt of *p*-hydroxyphenyl sulphonate, *aseptol;* and *a*-quinoline and oxyquinoline silver phenyl sulphonate, *argentol;* acetyl guaiacoltrisulphonate, *eosolate.* Silver salts of thio fatty acids, such as *ichthargon* or silver ichthyol sulphonate, have likewise been suggested. A few complex salts of the type of ethylene diamine silver phosphate, *argentamine,* are also to be noted, but by far the greater number of organic silver derivatives consist of colloidal silver protected by some suitable colloid (see p. 207), or adsorption compounds of silver ions with some complex organic acid which can easily effect reduction of the ion to the metallic state. Of these substances, which are to be regarded not so much as chemical compounds, but as protected colloids, may be mentioned the caseinates, *argonine, omaral* (10 per cent. Ag), and *protargol* (83 per cent. Ag);[2] the nucleinates, *sophol, argyrol, nargol,* and *navergan,* stated to be less toxic than *protargol;* the albuminates, *largin, hegonon,* and *choleval*—colloidal silver protected with sodium gallate and silver galactose. A report by the British Medical Association in 1906 gives the time in minutes required to kill *S. pyogenes aureus* by the following preparations:

[1] *Ber.*, 1907, **40,** 386.
[2] Neiszer, *Dermatol. Zentr.*, 1897, 1.

Substance.	*Concentration.*	*Time.*
Argonine ..	.. 5 per cent. ..	.. 3–6 minutes.
Protargol ..	.. 2–4 ,, ..	.. 3–5 ,,
Largin ..	.. 10 ,, ..	.. 2–5 ,,
Silver nitrate ..	.. ½–2 ,, ..	.. 2–5 ,,

The colloidal silver derivatives, such as *argyrol* (protected with gluten) and *collargol*, had but little bactericidal power.

Copper, Gold, and Platinum.—A few organo-metallic compounds of copper, gold, and the platinum group of metals have been investigated for germicidal activity. It would seem desirable to investigate those of copper in more detail, since germicides approaching the mercurials in activity could probably be prepared.

Copper salts of the type CuB_2X_4, Cu_2BX_3, where X is a halogen, —CN or —CNS and B a univalent-N-alkylhexamethylene tetramine, are suggested in the D.R.P., 284, 260.

Salvarsan derivatives, in which the copper is either linked direct to the arsenic or as a double salt of cupric chloride, are said to be strong bactericides and spirillocides.[1] Cupric chloride, stannate, and cinnamate, with lecithin (*lecutyl*), have been employed with success for tubercle infections.[2] S. Mackenzie has shown that copper alanine[3] has a low toxicity, is soluble, and does not precipitate proteins. It is fatal to protozoa in dilutions of 1 : 100,000. *Cupratin*, copper albuminate; *cuprol* and *cupragol*, the nucleinate; and *cupriaseptol*, copper *m*-hydroxyphenyl sulphonate, have likewise been prepared. Double salts of gold cyanide, such as cholineaurocyanide, piperazine, aurocyanide, and *aurocantan*, have been utilized for tubercular infections. *Crysolgan*, the sodium salt of the 4-amino-2-aurophenol-1-carboxylate, is stated to inhibit the growth of tubercle bacilli in a dilution of 1 : 1,000,000. *N*-alkyl-hexamethylene auric iodide and sulphocyanide are stated to be germicidal. The high cost of these preparations, however, limits their application; this is also true of the palladium compounds, chiefly employed as the double salts of palladium chloride.

Aluminium.—Aluminium salts have been incorporated in a number of organic preparations; the germicidal activity is, however, not due to the presence of the aluminium, which merely performs the function of an astringent. Of these, which are both astringent and antiseptic or feebly germicidal, may be mentioned *lutol* and *borol*, the borotartrate; *acetonal*, aluminium sodium acetate; *alsol*, the acetotartrate; *acetoform*, acetyl citrate of aluminium hexamine; *morinal*, normal basic aluminium sulphite and formaldehyde; *aluminol*, aluminium-β-naphthol sulphonate; *alkazal*,

[1] D.R.P., 355, 030.

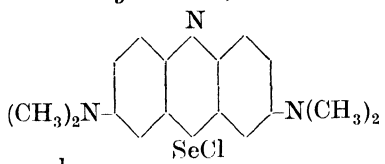
[2] V. Linden, *Zentr. Biochem. Biophys.*, 1915, **18**, 407; *Therap. Monats.*, 1917. **33**, 13.

[3] *Med. Press*, 1916, **50**, 2.

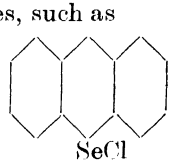
the potassium salicylate; *sozal*, aluminium-*p*-hydroxyphenyl sulphonate; *salumin*, the salicylate; *tannal*, a double salt of aluminium tartrate and tannate; *gallal*, the basic gallate; *autol*, aluminium borotannate; *boral*, aluminium borotartrate and boroformate. *Alformin* is basic aluminium formate.[1]

Of the organo-metalloids, in addition to arsenic derivatives, a number of substances containing antimony, selenium, tellurium, and especially sulphur, have been prepared, all possessing germicidal or spirillocidal activity.

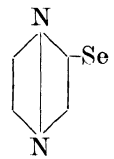
Wassermann has utilized selenium and tellurium compounds in the treatment of spirochetes and of protozoa, such as *eosine selenium* and *selenium methylene blue*,



Other derivatives, such as



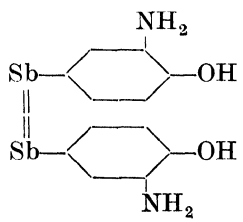
and



are also stated to be effective.

Antimony.

Antimony as well as bismuth organic compounds are trypanocidal, like arsenic, but much weaker in their action. As in the case of arsenic, trivalent antimony compounds are more effective than the pentavalent derivatives. Thus, according to Uhlenhut and Hügel,[2] *antimony atoxyl*, or sodium-*p*-aminophenyl stibnate, as well as its derivatives, have but little effect on spirilla; the sodium acetyl derivative appears to be slightly active, whilst the sodium-*m*-amino-*p*-urethano-phenyl stibnate possesses a marked spirillocidal activity. Derivatives of trivalent antimony, such as

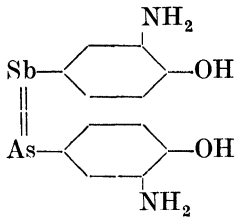


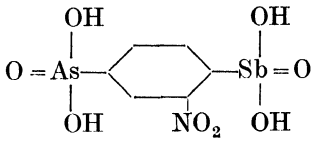
have been claimed as trypanocides.[3] *Stibacetin*, like *arsacetin*, is an effective trypanocide. Of the more important aliphatic anti

[1] Harzbecker, *Allg. Med. Zentr.*, 1916, **85**, 197. [2] *Deut. Med.*, 1915, 2455.

[3] Heyden, D.R.P., 268,451.

mony derivatives may be mentioned potassium ammonium antimonyl bitartrate, or *antiluetin*, a trypanocide, and antimony salts of fatty acids such as ethyl antimony tartrate.[1] Organic derivatives containing both antimony or bismuth and arsenic have been prepared as trypanocides by Ehrlich and Kamer.[2] The following compounds were found to be effective trypanocides:





and derivatives of the type RAsBiCl, where R indicates an aryl grouping. *Margol*, or antimonyl silver bromine arseno-benzene, is stated by Danysz and Raspail[3] to be as effective as salvarsan.

Bismuth.

Compounds precipitating basic bismuth salts have frequently been suggested as substitutes for iodoform,[4] and for internal antiseptics. The antiseptic power of these bismuth derivatives, as distinct from the organo-bismuth C—Bi linked derivatives, is to be attributed to the organic residue, the bismuth oxide itself possessing no germicidal and very weak (if any) antiseptic activity. The oxide, however, performs in certain cases a useful function as a protective agent.

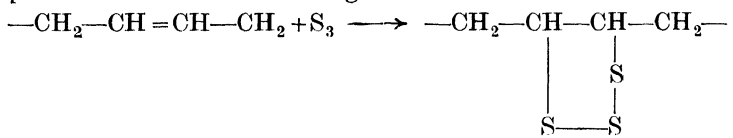
Amongst the aliphatic compounds are to be noticed the citrate, malate, and lactate, as well as complex bismuth oxide derivatives similar to tartar emetic, such as bismutho-tartaric acid.

Bismuth oxide and phenol; tribromophenol, *xeroform;* and β-naphthol, *orphol;* are found amongst the phenol derivatives. Amongst the organic aryl acid derivatives may be mentioned bismuth gallate, *dermatol* and *airol;* the tannate, *tannismut;* bismuth oxyiodogallate, *ibit* or *airoform;* *iodylin*, the salicylate; *thioform*, the dithiosalicylate; and *hetoform*, the cinnamate. More complex are the dilactomonotannate, *lactamin;* the borophenate, *marcasol*[2] the basic gallosulphonate; the bisalicylate, *gastrotan;* the iodosalicylate, *iodoybin;* the methylene gallate, *bismal;* and *helcosol*, the pyrogallate. *Crurin* is stated to be a double thiocyanate of quinoline and bismuth; *bismutose*, the albuminate and peptonate; and *parabismut*, the nucleinate.

[1] Thomson and Crosby, *Proc. Roy. Soc.*, **82B**, 249. [2] *Ber.*, 1913, **46**, 3564.
[3] *Münch. Med. Wochensch.*, 1916, 132, 836.
[4] Steinfeld and Meyer, *Arch. Path. Pharm.*, **20**, 40.

Sulphur.

The antiseptic and germicidal properties of the organic derivatives of hydrogen sulphide have already been referred to. Of the more complex organic thio compounds, those of *ichthyol* stand prominent for the treatment of skin infections such as scabies and eczema. *Ichthyol* is a water-soluble sulphonic salt of an aliphatic derivative containing 10 per cent. of sulphur; its composition, probably complex, is unknown, but the organic sulphur may exist in the form of a thiozonide resulting from the direct addition of sulphur to an unsaturated linkage:

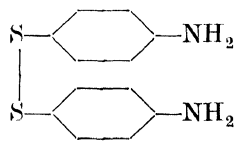


Ichthyol substitutes have been prepared in this way, the hydrocarbon being made water-soluble by sulphonation, whilst derivatives, such as *tumenol*, are prepared by the introduction of sulphur into cracked paraffin after sulphonation.

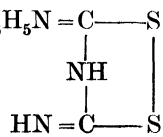
Of the more important ichthyol derivatives which have been proposed may be mentioned:

Ichthalbin, containing egg albumin; *ichthoform*, containing formaldehyde, *ichthargon* and *ferrichthol* containing colloidal silver and iron respectively. *Putinol* and *desichthol* appear to be ichthyol rendered odourless by steam distillation.

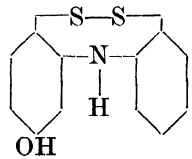
Of the other sulphur organic compounds which are weakly antiseptic may be mentioned *intramin*



suggested by MacDonagh[1] as a substitute for salvarsan; *thiuret*



and derivatives of thiourea; as well as thioresorcin and *sulfaminol*,



[1] *Lancet*, 1916, i., 236, 637; *Brit. Med. J.*, 1906, i., 202.

CHAPTER XIV

METHODS OF ANALYSIS AND TESTING

Bacteriological Methods of Standardizing Disinfectants.

That a chemical analysis of a disinfectant does not give sufficient data from which to determine its germicidal value is at once evident; for, although the activity is generally increased if we augment the quantity of the active ingredient present, we still have no method of determining which is the active substance, nor can we compare the relative value of different active ingredients in different germicides.

Furthermore, the germicidal power of a disinfectant is greatly affected, not only by its chemical composition, but also by its physical condition—*e.g.*, whether ionized or non-ionized, emulsified or in solution, hot or cold.

Many attempts have been made to derive a satisfactory test so conducted that the bactericidal efficiencies of disinfectants may be compared one with another. The preliminary work of Klein, Castro, and Wynter-Blyth in England; Sternberg in America; and Koch, Esmarch, Fraenkel, and Geppert on the Continent, showed to some extent the magnitude of the difficulties which had to be faced.

The first method to give anything like uniform results was devised by Robert Koch in 1892, and is generally known as the thread method. The test is briefly as follows: Threads loaded with anthrax spores are subjected to exposure for various lengths of time in the solution to be tested. After removal they are washed and placed in nutrient gelatine or used for inoculating animals. The germicidal value is estimated by the duration of the exposure necessary to cause the death of the spores.

At a later date Delépine at Manchester has used a modification of this method with cultures of non-sporing organisms, such as *B. coli* and *B. typhosus*.[1] There are several objections to the method which render the results uncertain. It is frequently difficult to remove the last traces of grease from off the threads, alternate washings with alkali and acid followed by alcohol being the most efficacious.

[1] *J. Roy. San. Inst.*, 1907, **28**, T.

A more serious error arises from the fact that when the threads are partially dried without any attempt being made to remove the organic matter of the broth emulsion, a film of dry albuminous matter is formed on the surface, acting as a protection to the organisms. According to V. Gerlach[1] the after-washing is, in the case of emulsified disinfectants, not sufficient to remove all the disinfectant, which may still be present in inhibiting quantities.

In 1897 Krönig and Paul suggested what is known as the garnet method, which had certain advantages over the thread method of Koch, inasmuch as the test bacteria were dried on the surface of little garnets of uniform size at a low temperature over calcium chloride, and could be washed and treated with chemical reagents to neutralize and prevent the carrying over of small quantities of the disinfectant fluid into the test culture, which occurrence, especially in the case of mercury salts, tends to inhibit, if not destroy, any subsequent growth where disinfection has originally not been completed.

In 1903 one of the authors, in conjunction with Mr. Ainslie Walker, devised a standard method for the examination of disinfectants which is the original basis of the many modifications in use at the present time. This method was devised to take into consideration as far as practicable the following factors:

1. Time.
2. Age of culture.
3. Choice of medium. Reaction of same.
4. Temperature of incubation.
5. Temperature of medication.
6. Variations in vital resistance of same species.
7. Variations in vital resistance of different species.
8. Proportion of culture to disinfectant.
9. Universal standard as control.

It was suggested at the time that pure phenol should be used as a control standard in preference to mercuric chloride, which suggestion has met with universal adoption. In making up solutions of phenol of any definite strength, it must be borne in mind that the so-called pure crystals contain at times as much as 7 or 8 per cent. of water,[2] and are frequently contaminated by cresols,[3] which may exert a considerable germicidal effect in the solution, although present in very small quantities. The purity of the crystals should, therefore, be ascertained by a melting-point determination (40·5° C.), whilst the stock solutions are conveniently standardized by bromine titration.

[1] *Zeitsch. Angew. Chem.*, 1901, **14** and **15.**

[2] Rideal and Walker, *J. San. Inst.*, 1903.

[3] J. M. Weiss, *J. Franklin Inst.*, December, 1912, 683.

With regard to the keeping properties of phenol solutions, the evidence is somewhat obscure; it has been suggested that polymerization and possible alteration of germicidal strength occur on storage. Our own experience is that, if not too much solution is made up at one time, and if the solutions are kept in the dark, in those laboratories where tests are frequently being made there is very little possibility of sufficient time elapsing to cause any considerable error in testing.

The following are the original details of the **Rideal-Walker method:**

MATERIALS REQUIRED FOR TEST.

Nutrient Broth.

Liebig's extract of meat	20 grammes.
Peptone (Witte's)	10 ,,
Salt (sodium chloride)	10 ,,
Distilled water	1 litre.

Boil the mixture for thirty minutes, then filter, and neutralize with normal sodium hydrate solution, using phenolphthalein as indicator. In order to avoid contaminating the broth with phenolphthalein, it is advisable to take an aliquot part of the filtered broth—say 10 c.c.—and titrate this with decincrmal sodium hydrate, calculating the amount of normal sodium hydrate necessary for the neutralization of the remainder of the broth. Add when quite neutral 15 c.c. of normal hydrochloric acid. This will give the broth a reaction of 1·5 per cent. The broth is then made up to the litre, filtered and sterilized. Where 2 or 3 litres are prepared at one time, as is customary, the broth is distributed in 500 c.c. flasks on the following day and again sterilized.[1] Five c.c. are then run with the aid of a small separating funnel into sterile test-tubes, which, after plugging with sterile cotton-wool, are placed in the steam sterilizer for half an hour or so.

Standard Carbolic Acid.—A 5 per cent. (by weight) stock solution is prepared and standardized by titration with stock bromine. From this solution the various working strengths are made up by diluting some comparatively large quantity, such as 100 c.c., to the desired volume; this serves to eliminate the error introduced by measuring out small quantities of strong acid.

Dilutions of the Disinfectant.—A stock solution or emulsion should be prepared in a 500 c.c. stoppered cylinder with sterilized distilled water—10 per cent. if the coefficient be under 1, and 1 per cent. if over 1. Ten c.c. of this stock solution are used in

[1] Cheap bad glassware frequently contains sufficient soluble alkali to effect the reaction.

preparing each of the four dilutions required for the test. Thus, working with a sample having a coefficient under 1, if it is desired to prepare a dilution of 1 : 70, 10 c.c. of the 10 per cent. stock solution are diluted with 60 c.c. of distilled water; and in the case of a preparation having a coefficient over 1, where the dilution required is 1 : 700, 10 c.c. of the 1 per cent. stock solution should be diluted with 60 c.c. of water. In preparing dilutions of the unknown, the limitations of the test must not be overlooked. The following is a safe rule for general work, expressing the dilutions as multiples of the carbolic acid dilution:

With coefficients of 1 and under	×0·1
With coefficients above 1, but not exceeding 10	×0·5
With coefficients above 10, but not exceeding 20 ..	×1·0

For example, assuming the strength of the carbolic acid control to be 1 : 100, when it is desired to test a sample having a coefficient of 10, the dilutions to be recommended would be 1 : 950, 1 : 1,000, 1 : 1,050, 1 : 1,100.

The Broth Culture.—*B. typhosus*, grown in R.W. broth and incubated for twenty-four hours at 37° C., provides the test culture. To ensure even distribution of the bacilli in the broth culture, and to avoid the necessity of filtration, the culture-tube should be shaken and allowed to rest for half an hour before it is finally removed from the incubator, the temperature of which should not vary more than half a degree from day to day. It is advisable to make a subculture every twenty-four hours from the previous twenty-four hours' culture, even if on many days no test is to be performed; but as this tends to attenuate the organism, it should be continued for not more than one month, after which a fresh subculture in broth should be taken from a month-old agar culture. By this means a culture not varying much from day to day in resistance to disinfectants is obtained, making the selection of the proper dilution of carbolic acid much easier than it would be if the culture from which the twenty-four-hour growth is obtained were older on one occasion than another.

Apparatus required for Test.

Test-Tube Rack.—A special rack is used. It contains two tiers, the upper having holes for thirty test-tubes, in two rows, each row containing three sets of five; this tier is for the sterilized broth-tubes, each of which is numbered with grease pencil. The lower tier is for the medication-tubes—four with disinfectant dilutions, and one with carbolic acid control dilution, the latter being placed in the fifth hole. The lower tier is provided with a copper water-

bath to keep the temperature of medication within the prescribed limit, —15° to 18° C. The test-tubes being numbered in rotation, it will be seen that the first medication-tube is used for inoculating broth-tubes 1, 6, 11, 16, 21, and 26; the second for 2, 7, 12, 17, 22, and 27, etc.

Inoculating Needle.—The needle used should be composed of thin aluminium rod, with a short piece of platinum wire (26 U.S. gauge) passed through and twisted round an eye in the end of the rod, or otherwise firmly fixed thereto. The wire is made into a loop at the end, and bent slightly in the centre to allow of a fair-sized drop being taken up for each inoculation. Satisfactory results cannot be expected when one tube is inoculated with a full drop and a mere film is introduced into another. The length of the wire to end of loop should be about $1\frac{3}{4}$ inches. After a little practice it is easy to obtain a satisfactory drop by dipping the needle in the medicated culture and bringing it out with a slight jerk. The loop has an internal diameter of 3 millimetres.

Test-Tubes.—The test-tubes should be of fairly strong glass, so as to minimize as far as possible the risk of breakage, and lipped, to facilitate manipulation of plugs. Five inches by $\frac{5}{8}$ inch is the size recommended for use. The cotton-wool plugs for both medication-tubes and broth-tubes should be well made, so that they can be withdrawn and replaced without loss of time. A convenient method is to place a thin flat piece of cotton-wool over the mouth of the test-tube, with a smaller piece in the centre to form a core, and to push both into position with the aid of a thin glass rod.

Dropping Pipette.—This is used for the broth culture, and is loosely plugged at the top with cotton-wool, and when not in actual use is kept in a sterile test-tube plugged at the mouth with cotton-wool. For greater convenience, the tube should be passed through the centre of the plug and fastened thereto with wire.

In addition to the above, one or two each of the following are required: 1, 5, and 10 c.c. capacity pipettes; 100 and 250 c.c. stoppered cylinders (with inverted beakers, to safeguard against dust after removal from sterilizer); wire baskets to receive tubes for incubation or sterilization. All pipettes and cylinders should be sterilized.

Technique.

Before commencing the test it is necessary to ascertain the carbolic acid control dilution which will give the desired result—*i.e.*, life in two and a half and five minutes. This is done by running a trial test with five dilutions of the carbolic acid only—say 1 : 80, 1 : 90, 1 : 100, 1 : 110, and 1 : 120. Five c.c. of the control solution

so ascertained are then pipetted into the fifth medication-tube, the other four receiving 5 c.c. of the various dilutions of the disinfectant under test. To save time and apparatus, one pipette can be made to do service at this stage by starting with the phenol solution, and following on with the highest or lowest dilution of the disinfectant, according as the coefficient is below or above 1, rinsing out the pipette in each case with the next dilution before measuring off the sample for test.

The plug of the culture-tube is now replaced by the culture pipette, which, as explained above, has a plug attached to it with wire at such a height that when the plug fits easily into the mouth of the culture-tube, the point of the pipette is half-way down the broth, and clear of the lumps. The first of the five medication-tubes is now inoculated with five drops of the culture. At intervals of half a minute each of the other medication-tubes is inoculated in turn. By the time the fifth tube has been inoculated the organism in the first will have been exposed to the action of the disinfectant for two minutes, and after the next half-minute a loopful of the latter is inoculated into the first broth-tube, loopfuls from the other medication-tubes being in turn inoculated into their respective broth-tubes at the rate of one every thirty seconds. By the time the fifth broth-tube has been inoculated from the fifth medication-tube, the disinfectant in the first medication-tube will have acted on the test organism for four and a half minutes, and after the next thirty seconds a loopful is introduced into broth-tube 6, and so on. The actual test, therefore, occupies seventeen minutes, and provides for six two and a half minute periods of contact in each of the five medication-tubes.

It is open to the worker, of course, to adopt any convenient method of manipulating the tubes and plugs. The following procedure is given for the guidance of the inexperienced: The first medication-tube is taken from the rack and the contents gently agitated for a second to ensure even distribution of the bacilli; the plug having been taken out and grasped by the left little finger, the tube is held by the back of the left forefinger and the front of the second. The corresponding broth-tube (No. 1) is taken up by the right hand and transferred to the left between the thumb and forefinger, the plug being extracted and held by the little finger of the right hand. The tubes now being in position for inoculation, the needle, which should have been sterilized before the tubes were touched, is introduced into the medication-tube, from which a loopful is taken and inoculated into the broth-tube. The needle is sterilized in the flame (placed to the right) and pushed with a movement of the thumb well up between the first and second

fingers of the right hand; the plugs are then replaced, the medication-tube going back to the rack, while the broth-tube is subjected to a gentle agitation and placed in a wire basket on the right of the rack. This basket, containing the thirty inoculation-tubes and the test form giving particulars of the dilutions, etc., is now placed in the incubator, where it is allowed to remain for forty-eight hours at blood heat, when the results are read off. A moment's consideration of the manner in which the test has been conducted will suffice to indicate where the results of each subculture should be placed in the table.

The strength of efficiency of the disinfectant under test is expressed in multiples of carbolic acid, and is obtained by dividing the dilution of the disinfectant showing life in two and a half and five minutes by the carbolic acid dilution, which, of course, must show the same result.

To avoid annoyance and loss of time caused by aerial contamination of tubes, etc., it is advisable to conduct the test in a room free from draughts; a further safeguard is provided by spraying or swabbing the floors and benches with an efficient disinfectant solution. Needless to add, all pipettes, etc., must be rigorously sterilized before use.

The following example represents a typical test:

DISINFECTANT A. BULK SAMPLE.

Temperature, 18° C.

Test organism, 24 hours' broth culture. *B. typhosus.* (Rawlins).

Dilution.	*Time of Exposure (Minutes).*					
	2½	5	7½	10	12½	15
'A' 1/1,700 ..	+	-	-	-	-	-
,, 1/2,000 ..	+	+	-	-	-	-
,, 1/2,300 ..	+	+	+	-	-	-
,, 1/2,600 ..	+	+	+	+	+	-
Carbolic Acid 1/100	+	+	-	-	-	-

Coefficient, $\frac{2{,}000}{110} = 18{\cdot}2$.

It should be borne in mind that no table can be accepted with this or any other method which does not show a harmonious curve.

It will be noticed that the conditions laid down in the method embrace all the factors alluded to above. Since the publication of this method of testing there have been several critical investiga-

tions made of the methods of conducting the test, with the result that there are now a large variety of tests embracing one or more ideas which the investigations have brought forth.

The following are some of the more important modification tests since introduced:

The Hygienic Laboratory Method.

This method, introduced by Professor J. F. Anderson and Dr. T. B. McClintic of the National Hygienic Laboratory, Washington, D.C., in 1912, closely follows the R.W. method, and is conducted as follows:

Media.—The broth made from Liebig's extract of beef of a reaction +1·5 is prepared in accordance with the standard methods adopted by the American Public Health Association for water analysis.

Ten c.c. of broth are put in each test-tube.

Organism.—A twenty-four hours old broth culture of the *B. typhosus* originally isolated from a patient in the Johns Hopkins Laboratory about the year 1906. Subculturings every twenty-four hours on at least three successive days is advised.

A 4-millimetre platinum loop of 23 U.S. gauge is used, and one loopful taken. (This size loop is also used for transfer of the culture after exposure to the disinfectant.) Before being added to the disinfectants the culture is well shaken and filtered through sterile filter-paper and placed in the water-bath at 20° C.

Temperature.—The standard temperature of 20° C. is adopted.

Proportion of Culture to Disinfectant.—One tenth c.c. of the broth culture is used, added to 5 c.c. of the disinfectant solution The amount is measured with a graduated pipette.

Incubation.—The subcultures are incubated forty-eight hours at 37° C., and the results read off and tabulated.

Dilutions are made with capacity pipettes and 5 per cent. phenol solution is used as stock standard.

Determination of the Coefficient.—Subcultures are made every two and a half minutes up to and including fifteen minutes. To determine the coefficient, the figure representing the degree of dilution of the weakest strength of the disinfectant that kills in two and a half minutes is divided by the figure representing the degree of dilution of the weakest strength of the phenol control that kills within the same time. The same is done for the weakest strength that kills in fifteen minutes. The mean of the two is the coefficient.

EXAMPLE.

Name "A."

Temperature of medication, 20° C.

Culture used, *B. typhosus*, twenty-four hours' extract broth, filtered.

Proportion of culture and disinfectant, 0·1 +5 c.c.

Sample.	*Dilution.*	*Time Culture exposed to Action of Disinfectants for Minutes.*						*Phenol Coefficient.*
		2½	5	7½	10	12½	15	
Phenol	1: 80	–	–	–				
	1: 90	+	–	–	–			
	1:100	+	+	+	–	–	–	
	1:110	+	+	+	+	+	–	
Disinfectant ..	1:350	–	–	–				$\frac{375}{80}+\frac{650}{110}$
	1:375	–	–	–				$\frac{2}{}$
	1:400	+	–	–	–			
	1:425	+	+	–	–	–	–	$=\frac{4\cdot69+5\cdot91}{2}$
	1:450	+	+	–	–	–	–	
	1:500	+	+	–	–	–	–	
	1:550	+	+	+	–	–	–	$=5\cdot30$
	1:600	+	+	+	+	–	–	
	1:650	+	+	+	+	+	–	
	1:700	+	+	+	+	+	+	
	1:750	+	+	+	+	+	+	

The "Lancet" Test.

This was originally published in November, 1907, and prominently brought forward at the Cambridge Meeting of the British Pharmaceutical Conference in 1910 by Professor Sims Woodhead and C. Ponder. It followed the R.W. principle, but with the following important departures:

1. **Number of Dilutions and Time Periods.**—The number of time periods was increased, the maximum length of time during which the disinfectant was allowed to act increased from fifteen to thirty minutes.

2. **The Organism and Medium.**—The *Bacillus coli communis* was substituted for the *B. typhosus*. McConckey's medium was used for subculturing.

3. The sample of the mixture taken after the action of the disinfectant on the micro-organism was taken by means of small platinum spoons of capacity 0·08 c.c.

4. The broth was prepared as follows: 1 pound minced fat-free bullock's heart broth macerated with cold water for two to three

hours, cooked slowly over a small flame for two or three hours more, then boiled and filtered and made up to 1 litre. Ten grammes of sodium chloride and 10 grammes of Witte's peptone were then added, and the solution standardized to an acidity of + 1·5 of phenolphthalein. The culture obtained in the broth was first shaken and then filtered through a double layer of Swedish filter-paper before use.

5. The coefficient was obtained by taking the mean of two figures:

(*a*) The weakest dilution of the disinfectant which kills in two and a half minutes.

(*b*) The coefficient for the thirty minutes period obtained in the same way.

6. The standard temperature lay between 62° and 67° F., room temperature.

The following table illustrates the results obtained by this method:

TABLE X.

Minutes.	*Dilutions.*											
	1/500 ·2 *per Cent.*	1/600 ·166 *per Cent.*	1/700 ·143 *per Cent.*	1/800 ·125 *per Cent.*	1/900 ·111 *per Cent.*	1/1000 ·1 *per Cent.*	1/1100 ·091 *per Cent.*	1/1200 ·083 *per Cent.*	1/1300 ·077 *per Cent*	1/1400 ·071 *per Cent.*	1/1500 ·068 *per Cent.*	1/1600 ·062 *per Cent.*
2½	0	0	0	+	+	+	+	+	+	+	+	+
5	0	0	0	0	+	+	+	+	+	+	+	+
7½	0	0	0	0	0	+	+	+	+	+	+	+
10	0	0	0	+	0	0	+	+	+	+	+	+
12½	0	0	0	0	0	0	0	+	+	+	+	+
15	0	0	0	0	0	0	0	+	+	+	+	+
20	0	0	0	0	0	0	0	0	+	+	+	+
25	0	0	0	0	0	0	0	0	0	+	+	+
30	0	0	0	0	0	0	0	0	0	+	+	+

CARBOLIC ACID CONTROL.

Minutes.	*Percentage Dilutions.*							
	1·37	1·22	1·10	1·00	0·917	0·846	0·786	0·73
2½	0	0	0	+	+	+	+	+
5	0	0	0	+	+	+	+	+
25	0	0	0	0	0	+	+	+
30	0	0	0	0	0	+	+	+

Room temperature, 64° F.

Coefficient is therefore $\frac{\frac{1{\cdot}10}{0{\cdot}143}+\frac{0{\cdot}917}{0{\cdot}077}}{2}=\frac{7{\cdot}7+11{\cdot}9}{2}=9{\cdot}8.$

The *Lancet* Commission further proposed certain chemical tests by which to classify the "tar acid" class of disinfectants. This will be dealt with under that section.

These two methods incorporate the results of all the criticisms levelled at the actual working operations of the R.W. test itself, which criticisms may be summarized as follows:

Choice of Organism.—The advantages claimed for *B. coli communis* as a test organism over the *B. typhosus* are:

1. It is non-pathogenic.

2. Constant biological characters may be obtained by carrying on a culture every twenty-four hours in broth of standard composition.

3. McConckey's bile salt medium for subculturing practically eliminates accidental contamination.

It has been found that *B. coli* is about 10 per cent. more resistant than *B. typhosus* in the R.W. test.

Anderson and McClintic, who devised the Hygienic Laboratory method of testing, had both the R.W. and the *Lancet* method before them in making their test, and chose *B. typhosus* in preference to *B. coli* on account of the greater reliability of strains in the former. They further found that the comparatively expensive bile salt media have a much greater restraining influence on attenuated organisms of the typhoid colon type, such as is the case after they have been exposed to the action of disinfectants. If *B. typhosus* is used and an error is suspected, an agglutination test may be conducted to prove the point. The pathogenic powers of cultures of *B. typhosus* grown for several years on culture media are not so great as to be a deterrent from using this organism.

It will be noted that both the modifications insist upon the necessity of filtration of the inoculated broth, while the Hygienic Laboratory go so far as to advise three twenty-four hours' subcultures before filtration. In regard to this point, our own experience has led us to believe that filtration is not by any means always necessary. The necessity or otherwise of filtration rests in the fact whether the culture gives a smooth curve or an irregular one, and we find that only very rarely does a good vigorous culture give a broth containing clotting groups which are responsible for erratic results and consequently necessitate filtration. Filtration has also the minor drawbacks of increasing the risk of contamination and relatively lowering the resistant action to disinfectants. The three subcultures advised by the Hygienic Laboratory make the test a somewhat lengthy one to carry out.

Choice of Culture Medium.—The disadvantages of bullock's heart broth in preference to "Lemco" broth are briefly:

Bullock's heart broth provides a more resistant culture medium to disinfectants than "Lemco" broth, although in both cases the resistance of bacteria to phenol is the same. The following tests illustrate the retarding action of the broth:

Disinfectant	*C.A./R.W.*	*C.A./R.W. with Bullock's Heart Broth*
(1) ..	.. 21·6 ..	.. 9·0
(2) ..	.. 19·0 ..	.. 10·0
(3) ..	.. 19·0 ..	.. 7·0
(4) ..	.. 19·5 ..	.. 13·0

If the bullock's heart broth is uniform in composition there will be no objection to its use, although lower figures are obtained with it. But such factors as to whether the bullock is young or old, under- or over-fed, or whether the heart be fresh or chilled, influence the growth of bacteria in the broth.

Time Factor.—The recommendations of the *Lancet* Commission to extend the time contact from fifteen to thirty minutes, and to take the mean of the two and a half and thirty minutes figures in order to incorporate the effect of both time and dilution in the coefficient, was found by the American investigators too long and tedious, with the result that they took two and a half and fifteen minutes as the requisite figures. In addition, the time allowed by the *Lancet* method for inoculation—viz., every twelve and a half seconds for half an hour—makes the test somewhat formidable. The advantages accruing from the determination of the two and a half and fifteen minutes figures have to be set off against the increased amount of work to tip off the low carbolic acid controls in the right place, and for any test devised for practical and not only for research work this latter item is of great significance.

Quantity of Broth Culture added to Disinfectant.

Solutions.—In both the *Lancet* and Hygienic Laboratory tests the feeling has been expressed that the original method of adding 5 drops to 5 c.c., and subsequent subculturing by means of a standard loop, was somewhat lacking in scientific accuracy, and that it would be more scientific to add either:

(1) 0·1 c.c. from a pipette to 5 c.c. of disinfectant solution, as in the Hygienic Laboratory method, subculturing by means of a standard loop; or

(2) A standard amount from a platinum spoon of fixed capacity, originally stated as 0·08 c.c., but subsequently found to be between 0·10 and 0·15 c.c., to 5 c.c. of disinfectant solution, and subculturing also by means of a spoon.

The use of a spoon for subculturing has the disadvantage of carrying over the disinfectant into the subculture-medium, and acts as an inhibitor, a criticism which has been raised against the loop method with its much smaller capacity.

The authors have carried out several experiments on the comparison between the drop method and the 0·1 c.c. method, and have found that—

(1) With phenol and an emulsified disinfectant of C.A./R.W. 18 no difference in the time required to ensure death of the organisms could be found if 5, 6, 7, or even more drops were added.

(2) With potassium permanganate in dilute solutions 1 in 4,200 to 1 in 4,500 an effect was only produced when 7 drops were added instead of 5, the permanganate apparently being taken up by the extra amount of organic matter present.

This permits an error of 2 in 5, or nearly 50 per cent. in drop measurement. Further 5 drops delivered from this actual pipette were equivalent to 0·27 c.c., and the error in dropping was a very small one. This point, it appears, is not of great significance.

The Standard Bacteriological Test (Rideal-Walker Method), adopted by all members of the British Disinfectant Manufacturers' Association, is as follows:

"The coefficient values of all disinfectant fluids manufactured by . . . are determined in the following manner:

Shake the bottle or other vessel containing the disinfectant well before proceeding to make the dilution. Make a 1 per cent. stock emulsion (5 c.c. of disinfectant added to 495 c.c. of boiled distilled water of 15° to 80° C.). From this stock emulsion prepare required dilutions in boiled distilled water, taking care that pipettes used for preparing stock emulsion as well as dilutions are, after emptying, always well washed out with and into the diluent, and that all dilutions, including stock emulsion, are well shaken before use. To 5 c.c. of a particular dilution add 0·2 c.c. (5 drops) of a broth culture of *B. typhosus* grown for twenty-four hours at 37° C. Shake immediately after medication. Keep medicated tubes at temperature of 15° to 18° C., and take subcultures into 5 c.c. broth every two and a half minutes up to ten minutes. Incubate for at least forty-eight hours at 37° C.[1]

Use as a stock organism *B. typhosus* from a single colony on an agar plate culture that has been grown at 21° to 22° C. from two to seven days, and removed by weekly transference for several uninterrupted generations from the original source (the human body).

Owing to the extremely important influence which the broth

[1] Rideal and Walker, *J. Soc. Ind.*, October, 1903, p. 424.

has on the characteristics of the *B. typhosus* employed as the test organism in the Rideal-Walker test, particularly as regards the peptone, attention is drawn to the fact that this is prepared according to the following modification of the formula of Dr. S. Rideal:[1]

"Lemco," 20 grammes; peptone,[2] 20 grammes; sodium chloride, 10 grammes; water to 1 litre. Boil the mixture for thirty minutes, neutralize with normal caustic soda (phenolphthalein indicator), add 15 c.c. of normal hydrochloric acid, make up to 1 litre with distilled water, filter, and finally sterilize.

The culture employed must conform with the requirements laid down by the authors of the test[3]—viz., "life in two and a half and five minutes, and no life thereafter," with "phenol dilutions not higher than 1 to 110 or lower than 1 to 90."

It has long been the hope of the authors that a standard test for disinfectants should be devised varying only in temperature of operation for temperate, subtropical, and tropical use, and it appears likely that such a test will conform to the general end-point method developed in the Rideal-Walker. The following points, however, are those on which agreement is by no means universal, and on which much further information is urgently needed before such a test can become actually operative:

The Stability of the Germicide.—It is well known that with the emulsified tar acid disinfectants the enhancement of germicidal activity with the dispersity of the emulsion is by no means inconsiderable, and the aim of manufacturers is to produce a fine emulsion. Such emulsions are, however, not always stable, and may actually separate into two distinct layers after a short period of standing either in cask before dilution or after making up for actual use. Again, although emulsoids are not very sensitive to electrolytes, when they are unstable electrolytes accelerate de-emulsification—*e.g.*, dilution with sea-water or hard water.

A stability test is thus necessary to ensure the uniformity of germicidal action with these emulsified disinfectants.

The Presence of Organic Matter.—The various types of organic matter which have been added to test the germicidal activity of germicides, such as milk, blood, blood-serum, dried fæces, all suffer from the disadvantage of lack of uniformity. Many disinfectants, especially those of the oxidizing class—*e.g.*, potassium permanganate, the halogens, ozone, and the like—suffer a remarkable diminution in germicidal activity. In the presence of easily

[1] Fourteenth International Congress for Hygiene and Demography, Berlin, 1907. [2] Allen and Hanbury's "Eupepton."

[3] *Vide Lancet*, September 25, 1915, p. 717.

oxidizable organic matter, the protein coagulating disinfectants, such as the salts of the heavy metals, are precipitated by non-living proteins, whilst the emulsified tar acids are absorbed by colloidal and discrete material particles. It is thus clear that the utilization of any particular type of organic material may unfavourably affect certain germicides and leave others unaffected.

If organic matter is to be added, it should embrace all these various factors—*i.e.*, it should be uniform in composition, capable of oxidation, of coagulation, and exhibitive of the phenomenon of absorption. Such a material may possibly be found in the synthetic polypeptides, where in derivatives with a high molecular weight colloidal solutions are readily obtained.

The Choice of Organism.—It is well known that many different strains of *B. typhosus* exist of appreciably different resistances to phenol, and that this resistance to other disinfectants does not vary *pro rata;* in fact, micro-organisms can by careful cultivation be immunized to quite strong solutions of any particular germicide. For this reason the limits or variation have been embraced in the modern tests. This point is of extreme importance in the case of the germicides of high R.W. figure, since the discrepancies obtained with different organisms are more serious. The ease with which organisms can be grown on agar and sent by post suggests the universal use of one organism—*e.g.*, *B. typhosus* (Johns Hopkins) or *B. typhosus* (Rawlings). Both these organisms fall within the limits suggested by the test, provided that continuity and regularity in subculturing is maintained. It would appear inadvisable at the present to place closer limits on the phenol control, since the seasonal variation in the resistance of the organism appears to be a difficult factor to eliminate.

The Choice of Culture Medium.—All the constituents of the culture medium—the "Lemco," peptone, and salt—have from time to time received their fair share of criticism, and it is certain that neither the original R.W. nor the Hygienic Laboratory broth is sufficiently uniform when made up by different investigators to give reproducible results, even with a limitation of the phenol control periods for the organism as stipulated in the present-day test. From time to time the writers have endeavoured to obtain a uniform "Lemco," since it is well known that the "Lemco" itself, although more perfect than any other nutrient medium proposed —*e.g.*, blood or bullock's heart broth—is subject to variations both in inorganic salts, but more especially in extractives which affect the R.W. figure. Wright[1] suggests that the cause of variation

[1] *J. Bacteriol.*, 1917, **2**, 319.

is due to the partial conversion of the fat glycerides into soaps when the media are boiled in alkaline solution. Doubtless, if the world's consumption of "Lemco" for bacteriological testing purposes were even approximately estimated, the "Lemco" Company would be prepared to set aside from their different batches material conforming to some agreed-upon figure for salts, nitrogen, fat, extractives, and hydrogen-ion concentration in a specified dilution under a suitable title, such as "'Lemco' for Bacteriological Purposes." A very small additional charge would cover the cost of analytical control and distribution through the larger retailers.

The addition of 10 grammes of sodium chloride has the sole advantage of minimizing (see a very comprehensive paper by J. H. Wright,[1] for a very detailed investigation on the problem of uniformity in culture media) slight variations in the inorganic salt content of broth, the "Lemco," and the peptone. Although the growth of the *B. typhosus* is not very sensitive to slight changes in electrolytic concentration, provided that this concentration is equal to or somewhat greater than that corresponding to physiological salt solution, small traces of electrolytes, on the other hand, in an otherwise nearly salt-free medium, do greatly affect the growth of the organisms. For the above reason it would appear inadvisable to reduce the salinity of the solution down to, and certainly not below, that of physiological salt solution. The addition of salt to the germicidal solution does, however, as has already been indicated, frequently alter the germicidal activity; thus in the case of phenol the activity is raised, due to an elevation in the chemical potential or activity of the phenol. That this is the true cause has been confirmed by Reichel[2] and Lash Millar,[3] who showed that phenol solutions of the same chemical activity, and consequently of the same fugacity, as determined by a partitive method, were equally germicidal. Similarly, in the case of mercuric chloride an increase on the addition of NaCl to the germicide is occasioned in spite of the lowering of the Hg″ concentration. This is doubtless in part due to the formation of the complex ion $HgCl_4$, which appears to be more basic than Hg″, although the unionized salt Na_2HgCl_4 has but slight germicidal activity.[4] The reaction of the medium is, however, a much more important factor. The rate of growth of *B. typhosus* and of other organisms is very dependent on the hydrogen-ion concentration. J. Wright[5] found the optimum hydrogen-ion concentration for *B. typhosus* as $P_H = 6$ . . . $P_H = 7$

[1] *J. Bacteriol.*, 1917, **2**, 4.
[2] *Biochem. Zeit.*, 1904, **22**, 149.
[3] *J. Phys. Chem.*, 1920, **24**, 566.
[4] See J. Clark, *J. Phys. Chem.*, 1901, **5**, 310.
[5] *Loc. cit.*

Schoenholtz and Meyer[1] obtained as optimum $P_H = 6{\cdot}8$ to $P_H = 7{\cdot}0$, variations in generation time being found as follows:

P_H	*Generation Time at* 30° *C.*
5·4	41·3
7·0	31·0
7·8	33·4

We may, therefore, assume that for uniformity in culture medium the hydrogen-ion concentration should be between the limits $P_H = 6{\cdot}5$ to $P_H = 7{\cdot}0$, and preferably the medium should be adjusted to a hydrogen-ion concentration of $P_H = 7{\cdot}0$, or that obtaining in pure water.

This concentration of hydrogen-ions can be adjusted in the medium by the addition of either caustic soda or hydrochloric acid, as is necessary, but the variation in hydrogen-ion concentration on the addition of alkali or acid to a neutral medium cannot be calculated if the solution contains an unknown concentration of "buffer" salts. Thus, the methods of preparing media by neutralization with caustic soda to a phenolphthalein end-point, followed by bringing the reaction up to +1·5 with hydrochloric acid, is not satisfactory, since in the presence of large quantities of buffer salts—*i.e.*, the salts of a strong base and weak acids such as are present in broth, peptone, and "Lemco"—the hydrogen-ion concentration will vary but little.

The only satisfactory method of adjusting the reaction of the medium is by direct measurement of the hydrogen-ion concentration; if a value of $P_H = 7$ be adopted, litmus solution will acquire a port-wine colour such as is obtained on the addition of litmus solution to water containing a little free carbonic acid.[2] Alternatively to colorimetric methods the electrometric hydrogen electrode may be employed. For accurate work the hydrogen electrode is to be recommended, but unless carefully manipulated and frequently used, hydrogen electrodes are often a source of much annoyance and trouble; for this reason it would seem preferable to use suitable indicators which give a marked colour change in the region $P_H = 6{\cdot}8$ to $P_H = 7$, and adjust the reaction of the medium by the addition of either acid or alkali, without any prior neutralization, until the colour change, as determined by the spotting-out method employing a white tile, indicates the correct hydrogen-ion concentration. Colorimetric methods are usually reproducible by independent observers to within 0·1 to 0·15 P_H.

[1] *Proc. Soc. Biol. Med.*, 1919, **16**, 151.

[2] For details as to the methods for the determination of the P_H of media, see "The Determination of Hydrogen Ions," by W. M. Clark; Williams and Wilkins, 1920.

The Peptone.—The original peptone suggested for the R.W. test was Witte's. This was employed for the simple reason that the manufacturers of this material have succeeded in producing a very uniform product. During the period of the war and subsequently home manufacturers have devoted more attention to the production of a uniform peptone. The Digestive Ferments Company in America and Allen and Hanbury in this country have succeeded in producing peptones which appear to be uniform in composition. The work in our own and in the Lederle Laboratories, New York, has conclusively shown that the hydrogen-ion concentration or the amount of buffer salts in a "Lemco" peptone broth is not the only controlling factor in the growth of *B. typhosus*, since certain peptones possess more easily assimilable foodstuffs than others, resulting in a luxuriant growth at identical hydrogen-ion concentrations. It would therefore appear probable that some proprietary peptone on the market would have to be incorporated in an international test.

The Reaction Kinetics and Disinfection.

The various drop methods, as well as the original thread method, of testing disinfectants are end-point tests, in so much as they give but an indirect method of determining exactly the rate of germicidal action. The garnet method of Krönig and Paul is thus a superior method of studying the reaction kinetics of disinfection, although it will be evident that by utilizing numerous short time intervals in any of the drop methods the variation in rate with the time may be approximated to.

The rate of disinfection was first examined in detail by Krönig and Paul[1] by the simple immersion of anthrax-loaded garnets in the disinfectant, and counting by subsequent incubation the number left alive after different intervals of time. The rate of disinfection or the rate of death at any time is proportional to the mumber left alive at that time and to the strength of the disinfectant, or

$$-\frac{dn}{dt} = Kcn,$$

where c is the concentration of active germicide, n the number of micro-organisms alive at time t.

On integration this expression becomes:

$$\frac{1}{t_1 - t_0} \cdot \log_e \frac{n_0}{n_1},$$

where n_0 and n_1 are the number of organisms alive at times t_0 and t_1 respectively.

[1] *Zeitsch. Hyg.*, 1907, **25**, 26.

Similar results have been obtained for various organisms with different types of germicides by Chick,[1] Lane Claypon,[2] Bronny and Gehnour,[3] Watson,[4] Churchmore,[5] and especially by Lee and Gilbert.[6]

As typical of the results obtained in this way may be quoted the following:

Observers, Krönig and Paul.[7]
Organism, anthrax spores.
Disinfectant, 0·11 per cent. $HgCl_2$.
Temperature, 18° C.

Time in Minutes.	*N (Surviving).*	$K = \frac{1}{t_n - t_0} . log \frac{N_0}{N}$.
$10 = t_0$	$2027 = N_0$	—
15	672	0·096
20	564	0·056
25	382	0·048
30	251	0·045
35	179	0·042
40	138	0·039
45	101	0·037
50	80	0·035
60	39	0·034
70	6	0·042
80	3	0·040

Observer, Chick.[8]
Organism, *B. typhosus*.
Disinfectant, 0·6 per cent. phenol.
Temperature, 20° C.

Time in Minutes.	*N (Surviving).*	*K.*
$0·5 = t_0$	231·3	—
1·5	190·0	0·085
2·6	167·0	0·067
4·6	119·2	0·075
6·6	77·8	0·077
10·5	31·6	0·086
15·0	11·3	0·090
20·0	2·4	0·102
30·0	0·35	0·096

Lee and Gilbert obtained the following values for the reaction velocity constants with a number of micro-organisms:

[1] *J. Hyg.*, 1910, **10**, 237.
[2] *Ibid.*, 1909, **9**, 239.
[3] *J. Path. Bact.*, 1913, **18**, 144.
[4] *J. Hyg.*, 1910, **10**, 237.
[5] *J. Exp. Med.*, 1913, **16**, 221, 822.
[6] *J. Phys. Chem.*, 1918, **12**, 348.
[7] *Zeitsch. Hyg.*, 1897, **25**, 26.
[8] *J. Hyg.*, 1910, **10**, 237.

Organism.	*Disinfectant.*	*Temperature.*	*K.*
B. typhosus	0·2 per cent. phenol	37·5° C.	0·067 - 0·056
Anthrax spores ..	0·1 per cent $HgCl_2$	20·0° C.	0·057 - 0·043
Staph. pyog. aureus	0·2 per cent phenol	0·0° C.	0·0146 - 0·0132
B. coli communis ..	Electric lamp exposure (100 watts)	—	0·021 - 0·013

The time required for complete disinfection was also determined by these latter observers. These data are usually obtained in the usual end-point methods already described.

In the case of phenol with *B. typhosus* at 37·5° C. and *Staph. pyog. aureus* at 20° C., the following figures were obtained:

Percentage Phenol.	*T (for Complete Disinfection) Minutes.*	
	B. typhosus.	*Staph. pyog. aureus.*
1·5	4	—
1·3	9·5	—
1·2	—	7
1·0	25	26
0·9	50	—
0·8	—	100
0·7	155	—
0·6	300	400
0·5	—	1,200

It is well known that an increase of temperature greatly augments the velocity of disinfection. For most measurable chemical reactions the temperature coefficient of the velocity constant is ca 2 to 4 for a rise of 10° C. The same holds good for many disinfectants—*e.g.*, $HgCl_2$ and $AgNO_3$; for phenol and the emulsified disinfectants the reaction velocity temperature coefficient is much higher; thus Lee and Gilbert found the following values:

Organism.	*Disinfectant.*	*Temperature Coefficient of Reaction Velocity.*
B. typhosus	0·01 per cent $HgCl_2$	3·0
,, ...	0·6 per cent. phenol	7·5

Watson, Lee, and Gilbert[1] have attempted to find out the number of molecules reacting with each organism by determining the time necessary for complete disinfection with various concentrations

[1] *Loc. cit.*

of disinfectants. If this latter be in large excess Watson found that $n \log C + Gt = \text{constant}$, where n is the number of molecules reacting with a micro-organism at any instant; for *Staph. pyog. aureus* $n = 5{\cdot}5$, for anthrax spores and $HgCl_2$ $n = 4{\cdot}9$, with *B. paratyphosus* $n = 3{\cdot}8$. For *B. typhosus* and phenol $n = 6$. Thus one micro-organism requires from 3·8 to 6 molecules of disinfectant for destruction. Attempts have likewise been made in the case of ionized disinfectants to determine the number of ions reacting with each micro-organism. Experiments with the heavy metallic ions, such as copper, silver, and mercury, which react with proteins, can easily be made by either electrical conductivity or preferably by potentiometric methods,[1] but it remains to be proved how many ions are actually required to produce death.

We have already indicated that the mechanism of disinfection is relatively complicated, and that the rate of disinfection follows approximately a monomolecular reaction when the disinfectant is in large excess. As a result of these experiments, numerous experimenters have been led to the conclusion that the micro-organism can be regarded as a simple molecular species, and that disinfection is a simple chemical process. This is certainly not the case, as diffusion and osmosis, as well as phenomena such as reversible and irreversible chemical coagulation, play an important part in the operation. These actions are not the same as a purely chemical reaction, although due to the same chemical and electrical forces. They do, however, follow the same mathematical law—viz., $\frac{dn}{dt} = Kn$ as a monomolecular reaction. As instances where the same law holds approximately for widely diverse phenomena may be mentioned the rate of unrestricted growth of bacteria,[2] the adsorption of acids by wool,[3] the rates of solution of substances in water (diffusion) and also in acids,[4] the rate of precipitation of solids from solids,[5] and the rate of evolution of gases from liquids.[6]

It is thus evident that to obtain a satisfactory monomolecular reaction curve (which incidentally was not obtained with 0·6 per cent. phenol at 20° C. on *S. pyog. aureus*, when for the first four minutes a constant surface diffusion expression

[1] See La Franca, *Zeitsch. Physikal. Chem.*, 1906, **48**, 481.

[2] Lane Claypon, *J. Hyg.*, 1909, **9**, 239; Penfold and Morris, *ibid.*, 1913, **12**, 527; Slater, *Biochem. J.*, 1913, **7**, 197.

[3] See Diett. *Monatsh.*, 1914, **35**, 787.

[4] See Noyes and Whitney, *Zeitsch. Physikal. Chem.*, 1897, **23**, 689; Bruner, *ibid.*, 1900, **35**, 283; *Zeitsch. Anorg Chem.*, 1901, **28**, 314; 1903, **35**, 23; 1903, **37**, 455.

[5] Langley, *Chem. Soc. Trans.*, 1884, **45**, 633.

[6] Penman, *ibid.*, 1898, **73**, 515; 1903, **83**, 1168.

$\frac{dn}{dt}=K$ was obtained by Lee and Gilbert) does not necessarily indicate that the progress of the reaction actually measured was a chemical reaction, although, as has already been indicated, death is due in the ultimate analysis to a problem in chemistry.

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