UNIVERSAL
LIBRARY

OU_170685

UNIVERSAL
LIBRARY


M



THE MODERN LIBRARY

OF THE WORLD'S BEST BOOKS

# CONTEMPORARY SCIENCE

The publishers will be glad to mail upon request a forty-page illustrated catalogue descriptive of the Modern Library. This booklet sets forth the purposes and ideals of the series, and gives a brief outline of each book included in the Modern Library. Every reader of books will find titles he needs at a low price in an attractive form.

# CONTEMPORARY SCIENCE

EDITED WITH AN INTRODUCTION BY

BY BENJAMIN HARROW, PH.D.

AUTHOR OF "FROM NEWTON TO EINSTEIN," "EMINENT CHEMISTS OF OUR TIME," "VITAMINES," "ESSENTIAL FOOD FACTORS"




BONI AND LIVERIGHT

PUBLISHERS NEW YORK

CONTEMPORARY SCIENCE

COPYRIGHT, 1921, BY
BONI & LIVERIGHT, INC.

PRINTED IN THE UNITED STATES OF AMERICA

The men who have been good enough to coöperate with me in the preparation of this volume are masters of their respective subjects; and what they say represents, in summary form, some of the latest achievements in science. The book does not pretend to be an exhaustive treatise, but it does claim to review some of the more recent and more suggestive work.

My thanks are due to the distinguished contributors not only for permitting me to use their articles, but for affording me the pleasure and instruction these articles have given me.

I am also indebted to the editors of the *Transactions of the American Institute of Electrical Engineers,* the *Journal of Industrial and Engineering Chemistry,* the *Journal of the Washington Academy of Sciences,* the *Scientific Monthly, Science,* and the *Journal of the American Medical Association,* for permission to reprint some of these articles.

THE EDITOR.

# CONTENTS


PAGE

INTRODUCTION . . . . . 9

MODERN PHYSICS . . . . . 13
By R. A. MILLIKAN

THE STRUCTURE OF ATOMS AND ITS BEARING ON CHEMICAL VALENCE . . . . . 23
By IRVING LANGMUIR

ENGINEERING BEFORE AND AFTER THE WAR . . . . . 34
By SIR CHARLES PARSONS

METHODS OF GAS WARFARE . . . . . 61
By S. J. M. AULD, D.S.M.

WHAT ARE ENZYMES? . . . . . 76
By BENJAMIN HARROW

NATURAL DEATH AND THE DURATION OF LIFE . . . . . 85
By JACQUES LOEB

THE PHYSIOLOGY OF THE AVIATOR . . . . . 95
By YANDELL HENDERSON

TWENTY-FIVE YEARS OF BACTERIOLOGY: A FRAGMENT OF MEDICAL RESEARCH . . . . . 115
By SIMON FLEXNER

BEFORE AND AFTER LISTER . . . . . 152
By W. W. KEEN

THE MEASUREMENT AND UTILIZATION OF BRAIN POWER IN THE ARMY . . . . . 192
By R. M. YERKES

CONCEPTIONS AND MISCONCEPTIONS IN PSYCHOANALYSIS . . 211
By TRIGANT BURROW, M.D.

EINSTEIN'S LAW OF GRAVITATION . . . . . 230
By J. S. AMES

INDEX . . . . . 247

# INTRODUCTION

BY

BENJAMIN HARROW

*Associate in Physiological Chemistry,*
*Columbia University*

THE Greeks were the first to advance the idea that matter cannot be subdivided indefinitely. According to them a stage would be reached beyond which no further subdivision would be possible; this they called the atomic stage.

The Greek idea of atoms lay dormant until early in the nineteenth century, when John Dalton revived it. In Dalton's hands the hypothesis of atoms became the very basis for building the superstructure of chemistry.

It may be doubted whether, with the possible exception of Lavoisier, any man was more responsible for laying the foundations of modern physics and chemistry than Dalton, native of Manchester.

Not till the latter part of the last century did the rumblings of a storm make themselves heard. Then began those celebrated experiments on the electrical properties of gases, by J. J. Thomson and others, followed by Roentgen's discovery of X-rays and Madame Curie's isolation of radium, which opened up to view a new continent in science. For the gist of these achievements was to show that the atom was by no means the smallest particle of matter; that the atom, in fact, inconceivably small though it be, was yet complex enough to resemble, in minia-

ture, our solar system, with a positive particle of electricity for its sun, and negative particles (electrons) to represent the planets.

The more recent activities in physics and chemistry have mainly focussed themselves on elucidating the structure of the atom. The successive stages in the development of these researches are summed up by Professor Millikan, the master in the measurement of the electron.

The latest, and so far the most probable, hypothesis of the structure of the atom is that due to Dr. Langmuir.

The breaking up of the atom is accompanied by the release of enormous quantities of energy. If a catalyzer could be found to accelerate such a reaction, then the solution of the problem, the Energy of the Future, would be in sight. So far we have not been able either to accelerate or to retard radium disintegration, though Professor Rutherford, of Cambridge, has recently been successful in breaking up the nitrogen into hydrogen atoms by means of alpha particles obtained from radium. Chemists and engineers are busy casting their eyes upon objects other than fossilised wood, because of our prodigal expenditure of the coal resources of the earth. In this connection Sir Charles Parsons, English engineer, suggests sources of energy that have so far been neglected.

Not without reason has the Great War been called the Chemists' War, yet there is an element of injustice in the name. The layman assumes, from the activities of the chemist during the seven critical years from which we are emerging, that the function of this type of scientist is to destroy, just as the function of the physician, on the other hand, is to heal. I say this opinion of the chemist is an unjust one. He cannot be blamed if the weapons he forges are misused. The several varieties of the nitro compounds that form the series of modern explosives are indispensable in the building of a Panama Canal; and the very gas that has tortured the bodies of thousands of innocent youngsters saved the lives of thousands during the

late war when applied in small doses in somewhat modified form.

Colonel Auld's authoritative exposition of gas warfare is not included to make the reader as enthusiastic about this tool of civilized man as it has made a number of generals belonging to the five continents. The introduction of "gas" in war has done as much to revolutionize warfare as the introduction of the aeroplane. For good or for evil, gas warfare has come to stay, unless a miracle happens and men begin to use their hearts as well as their heads.

We can at least point to one constructive achievement indirectly due to the development of gas warfare. Several types of gas masks have already been successfully used by miners and others as protection against poisonous fumes.

The physicist needs his mathematics; the chemist rests more and more on physics; and so it is no wonder that the biologist and the medical man have turned to physics and chemistry for further inspiration. Some of the most notable achievements in biology and medicine in recent years have been due to the application of the two more fundamental sciences to them. The elucidation of the nature of enzymes is a case in point; Professor Loeb's and Professor Henderson's articles are other and noteworthy examples.

Still it is true to say that in medicine the most notable achievement so far has been the development of the science of bacteriology, the foundation of which we owe to the chemist Pasteur. The story of this development is told by Dr. Flexner.

The chemist Pasteur inspired Lister the surgeon; and Dr. Keen, who served in the Civil as well as in the late war, tells the story of Before and After Lister.

From the physical, through the biological, to the psychological sciences is a very natural evolutionary process. Experimental psychology, of which psycho-analysis may

be considered a part, is still in its swaddling clothes; but the two articles by Professor Yerkes and Dr. Burrow give an idea of future possibilities.

I have put Professor Ames's article dealing with Einstein's theory last on the list because in some ways it can be regarded as a summation or a crystallization of all of the sciences. In its conception of a cosmos decidedly at variance with anything yet conceived by any school of philosophy, it will attract the attention of thinking men in all countries. The scientist is immediately struck by the way Einstein has utilized the various achievements in physics and mathematics to build up a coördinated system showing connecting links where heretofore none was perceived. The philosopher is equally fascinated by a theory which, in detail extremely complex, shows a singular beauty of unity in design when viewed as a whole. The revolutionary ideas propounded regarding time and space, the brilliant way in which the most universal property of matter, gravitation, is for the first time linked up with other properties of matter, and above all, the experimental confirmation of several of his more startling predictions—always the finest test of scientific merit—stamp Einstein as one of those super-men who from time to time are sent to give us a peep into the beyond.

# MODERN PHYSICS

(A lecture delivered at the Fifth Midwinter Convention of the American Institute of Electrical Engineers, New York, Feb. 15, 1917)

BY

R. A. MILLIKAN

*Professor of Physics, Chicago University*

Let me run over a list of ten discoveries which I will call the ten most important advances [in physics] of the last twenty years.

We may aptly characterize the physics of the last twenty years as the physics of atomism, and the first discovery on my list of ten advances is the recent verification of the adumbrations of the Greeks regarding the atomic and the kinetic theories—the proof that, as Democritus had imagined 500 B. C., this world does indeed consist, in every part of it, of matter which is in violent motion.

Up to within six years there were not a few distinguished scientists who withheld their allegiance even from these atomic and kinetic theories of matter. The most illustrious of them was Professor Wilhelm Ostwald, but in the preface to a new edition of his *Outlines of Chemistry* he now says frankly:

"I am convinced that we have recently become possessed of experimental evidence of the discreet or grained nature of matter for which the atomic hypothesis sought in vain *for hundreds and thousands of years.* The isola-

tion and counting of gaseous ions on the one hand . . . and on the other the agreement of the Brownian movements with the kinetic hypothesis . . . justify the most cautious scientist in now speaking of the experimental proof of the atomic theory of matter. The atomic hypothesis is thus raised to the position of scientifically well-founded theory."

The second advance is the proof of the divisibility of the atom, a proof which grew out of the discovery of X-rays. Let me tell you how. If you have here two plates with an electric field between them, and nothing else but a monatomic gas like helium, then it is found that when the field is thrown on, the helium is perfectly stagnant; but when a beam of X-rays is shot between the plates, some of the molecules become electrically charged and begin to jump,—some toward the upper, and some toward the lower plate, where their presence can be detected by an electrical measuring instrument. What does that show? It shows that the thing which we call an atom has electrical charges as its constituents; and the history of the last twenty years in physics has consisted pretty largely in determining what are the properties of these electrical constituents.

The third is the discovery of radio-activity, which occurred just a little after the discovery of X-rays. And here again we found matter doing things we had never dreamed it was doing; *viz,* shooting off from itself both negatively and positively charged particles, the negatives with a speed which may approach close to the velocity of light, 186,000 miles per second, and the positives with a speed of one-tenth of that, or 18,000 miles. The fact that such speeds could be imparted to projectiles of any kind was undreamed of twenty years ago.

The fourth discovery that I wish to mention is the discovery of the atomicity of electricity,—the proof that the thing we call electricity is built up out of a definite number of specks of electricity, all exactly alike; and that

what we call an electrical current consists simply in the journey along the conductor of these electrical specks, which we may call with perfect justice definite *material* bodies. Now, I can give you in just a word the proof of that statement. There are half a dozen ways in which it could be approached. I will mention the one with which I am most familiar, because it is the particular proof which we worked out in our laboratory.

We took these plates with a field of 10,000 volts between them, with a little hole in the top plate, and blew an oil spray above the top plate so as to get an electrically charged body just as small as we could; for we expected that the frictional process involved in blowing the spray would charge the drops; and this, indeed, it was found to do. We let one of those drops come into the space between the plates, and then moved it up and down by an electrical field, throwing it on the field as it came close to the bottom plate, and throwing it off as it approached the upper one. And so we kept that oil drop going up and down between the plates, in the hope that it would capture some of the ions which we knew existed in the air, put there by radium or other agencies. The drop met our fullest expectations. It captured ions frequently and signalled the fact of each capture to the observer by the change in its speed in the field. For the oil drop is an electrically charged body, and in a given field it moves with a definite speed. If, however, it captures an ion, its charge increases or decreases, and hence its speed increases or decreases. If the charges on ions are all alike, then we can only get one particular change in speed. If the charge that is already upon it, put there by the frictional process, is built up out of these same units, then the total speed which the field will impart must be an exact multiple of the change in speed which the capture of an ion produces. In other words, if electricity is atomic in structure, you cannot get in a given field anything except a definite number of speeds, which will make an arith-

metical series; that is, which will come up by steps,—one, two, three, etc. That is exactly what we found. We have experimented with thousands of drops and scores of different substances, and they always work exactly that way. Both positively and negatively charged drops are found to act in quite the same way, showing that both positive and negative electrical charges are built up of specks of electricity. Further we can count the number of those specks, which we will call electrons, in a given drop, with the same certainty with which you can count the number of fingers that are on your hand. And again since Rowland showed that an electrical current is nothing but a charge in motion, you have here the proof that the electrical current that goes through these lamps, for example, is nothing except the motion of a certain number of electrical specks through or over the filament of the lamp. Add to that J. J. Thomson's discovery made in 1881, that an electrical charge possesses inertia, the only distinguishing property of matter, and you have made it perfectly legitimate to say that an electrical current in a wire is a definite, material, granular something which is moving along that wire.

The fifth great discovery of modern physics is the bringing forward of evidence for the electrical origin of mass. I have just said that electricity is material. Can we turn it around, and say that all matter is electrical in origin? The last is not exactly the same as the first, and it needs evidence. When we have proved that an electrical charge possesses inertia or mass we have not shown that there is no inertia in matter which is not electrical in its origin. Now we have a certain amount of evidence upon this point and I wish to state what that evidence is. We can measure the inertia of the negative electron and it is found to be one-one thousand eight hundred and forty-fifth part of the inertia of a hydrogen atom, but the positive electron is never found with an inertia less than the inertia of a hydrogen atom. Let us consider the inertia of the negative.

So long as it is moving slowly compared with the speed of light its inertia remains constant because the shape of its electromagnetic field is not appreciably distorted by its motion. But as soon as you imagine it to be moving with a speed which is close to the speed of light, that is with a speed which is nearly as great as the speed with which its own electro magnetic field can travel forward, then further change in speed will distort the field and hence change the inertia. In other words, the inertia of a charge ought to be a function of speed only when the speed approaches the speed of light. As a matter of fact, when it is from 0.1 up to 0.9 of the speed of light, you can compute just how it ought to vary. Now, by some happy chance the physicist has found negative electrons, namely those shot off by radium, which are going with these speeds, and hence it is possible to test our theory for these particles and see whether the rate of change of their inertia with the speed checks with the theoretical value. It is found that there is such a check. This means that there isn't any inertia in those particles which does not obey the electromagnetic laws. Therefore, we *have good reason for assuming that the negative electron is nothing but a disembodied electrical charge, and that its inertia is wholly of electrical origin.*

With respect to the positive electron, we have not such convincing evidence as yet, but it is obviously in the interest of simplicity to assume one kind of inertia rather than two kinds. Further, we have a little bit of evidence of this kind, and I wish to mention what it is, because that will furnish an introduction to my sixth important modern discovery. We have good reasons for thinking that there is only one positive electron in the hydrogen atom, but that the mass, or inertia of that positive is almost the mass of the hydrogen atom—at any rate we never find it any less. If this inertia is all electrical, then we know from theory that the charge must be more condensed in the positive than in the negative; consequently, if we are

going to make the observed inertia of the hydrogen nucleus all electrical, it must possess an even denser charge than that on the negative.

This brings me to the sixth of our discoveries, namely *the discovery of the nucleus atom.* Let me give you just a brief statement of how we know that the atom is somewhat like a miniature solar system, with an extraordinarily minute nucleus, the size of which is never more than one-one hundred thousandth part of the diameter of the atom —and with a certain number of subsidiary bodies—negative electrons—which we may liken to the planets, and which are somewhere around the outside. How do we know that is the case? We have this direct evidence. Nature takes a helium atom which is going with a speed of 18,000 miles per second, and Nature shoots that atom right through a glass wall without leaving any hole behind, and without in any way interferring with the structure of the molecules of the glass. I can show you photographs that make the thing so clear that the man in the street can see it. This obviously means that the positive nucleus itself must be extraordinarily minute. Indeed the fact that the negative electron actually shoots through those hundreds of thousands of atoms without ever going near enough to any constituent of those atoms to knock any one of them out, and the fact that the positive nucleus of helium, *viz.*, the alpha particle, shoots through even more molecules without being deflected at all from its course, causes one to wonder whether there is anything at all that is impenetrable in the atom. Why do we say there is a nucleus there? Because direct experiment says there is. There is a certain portion of the atom which the alpha particle itself cannot penetrate. If the impact is head on, the alpha particle goes right up to the atom and then it backs out again. Or if it comes up to the atom at an angle, it glances off that way. Rutherford, Geiger and Marsden counted the percentage of alpha particles which go straight on, and the percentage which go off at a

tangent; and in this manner we find how big that nucleus is. By the size of the nucleus I mean the size of that portion of the atom which is impenetrable to the alpha particles. It amounts to about $10^{-13}$,000,000,000,000 centimeters. The diameter of the atom is $10^{-8}$. Furthermore, by counting how the deflections of the alpha particles are distributed around this sphere, which we can do directly with the aid of zinc sulphide spread over the inside of the sphere, we can obtain the number of alpha particles deflected through any given angle. With a little analysis of unquestionable correctness, we find how many unit charges,—positive electrons,—there are in this exceedingly small nucleus, and it comes out approximately to one-half of the atomic weight.

I now come to another extraordinary discovery. This one does not merely tell us approximately how many electrons there are in the nucleus but it tells us *exactly* how many there are, and the result checks with the number obtained by the foregoing approximate method. This brings me to the recent discoveries in the field of X-rays, and I will call the seventh of the modern advances the discovery of the nature of X-rays, which was virtually made by Barkla in 1904. For Barkla and others had proved that there are two types of X-rays: first, X-rays which consist in simple ether pulses pushed off from an electron when it changes its speed; and second, so-called characteristic X-rays. When the electrons bump into a target they set something in the target into vibration, and this something sends off perfectly definite characteristic X-rays, which are like monochromatic light. So that we have two types of X-rays,—pulse X-rays, like white light; and monochromatic X-rays, like monochromatic light (such as mercury gives rise to). That is the seventh of our great modern discoveries, and it must be credited chiefly to Barkla.

The eighth I will call the discovery of crystal structure by the study of X-rays, which is due to Laue in Munich,

and Bragg, in England. The method is simply this. We analyze light by a grating which consists of a series of equally spaced lines on a reflecting or transmitting surface. With such a device we can split light up into a spectrum; but we cannot do this unless the width of the grating space is comparable with the wave length of the light. In the case of X-rays, we had no knowledge of gratings whose grating spaces were anything like as small as the wave length of X-rays. In fact such gratings were unknown until Laue had the bright idea of using the regular arrangement of the atoms in a crystal for a grating to see whether that would not do the work, and it did the work marvelously well. It was found that we could compute the grating space of certain crystals from the density and the atomic weight, and then from the observed spectrum find the wave length of X-rays. And now knowing the wave length we can work backward and find the grating-space for other crystals. We are now using this method for finding the positions and the arrangements of the atoms in crystalline bodies. Prof. Bragg in his recent book on X-rays and crystal structure has described this work very beautifully. Thus a whole new field of experimentation has been opened up and is being pursued in a great many laboratories, and with particular success by A. W. Hull at the laboratory of the General Electric Company. There are almost unlimited possibilities for the chemist in the discovery of the exact position of the atoms in any kind of crystal by this method.

But the results of this discovery as of most of the others which I have mentioned are rather insignificant when compared with those of the ninth which I am going to mention, namely the discovery of the relations between the elements, and the extension of our knowledge of the radiations emitted by different substances. This discovery was made by a young Englishman, Moseley, only twenty-six years old, who has already, unfortunately, fallen a victim to this juggernaut which is at the present time

crushing out the finest scientific brains in the world. Moseley was killed at the age of twenty-seven, a year after he had made his epoch-making discovery, and all the lives and all the interests of the eternally infamous men who made this war are not to be compared in value to the world with a hair of Moseley's head. Yet he had to be sacrificed to save a threatened civilization. A double honor to Moseley.

His discovery was this: He was analyzing the characteristic X-rays which are given off when any kind of a substance is bombarded with cathode rays. The experiment was in my judgment as brilliantly conceived, as carefully and skillfully carried out, and as illuminating in its results, as any which has been done in the last fifty years. What he found was this, that the atoms of all the different substances emit radiations or groups of radiations which are extraordinarily similar, but that these radiations differ in their wave lengths as we go from substance to substance. The whole discovery can be stated in this fashion: If you take the highest frequency emitted by a given atom, and if you lay down on a table a length which is equal to the square root of this frequency, and if on top of that you lay down the square root of the frequency of the atom which has the next lower frequency, and so if you continue to lay down, with one group of ends together, the measured square root frequencies of all the elements that you can study, then what have you got? You find that you have a flight of stairs, with perfectly definite equal treads; that is, the frequencies change by definite steps as you go from element to element. And there are only four vacant treads between the lightest element which Moseley could study, namely aluminum and the heaviest one, namely lead; thus indicating that there are only four elements in this range which we have not already found.

We may then picture with considerable confidence this whole physical world as built up out of one positive and one negative electron. The positive electron is the nu-

cleus of the hydrogen atom. It is very minute in comparison with the negative, but much more massive. When two free positive electrons are tied together we have the helium atom. We don't know why these positives cling together.

My last of the great discoveries of modern physics is one that I will just touch upon. It is the discovery of quantum relations in photo-electricity, in X-rays, and in optical spectra; but here I am coming to a field which we do not know very much about, which we do not yet understand, and my main motive in introducing it is to convince you that the physicist, in spite of all he knows, or thinks he knows, is a fairly modest fellow; because there are some things he knows he doesn't know, and one at present is the nature of radiation. However, we know some things about it that are new. For example, it is an extraordinarily interesting fact that when light of the X-ray type, or indeed, light of any frequency falls upon say a lithium or sodium surface, or upon almost any surface, it has the property in some way of taking hold of a negative electron in the atoms of that surface and of hurling that electron out with a speed which can be measured, and which we find to be exactly proportional to the frequency of the light. That is an extraordinary phenomenon, and it is one that we explain on a kind of quantum theory which I will not attempt to go into here, because of the fact that we have not yet worked it out fully; but at any rate, the quantum constant comes out of the photo-electric effect, as shown in my own work, out of X-ray work as discovered by Duane and Hunt at Harvard, and out of spectroscope work, as shown by Bohr in the beautiful theory of the atom which he has developed within the last three or four years.

# THE STRUCTURE OF ATOMS AND ITS BEARING ON CHEMICAL VALENCE

BY

IRVING LANGMUIR

*General Electric Company*

ACCORDING to the well-established Rutherford-Bohr theory, all the positive electricity in an atom is concentrated in a *nucleus* at its center. The dimensions of this nucleus are negligibly small compared with those of the rest of the atom, its diameter being of the order of 0.00001 of that of the atom. The charge on the nucleus is an integral multiple of the charge of an electron but of course opposite in sign. The remainder of the atom consists of electrons arranged in space about the nucleus, the normal number of such electrons (called the *atomic number*) being equal to the number of unit positive charges on the nucleus, so that the atom as a whole is electrically neutral. If the number of electrons in the atom exceeds the atomic number we have a negatively charged atom or ion while in the reverse case a positively charged atom or ion results. The atomic number of any element has been found to be equal to the ordinal number of the element in the periodic table. Thus hydrogen has the atomic number one, helium 2, lithium 3, carbon 6, neon 10, chlorine 17, nickel 28, silver 47, cerium, 58, tungsten 74, radium 88, and uranium 92. The atomic numbers can be determined

experimentally from the X-ray spectrum so that we are not dependent upon the periodic table for our knowledge of these numbers.

Bohr, Sommerfeld and others have developed an extensive and very successful theory of spectra upon the hypothesis that the electrons in atoms are in rapid rotation in plane orbits about the nucleus in much the same way as the planets revolve around the sun. Stark, Parson, and G. N. Lewis on the other hand, starting from chemical evidence, have assumed that the electrons are stationary in position. It should be noted that Bohr's theory has had its greatest success when applied to atoms or ions containing only one electron and that it seems incapable of explaining the chemical or ordinary physical properties of even such simple elements as lithium, carbon, or neon.

The two theories can, however, be reconciled if we consider that the electrons, as a result of forces which they exert on one another, rotate about certain definite positions in the atom which are distributed symmetrically in three dimensions. Thus for atoms containing only a single electron the chemical theory is in agreement with Bohr's theory. But for an atom such as neon the eight electrons in the outside layer would revolve around positions which are located about the nucleus in the same way that the eight corners of a cube are arranged about the center of the cube. This structure is not inconsistent with those parts of Bohr's theory which have received experimental confirmation. In fact, Born and Landé,[1] starting from Bohr's theory and without knowledge of Lewis' work, arrived at exactly this conception of the structure of atoms (*i.e.*, the cubic atom) from a study of the compressibility of the salts of the alkali metals.

The atomic numbers and the properties of the inert gases furnish us with a clue to the arrangement of the electrons within atoms. The low boiling point, the high

[1] *Verh. d. Phys. Ges.*, 20 (1918), 210.

ionizing potential, the chemical inertness, etc., of helium, prove that the arrangement of the electrons in the helium atom is more stable than that in any other atom. Since this atom contains two electrons we must conclude that a pair of electrons in the presence of a nucleus represents a very stable group. It is reasonable that with elements of higher atomic number there should be an even greater tendency for this stable pair of electrons to form about the nucleus. There are two sets of facts which furnish conclusive experimental evidence that this stable pair exists in all atoms above helium.

In the first place, the properties of lithium, beryllium, etc., show that in these elements also the first two electrons are held firmly while the remainder are easily detached. Thus, lithium readily forms a univalent positive ion by the detachment of one of the three electrons in its neutral atom. The divalence and other properties of beryllium prove that there is little or no tendency for a second stable pair of electrons to surround the first pair.

In the second place, the absence of irregularities in the observed K and L series of the X-ray spectra of the various elements proves that there are no sudden changes in the number of electrons in the innermost layers of electrons about the nucleus. From these two sets of facts, as well as from other evidence, we may take it as a fundamental principle that the arrangement of the inner electrons undergoes no change as we pass from elements of smaller to those of higher atomic number.

The properties of neon indicate that its atoms are more stable than those of any other element except helium. Since the atomic number is 10, and the first 2 electrons form a stable pair about the nucleus as in the helium atom, it follows directly that the other eight electrons arrange themselves in a second layer or shell possessing a very high stability. If these 8 electrons revolved about the nucleus in a single circular orbit or ring, as would be suggested by Bohr's theory, there is no apparent reason why

there should be any very great difference in stability between rings having 7, 8 or 9 electrons. On the other hand, we readily see that the geometrical symmetry of the arrangement of the 8 electrons at (or rotating about) the 8 corners of a cube would not only account for a high degree of stability but for the fact that an arrangement of 7 or 9 electrons would have no such stability. Chemical considerations and Born and Landé's work on compressibility also lead us to this spatial arrangement of the electrons. We shall refer to the stable group of 8 electrons by the term *octet*. From the principles already enunciated it is clear that in the atoms of all the elements above neon the inner electrons are arranged in the same way as those of neon.

From the atomic numbers of the inert gases we are thus able to determine the number of electrons in the various layers or shells of electrons which exist in the atoms. The results are summarized in Table I.

TABLE I—DISTRIBUTION OF ELECTRONS IN THE VARIOUS SHELLS

| Shell | Number of Electrons | Inert Gas Corresponding to Completed Layer |
|---|---|---|
| 1st shell | $2 = 2 \times 1^2$ | He 2 |
| 2nd shell, 1st layer | $8 = 2 \times 2^2$ | Ne 10 |
| 2nd shell, 2nd layer | $8 = 2 \times 2^2$ | Ar 18 |
| 3rd shell, 1st layer | $18 = 2 \times 3^2$ | Kr 36 |
| 3rd shell, 2nd layer | $18 = 2 \times 3^2$ | Xe 54 |
| 4th shell, 1st layer | $32 = 2 \times 4^2$ | Nt 86 |

Thus the xenon atom with an atomic number 54 contains 54 electrons arranged as follows: Close to the nucleus are two electrons which constitute the first shell. This is surrounded by the second shell which contains two "layers" of 8 electrons each. The third shell, which in the xenon atom is the outside shell, contains 18 electrons.

An examination of the number of electrons in the layers (Table I, 2nd column) shows that they bear a simple

mathematical relation to each other, namely, that they are proportional to the squares of the successive integers 1, 2, 3, and 4. This is to be looked upon as perhaps the most fundamental fact underlying the periodic arrangement of the elements. It is significant that in Bohr's theory these same numbers, 1, 4, 9, 16, etc., play a prominent part. Thus the energies of the electron in the various "stationary states" are proportional to one, one-quarter, one-ninth, one-sixteenth, etc., and the diameters of the various possible orbits in Bohr's theory are proportional to 1, 4, 9, 16, etc. In Bohr's theory the various stationary states correspond to different number of quanta (Planck's quantum theory), the innermost orbit corresponding to one quantum, the second orbit to two quanta, etc. We should thus consider (Table I) that the electrons in the 1st shell are monoquantic, those in both layers of the 2nd shell are diquantic, etc. It is interesting that Born and Landé from quite other evidence have concluded that the outermost electrons of the chlorine atom (2nd layer of the 2nd shell) are diquantic instead of triquantic as was at first assumed.

The foregoing theory of the arrangement of electrons in atoms explains the general features of the entire periodic system of the elements and is particularly successful in accounting for the position and the properties of the so-called 8th group and the rare earth elements. It also serves to correlate the magnetic properties of the elements.

Let us now consider the bearing of this theory of atomic structure on the phenomena of chemical valence. The outstanding feature of the theory is that there are certain groups of electrons, such as the pair in the first shell and the octet in the second, that have a remarkable stability. Those atoms in which all the electrons form parts of such stable groups (*viz.*, the inert gases) will have no tendency to change the arrangement of their electrons and will thus not undergo chemical change. Suppose, however, we bring together an atom of fluorine ($N = 9$)[1] and an atom

[1] We will denote the atomic number of an element by N.

of sodium (N = 11). Ten electrons are needed for the stable pair in the first shell and the octet in the second shell, as in the neon atom. The sodium atom has one more electron than is needed to give this stable structure while the fluorine atom has one electron too few. It is obvious then that the extra electron of the sodium atom should pass over *completely* to the *fluorine* atom. This leaves the sodium atom with a single positive charge while the fluorine becomes negatively charged. If the two charged atoms or ions[2] were alone in space they would be drawn together by the electrostatic force and would move as a unit and thus constitute a molecule. However, if other sodium and fluorine ions are brought into contact with the "molecule" they will be attracted as well as the first one was. There will result (at not too high temperature) a space lattice consisting of alternate positive and negative ions and the "molecule" of sodium fluoride will have disappeared. Now this is just the structure which we find experimentally for sodium fluoride by Bragg's method of X-ray crystal analysis. There are no bonds linking individual pairs of atoms together. The salt is an electrolytic conductor only in so far as its ions are free to move. In the molten condition or when dissolved in water, therefore, it becomes a good conductor.

The case of magnesium (N = 12) and oxygen (N = 8) is similar except that two electrons are transferred from the magnesium to the oxygen atom. The resulting ions

[2] It is convenient and it has been customary with many physicists to speak of a charged atom or molecule as an ion, irrespective of whether or not the particle is able to wander under the influence of an electric field. The writer has used the term in this way in his recent publications. This practice is very distasteful to many physical chemists and is likely to be misunderstood by them. Nevertheless, it seems to me probable, especially in view of the recent work of Milner and Ghosh, that it will be desirable to abandon the physical chemists' definition of the ion and to apply it to all charged atoms or molecules. The ion which wanders may then be referred to as a "free ion."

have their electrons arranged exactly like those of the neon atoms and the ions of sodium and fluorine. Therefore, the crystalline form of magnesium oxide and sodium fluoride should be identical, and this prediction of the theory has been confirmed experimentally by Dr. A. W. Hull by the X-ray method. Because of the much greater forces acting between the ions as a result of the double charges, the stability of the magnesium oxide is much higher than that of the sodium fluoride. This is manifested by the high melting point, low conductivity, low solubility, and hardness of magnesium oxide.

Phosphorus ($N = 15$) and sulfur ($N = 16$) have, respectively, 5 and 6 electrons more than neon, and are thus capable of giving up these numbers of electrons. If these elements are brought into contact with an excess of fluorine (which because of its proximity to neon has a particularly strong tendency to take electrons) all the extra electrons pass to fluorine atoms. Thus a sulfur atom will supply electrons to 6 fluorine atoms and will form the compound $SF_6$. The force acting between the fluorine ions and the central sulfur ion is still electrostatic in nature but it must be nearly 6 times greater than the force between sodium and fluorine ions. Furthermore, the 6 fluorine ions would surround the sulfur ion so that there would be little stray field of force. Therefore, we should not expect sulfur fluoride to be salt-like in character but to consist of very stable molecules having weak external fields of force and, therefore, readily existing in the form of a gas. As a matter of fact this extraordinary substance has these properties developed to such a degree that it is an *odorless* and *tasteless* gas with a boiling point of —62°. Phosphorus pentafluoride, as would be expected from its less symmetrical structure, is a gas having greater chemical activity.

The fluosilicate ion $SiF_6^{--}$ has a structure exactly like that of the sulfur fluoride molecule since the number and arrangement of the electrons are the same. This is clear

if we consider that the atomic number of silicon is 14 while that of sulfur is 16. Thus if we should replace the nucleus of the sulfur atom in a molecule of sulfur fluoride by the nucleus of a silicon atom, without disturbing any of the surrounding electrons, we would have removed two positive charges and would obtain a negative ion with two negative charges of the formula $SiF_6^{--}$. In the presence of potassium ions we would then have the familiar salt potassium fluosilicate. The theory is thus capable of explaining typical complex salts. In fact, it is applicable to the whole field of inorganic compounds covered by the work of Werner, and helps to simplify the theory of such compounds. There is no time, however, to go into this subject.

The simple theory of atomic structure which we have discussed thus far explains perfectly what has usually been called "the maximum positive and negative valance." The maximum positive valence represents the number of electrons which the atom possesses in excess of the number needed to form one of the particularly stable configurations of electrons. On the other hand, the maximum negative valence is the number of electrons which the atom must take up in order to reach one of these stable configurations.

For example, magnesium has a positive valence of two, since its atomic number is 12 while that of neon is 10. Sulfur has a positive valence of 6 since it has 6 electrons more than neon; but it has a negative valence of two because it must take up two more electrons before it can assume a form like that of the argon atom.

It is clear, however, that this theory of valence is not yet complete.[1] It is not applicable to those cases where we have usually taken valences of 4 for sulfur, or 3 and

[1] The theories of Kossel, Lacomblé, Teudt, etc., which have recently been proposed in Germany, have not advanced beyond this point and are therefore very unsatisfactory as a general theory of valence.

5 for chlorine, etc. But more especially it does not explain the structure of organic compounds and such substances as $H_2$, $Cl_2$, $O_2$, $N_2H_4$, $PCl_3$, etc.

J. J. Thomson, Stark, Bohr, and others had suggested that pairs of electrons held in common by two adjacen atoms may function in some cases as chemical bonds between the atoms, but this idea had not been combined with the conception of the stable groups of electrons or octets. G. N. Lewis, in an important paper in 1916, advanced the idea that the stable configurations of electrons in atom could share *pairs* of electrons with each other and he identified these pairs of electrons with the chemical bond of organic chemistry. This work of Lewis has been the basis and the inspiration of my work on valence and atomic structure.

As a result of the sharing of electrons between octets, the number of octets that can be formed from a given number of electrons is increased. For example, two fluorine atoms, each having seven electrons in its outside shell, would not be able to form octets at all except by sharing electrons. By sharing a single pair of electrons, however, two octets can be formed since two octets holding a pair in common require only 14 electrons. This is clear if we consider two cubes with electrons at each of the eight corners. When the cubes are placed so that an edge of one is in contact with an edge of the other a single pair of electrons at the ends of the common edge will take the place of four electrons in the original cubes. For each pair of electrons held in common between two octets there is a decrease of two in the total number of electrons needed to form the octets.

Let $e$ represent the number of electrons in the outside shell of the atoms that combine to form a molecule. Let $n$ be the number of octets that are formed from these $e$ electrons, and let $p$ be the number of pairs of electrons which the octets share with one another. Since every pair of electrons thus shared reduces by two the number

of electrons required to form the molecule it follows that $e = 8n - 2p$ or

$$p = \tfrac{1}{2}(8n - e).$$

This simple equation tells us in each case how many pairs of electrons or chemical bonds must exist in any given molecule *between the octets formed.* Hydrogen nuclei, however, may attach themselves to pairs of electrons in the octets which are not already shared. For example, in the formation of hydrogen fluoride from a hydrogen atom and a flourine atom there are 8 electrons in the shells ($e = 8$). We place $n - 1$ in the above equation and find $p = 0$. In other words, the fluorine atoms do not share electrons with each other. The hydrogen nucleus having given up its electron to the flourine atom attaches itself to one of the pairs of electrons of the fluorine octet, and thus forms a molecule having a relatively weak external field of force. As a result, hydrogen fluoride is a liquid of low boiling point instead of being salt-like in character.

The equation given above is applicable to all types of compounds. For example, if we apply it to substances such as sodium fluoride, sulfur fluoride, or potassium fluosilicate, which were previously considered, we find in each case $p = 0$. In other words, there are no pairs of electrons holding the atoms of these compounds together. On the other hand if we consider the compound $N_2H_4$, we find $p = 1$. Since there are only two octets the pair of electrons must be between the two nitrogen atoms while the hydrogen nuclei attach themselves to pairs of electrons of the nitrogen octets. It can be readily shown that this simple theory is in fact identical with the accepted valence theory of organic chemistry and leads to the same structural formulas as the ordinary theory in all those cases where we can take the valance of nitrogen to be 3, oxygen and sulfur 2, chlorine and hydrogen one. In other cases such as those where quinquivalent nitrogen has been assumed, the new theory gives results different

from the old but in each case in better agreement with the facts.

The theory indicates a series of new relationships between certain types of substances which I have termed *isosteric* substances. For example, it indicates that the molecules of carbon dioxide and nitrous oxide should have nearly identical structures and this is borne out by the extraordinary similarity in the physical properties of these gases. Nitrogen and carbon monoxide constitute another pair of gases which are similarly related. The same theory also points out a number of previously unsuspected cases of similarity of crystalline form (isomorphism).

It is clear that in the past the term valence has been used to cover what we may now recognize as three different types of valence, as follows:

1—Positive valence: the number of electrons an atom can give up,

2—Negative valence: the number of electrons an atom can take up,

3—Covalence: the number of pairs of electrons which an atom can share with its neighbors.

It is recommended that only for valences of the covalence type should definite bonds be indicated in chemical formulas. One of the particular advantages of the present theory is that it becomes easy to distinguish between covalence and the other types and thus to predict with certainty in what way electrolytic dissociation will occur if at all.

## REFERENCES

K. Kossel, *Ann. Physik*, 49 (1916), 229.

G. N. Lewis, *J. Am. Chem. Soc.*, 38 (1916), 762.

Langmuir, *J. Frank. Inst.*, 187 (1919), 359; *J. Am. Chem. Soc.*, 41 (1919), 868, 1543; 42 (1920), 274; *Proc. Nat. Acad. Sci.*, 5 (1919), 252.

# ENGINEERING BEFORE AND AFTER THE WAR

(Address of the president of the British Association for the Advancement of Science, Bournemouth, 1919.)

BY

SIR CHARLES PARSONS

## *Developments Prior to the War*

*James Watt.*—No excuse is necessary for entering upon this theme, because this year (1919) marks the hundredth anniversary of the death of James Watt, and in reviewing the past, it appears that England has gained her present proud position by her early enterprise and by the success of the Watt steam engine, which enabled her to become the first country to develop her resources in coal, and led to the establishment of her great manufactures and her immense mercantile marine.

The laws of steam which James Watt discovered are simply these: That the latent heat is nearly constant for different pressures within the ranges used in steam engines, and that, consequently, the greater the steam pressure and the greater the range of expansion the greater

will be the work obtained from a given amount of steam. Secondly, as may now seem to us obvious, that steam from its expansive force will rush into a vacuum. Having regard to the state of knowledge at the time, his conclusions appear to have been the result of close and patient reasoning by a mind endowed with extraordinary powers of insight into physical questions, and with the faculty of drawing sound practical conclusions from numerous experiments devised to throw light on the subject under investigation. His resource, courage and devotion were extraordinary.

In commencing his investigations on the steam engine he soon discovered that there was a tremendous loss in the Newcomen engine, which he thought might be remedied. This was the loss caused by condensation of the steam on the cold metal walls of the cylinder. He first commenced by lining the walls with wood, a material of low thermal conductivity. Though this improved matters, he was not satisfied; his intuition probably told him that there should be some better solution of the problem, and doubtless he made many experiments before he realised that the true solution lay in a condenser separate from the cylinder of the engine. It is easy after discovery to say, "How obvious and how simple," but many of us here know how difficult is any step of advance when shrouded by unknown surroundings, and we can well appreciate the courage and the amount of investigation necessary before James Watt thought himself justified in trying the separate condenser. But to us now, and to the youngest student who knows the laws of steam as formulated by Carnot, Joule, and Kelvin, the separate condenser is the obvious means of constructing an economical condensing engine.

Watt's experiments led him to a clear view of the great importance of securing as much expansion as possible in his engines. The materials and appliances for boiler and machine construction were at that time so undeveloped

that steam pressures were practically limited to a few pounds above atmospheric pressure. The cylinders and pistons of his engines were not constructed with the facility and accuracy to which we are now accustomed, and chiefly for these reasons expansion ratios of from two to threefold were the usual practice. Watt had given to the world an engine which consumed from five to seven pounds of coal per horse-power hour, or one-quarter of the fuel previously used by any engine. With this consumption of fuel its field under the conditions prevailing at the time was practically unlimited. What need was there, therefore, for commercial reasons, to endeavor still further to improve the engine at the risk of encountering fresh difficulties and greater commercial embarrassments? The course was rather for him and his partners to devote all their energy to extend the adoption of the engine as it stood, and this they did, and to the Watt engine, consuming from five to seven pounds of coal per horse-power, mankind owes the greatest permanent advances in material welfare recorded in history.

With secondary modifications, it was the prime mover in most general use for eighty years—*i.e.*, till the middle of last century. It remained for others to carry the expansion of steam still further in the compound, triple, and, lastly, in the quadruple expansion engine, which is the most economical reciprocating engine of to-day.

Watt had considered the practicability of the turbine. He writes to his partner, Boulton, in 1784: "The whole success of the machine depends on the possibility of prodigious velocities. In short, without God makes it possible for things to move them one thousand feet per second, it cannot do us much harm." The advance in tools of precision, and a clearer knowledge of the dynamics of rotating bodies, have now made the speeds mentioned by Watt feasible, and indeed common, everyday practice.

*Turbines* —The turbine of to-day carries the expansion

of steam much further than has been found possible in any reciprocating engine, and owing to this property it has surpassed it in economy of coal, and it realises to the fullest extent Watt's ideal of the expansion of steam from the boiler to the lowest vapor pressure obtainable in the condenser.

Among the minor improvements which in recent years have conduced to a higher efficiency in turbines are the more accurate curvature of the blades to avoid eddy losses in the steam, the raising of the peripheral velocities of the blades to nearly the velocity of the steam impinging upon them, and details of construction to reduce leakages to a minimum. In turbines of 20,000 to 30,000 horse-power 82 per cent. of the available energy in the steam is now obtainable as brake horse-power; and with a boiler efficiency of 85 per cent. the thermo-dynamic efficiency from the fuel to the electrical output of the alternator has reached 23 per cent., and shortly may reach 28 per cent., a result rivalling the efficiency of internal combustion engines worked by producer gas.

During the twenty years immediately preceding the war turbo generators had increased in size from 500 kilowatts to 25,000 kilowatts, and the consumption of steam had fallen from 17 lb. per kw. hour to 10.3 lb. per kw. hour. Turbines have become the recognised means of generating electricity from steam on a large scale, although they have not superseded the Watt engine for pumping mines or the drawing of coal, except as a means for generating electricity for these purposes. In the same period the engine power in the mercantile marine had risen from 3,900 of the *King Edward* to 75,000 of the *Mauretania*.

As regards the Royal Navy, the engine power of battleships, prior to the war, had increased from 12,000 i.h.p. to 30,000 s.h.p., while the speed advanced from 17 knots to 23 knots, and during the war, in ships of the *Queen Elizabeth* class, the power amounted to 75,000 s.h.p.,

with a speed of 25 knots. In cruisers similar advances were made. The i.h.p. of the *Powerful* was 25,000, while the s.h.p. of the *Queen Mary* was 78,000, with a speed of 28 knots. During the war the power obtained with geared turbines in the *Courageous* class was 100,000 s.h.p. with a speed of 32 knots, the maximum power transmitted through one gear wheel being 25,000 h.p., and through one pinion 15,500 h.p., while in destroyers, speeds up to 39 knots have been obtained. The aggregate horse-power of war and mercantile turbined vessels throughout the world is now about 35 millions.

These advances in power and speed have been made possible mainly by the successive increase in economy and diminution of weight derived from the replacement of reciprocating engines by turbines direct coupled to the propellers, and, later, by the introduction of reduction gearing between the turbines and the propellers; also by the adoption of water-tube boilers and oil fuel. With these advances the names of Lord Fisher, Sir William White, and Sir Henry Oram will always be associated.

The British Navy has led the world for a century and more. Lord Fisher has recently said that many of the ships are already obsolete and must soon be replaced if supremacy is to be maintained; and there can be no question that to guide the advance and development on the best lines, continuous scientific experiment, though costly at the time, will prove the cheapest in the long run.

*The Work of Sir Wm. White.*—With the great work of the Royal Navy fresh in our minds, we cannot but recall the prominent part taken by the late Sir William White in its construction. His sudden death, when President-elect for 1913, lost to the nation and to the Association the services of a great naval architect who possessed remarkable powers of prevision and dialectic. He was Chief Constructor to the Admiralty from 1885 to 1901, and largely to him was due the efficiency of our vessels in the Great War.

White often referred to the work of Brunel as the designer of the *Great Eastern,* and spoke of him as the originator of the cellular construction of the bottoms of ships, since universally adopted, as a means of strengthening the hull and for obtaining additional safety in case of damage. Scott Russell was the builder of this great pioneer vessel, the forerunner of the Atlantic liners, and the British Association may rightly feel satisfaction in having aided him when a young man by pecuniary grants to develop his researches into the design and construction of ships and the wave-line form of hull which he originated, a form of special importance in paddle-wheel vessels.

So much discussion has taken place in the last four years as to the best construction of ship to resist torpedo attacks that it is interesting to recall briefly at the present time what was said by White in his Cantor Lectures to the Royal Society of Arts in 1906: "Great attention has been bestowed upon means of defence against underwater torpedo attacks. From the first introduction of torpedoes it was recognised that extreme watertight subdivision in the interior of warships would be the most important means of defence. Experiments have been made with triple watertight skins forming double cellular sides, the compartments nearest the outer bottom being filled, in some cases, with water, coal, cellulose, or other materials. Armor plating has been used both on the outer bottom and on inner skins." He also alludes to several Russian ships which were torpedoed by the Japanese, and he concludes by saying: "Up to date the balance of opinion has favored minute watertight subdivisions and comparatively thin watertight compartments, rather than the use of internal armor, whose use, of course, involves large expenditure of weight and cost."

The present war has most amply confirmed his views and conclusions, then so lucidly and concisely expressed.

While on the subject of steamships, it may perhaps be

opportune to say one word as to their further development. The size of ships has been steadily increasing up to the time of the war, resulting in a reduction of power required to propel them per ton of displacement. On the other hand, thanks to their greater size and more economical machinery, speeds have been increased when the traffic has justified the greater cost. The limiting factor to further increase in size is the depth of water in the harbors. With this restriction removed there is no obstacle to building ships up to 1,000 feet in length or more, provided the volume and character of the traffic are such as to justify the capital outlay.

*Tungsten Steel.*—Among other important pre-war developments that have had a direct bearing upon the war, mention should be made of the discovery and extensive use of alloys of steel. The wonderful properties conferred upon steel by the addition of tungsten were discovered by Muschet[1] in 1868, and later this alloy was investigated and improved by Maunsel White and Taylor, of Philadelphia. The latter showed that the addition of tungsten to steel has the following effect: That after the steel has been quenched at a very high temperature near its melting point it can be raised to a much higher temperature than is possible with ordinary carbon tool steel, without losing its hardness and power of cutting metal. In other words, it holds the carbon more tenaciously in the hardened state, and hence tungsten steel tools, even when red hot, can cut ordinary mild steel. It has revolutionised the design of machine tools and has increased the output on heavy munition work by 100 per cent., and in ordinary engineering by 50 per cent.

The alloys of steel and manganese with which the name of Sir Robert Hadfield is associated have proved of utility in immensely increasing the durability of railway and tramway points and crossings, and for the hard

[1] Who has not been sufficiently credited with his share in making the Bessemer process a practical success.

teeth of machinery for the crushing of stone and other materials, and, in fact, for any purposes where great hardness and strength are essential.

*Investigation of Gaseous Explosions.*—Brief reference must also be made—and it will be gratifying to do so—to the important work of one of the Committees of the British Association appointed in 1908, under the chairmanship of the late Sir William Preece, for the investigation of gaseous explosions, with special reference to temperature. The investigations of the Committee are contained in seven yearly reports up to 1914. Of the very important work of the Committee I wish to refer to one investigation in particular, which has proved to be a guiding star to the designers and manufacturers of internal combustion engines in this country. The members of the Committee more directly associated with this particular investigation were Sir Dugald Clerk, Professor Callendar, and the late Professor Bertram Hopkinson.

The investigation showed that the intensity of the heat radiated by the incandescent gases to the walls of the cylinder of a gas engine increases with the size of the cylinder, the actual rate of this increase being approximately proportional to the square root of the depth of the radiating incandescent gas; the intensity was also shown to increase rapidly with the richness of the gas. It suffices now to say that the heat in a large cylinder with a rich explosive mixture is so intense that the metal eventually cracks. The investigation shows why this occurs, and by doing so has saved enormous sums to the makers of gas and oil engines in this country, and has led them to avoid the large cylinder, so common in Germany before the war, in favor of a multiplicity of smaller cylinders.

## SCIENCE AND THE WAR

Four years is too short a time for much scientific invention to blossom to useful maturity, even under the

forced exigencies of war and Government control. It must be remembered that in the past the great majority of new discoveries and inventions of merit have taken many years—sometimes generations—to bring them into general use. It must also be mentioned that in some instances discoveries and inventions are attributable to the general advance in Science and the Arts which has brought within the region of practical politics an attack on some particular problem. So the work of the scientists during the war has perforce been directed more to the application of known principles, trade knowledge, and properties of matter to the waging of war, than to the making of new and laborious discoveries; though, in effecting such applications, inventions of a high order have been achieved, some of which promise to be of great usefulness in time of peace.

The advance of Science and the Arts in the last century had, however, wrought a great change in the implements of war. The steam engine, the internal combustion engine, electricity, and the advances in metallurgy and chemistry had led to the building up of immense industries which, when diverted from their normal uses, have produced unprecedented quantities of war material for the enormous armies, and also for the greatest Navy which the world has ever seen.

The destructive energy in the field and afloat has multiplied many hundredfold since the time of the Napoleonic wars; both before and during the war the size of guns and the efficiency of explosives and shell increased immensely, and many new implements of destruction were added. Modern Science and Engineering enabled armies unprecedented in size, efficiency and equipment to be drawn from all parts of the world and to be concentrated rapidly in the fighting line.

To build up the stupendous fighting organization, ships have been taken from their normal trade routes, locomotives and material from the home railways, the normal

manufactures of the country have been largely diverted to munitions of war; the home railways, tramways, roads, buildings and constructions, and material of all kinds have been allowed to depreciate. The amount of depreciation in roads and railways alone has been estimated at 400 millions per annum at present prices. Upon the community at home a very great and abnormal strain has been thrown, notwithstanding the increased output per head of the workers derived from modern methods and improved machinery. In short, we have seen for the first time in history nearly the whole populations of the principal contending nations enlisted in intense personal and collective effort in the contest, resulting in unprecedented loss of life and destruction of capital.

A few figures will assist us to realize the great difference between this war and all preceding wars. At Waterloo, in 1815, 9,044 artillery rounds were fired, having a total weight of 37.3 tons, while on one day during the last offensive in France, on the British Front alone, 943,837 artillery rounds were fired, weighing 18,080 tons—over 100 times the number of rounds, and 485 times the weight of projectiles. Again, in the whole of the South African War, 273,000 artillery rounds were fired, weighing approximately 2,800 tons; while during the whole war in France, on the British Front alone, over 170 million artillery rounds were fired, weighing nearly 3½ million tons—622 times the number of rounds, and about 1,250 times the weight of projectiles.

However great these figures in connection with modern land artillery may be, they become almost insignificant when compared with those in respect of a modern naval battle squadron. The *Queen Elizabeth* when firing all her guns discharges 18 tons of metal and develops 1,870,000 foot-tons of energy. She is capable of repeating this discharge once every minute, and when doing so develops by her guns an average of 127,000 effective horse-power, or more than one-and-a-half times the power of her pro-

pelling machinery; and this energy is five times greater than the maximum average developed on the Western Front by British guns. Furthermore, if all her guns were fired simultaneously, they would for the instant be developing energy at the rate of 13,132,000 horse-power. From these figures we can form some conception of the vast destructive energy developed in a modern naval battle.

## *Engineering and the War.*

*Sound-ranging and Listening Devices.*—Probably the most interesting development during the war has been the extensive application of sound-listening devices for detecting and localizing the enemy. The Indian hunter puts his ear to the ground to listen for the sound of the footsteps of his enemy. So in modern warfare science has placed in the hands of the sailor and soldier elaborate instruments to aid the ear in the detection of noises transmitted through earth, water, air, or ether, and also in some cases to record these sounds graphically or photographically, so that their character and the time of their occurrence may be tabulated.

The sound-ranging apparatus by which the position of an enemy gun can be determined from electrically recorded times at which the sound wave from the gun passes over a number of receiving stations, has enabled our artillery to concentrate their fire on the enemy's guns, and often to destroy them.

The French began experimenting in September, 1914, with methods of locating enemy guns by sound. The English section began work in October, 1915, adopting the French methods in the first instance. By the end of 1916 the whole Front was covered, and sound-ranging began to play an important part in the location of enemy batteries. During 1917 locations by sound-ranging reached about 30,000 for the whole army, this number

being greater than that given by any other means of location. A single good set of observations could be relied upon to give the position of an enemy gun to about 50 yards at 7,000 yards range. It could also be carried on during considerable artillery activity.

The apparatus for localizing noises transmitted through the ground has been much used for the detection of enemy mining and counter-mining operations. Acoustic tubes, microphones, and amplifying valves have been employed to increase the volume of very faint noises.

For many years before the war the Bell Submarine Signaling Company, of which Sir William White was one of the early directors, used submerged microphones for detecting sound transmitted through the water, and a submerged bell for sending signals to distances up to one mile. With this apparatus passing ships could be heard at a distance of nearly a mile when the sea was calm and the listening vessel stationary.

Of all the physical disturbances emitted or produced by a moving submarine, those most easily detected, and at the greatest distance, are the pressure waves set up in the water by vibrations produced by the vessel and her machinery. A great variety of instruments have been devised during the war for detecting these noises, depending on microphones and magnetophones of exceedingly high sensitivity. Among them may be particularly mentioned the hydrophones devised by Captain Ryan and Professor Bragg, being adaptations of the telephone transmitter to work in water, instead of air. These instruments, when mounted so as to rotate, are directional, being insensitive to sound waves whose front is perpendicular to the plane of the diaphragm, and giving the loudest sound when the diaphragm is parallel to the wave front.

Another preferable method for determining direction is to use two hydrophones coupled to two receivers, one held to each ear. This is called the biaural method, and

enables the listener to recognize the direction from which the sound emanates.

When the vessel is in motion or the sea is rough the water noises from the dragging of the instrument through the water and from the waves striking the ship drown the noises from the enemy vessel, and under such conditions the instruments are useless. The assistance of eminent biologists was of invaluable help at this juncture. Experiments were made with sea-lions by Sir Richard Paget, who found that they have directional hearing under water up to speeds of six knots. Also Professor Keith explained the construction of the hearing organs of the whale, the ear proper being a capillary tube, too small to be capable of performing any useful function in transmitting sound to the relatively large aural organs, which are deep set in the head. The whale therefore hears by means of the sound waves transmitted through the substance of the head. It was further seen that the organs of hearing of the whale to some degree resembled the hydrophone.

The course now became clear. Hollow towing bodies in the form of fish or porpoises were made of celluloid, varnished canvas, or very thin metal, and the hydrophone suitably fixed in the center of the head. The body is filled with water, and the cable towing the fish contains the insulated leads to the observer on board the vessel. When towed at some distance behind the chasing ship disturbing noises are small, and enemy noises can be heard up to speeds of 14 knots, and at considerable distances. Thermionic amplifying valves have been extensively used, and have added much to the sensitiveness of the hydrophone in its many forms.

After the loss of the *Titanic* by collision with an iceberg, Lewis Richardson was granted two patents in 1912 for the detection of above-water objects by their echo in the air, and underwater objects by their echo transmitted through the water. The principles governing the produc-

tion and the concentration of beams of sound are described in his specifications, and he recommends frequencies ranging from 4,786 to 100,000 complete vibrations per second, and also suggests that the rate of approach or recession from the object may be determined from the difference in the pitch of the echo from the pitch of the blast sent out. Hiram Maxim also suggested similar apparatus a little later.

The echo method of detection was not, however, practically developed until French and English scientists, with whom was associated Professor Langevin, of the College de France, realizing its importance for submarine detection, brought the apparatus to a high degree of perfection and utility shortly before the Armistice. Now, with beams of high-frequency sound waves, it is possible to sweep the seas for the detection of any submerged object, such as icebergs, submarines, surface vessels, and rocks; they may also be used to make soundings. It enables a chasing ship to pick up and close in on a submarine situated more than a mile away.

The successful development of sound-ranging apparatus on land led to the suggestion by Professor Bragg that a modified form could be used to locate under-water explosions. It has been found that the shock of an explosion can be detected hundreds of miles from its source by means of a submerged hydrophone, and that the time of the arrival of the sound wave can be recorded with great precision. At the end of the war the sound-ranging stations were being used for the detection of positions at sea, required for strategical purposes. The same stations are now being used extensively for the determination of such positions at sea as light-vessels, buoys which indicate channels, and obstructions such as sunken ships. By this means ships steaming in fog can be given their positions with accuracy for ranges up to 500 miles.

Among the many other important technical systems and devices brought out during the war which will find useful

application under peace conditions as aids to navigation I may mention directional wireless, by which ships and aircraft can be given their positions and directed.

Leader gear, first used by the Germans to direct their ships through their minefields, and subsequently used by the Allies, consists of an insulated cable laid on the bottom of the sea, earthed at the farther end, and through which an alternating current is passed. By means of delicate devices installed on a ship, she is able to follow the cable at any speed with as much precision as a railless electric 'bus can follow its trolley wire. Cables up to 50 miles long have been used, and this device promises to be invaluable to ships navigating narrow and tortuous channels and entering or leaving harbors in a fog.

*Aircraft.*—It may be justly said that the development in aircraft design and manufacture is one of the astonishing engineering feats of the war. In August, 1914, the British Air Service possessed a total of 272 machines, whereas in October, 1918, just prior to the Armistice, the Royal Air Force possessed over 22,000 effective machines. During the first twelve months of the war the average monthly delivery of aeroplanes to our Flying Service was fifty, while during the last twelve months of the war the average deliveries were 2,700 per month. So far as aero-engines are concerned, our position in 1914 was by no means satisfactory. We depended for a large proportion of our supplies on other countries. In the Aerial Derby of 1913, of the eleven machines that started, not one had a British engine. By the end of the war, however, British aero-engines had gained the foremost place in design and manufacture, and were well up to requirements as regards supply. The total horse-power produced in the last twelve months of the war approximated to eight millions of brake horse-power, a figure quite comparable with the total horse-power of the marine engine output of the country.

In view of the recent trans-Atlantic flights, I feel that

it may be opportune to make the following observations on the comparative utility of aeroplanes and airships for commercial purposes. In the case of the aeroplane, the weight per horse-power increases with the size, other things being equal. This increase, however, is met to some extent by a multiplicity of engines, though in the fusilage the increase remains.

On the other hand, with the airship the advantage increases with the size, as in all ships. The tractive effort per ton of displacement diminishes in inverse proportion to the dimensions, other things, including the speed, being the same. Thus, an airship of 750 feet length and 60 tons displacement may require a tractive force of 5 per cent., or 3 tons, at 60 miles per hour; while one of 1,500 feet in length and $8 \times 60 = 480$ tons displacement would only require $2\frac{1}{2}$ per cent. $\times$ 480 = 12 tons at the same speed, and would carry fuel for double the distance.

With the same proportion of weight of hull to displacement, the larger airship would stand double the wind pressure, and would weather storms of greater violence and hailstones of greater size. It would be more durable, the proportional upkeep would be less, and the proportional loss of gas considerably less. In other words, it would lose a less proportion of its buoyancy per day. It is a development in which success depends upon the project being well thought out and the job being thoroughly well done. The equipment of the airsheds with numerous electric haulage winches, and all other appliances to make egress and ingress to the sheds safe from danger and accident, must be ample and efficient.

The airship appears to have a great future for special commerce where time is a dominant factor and the demand is sufficient to justify a large airship. It has also a great field in the opening up of new countries where other means of communication are difficult. The only limitation to size will be the cost of the airship and its sheds, just as in steam vessels it is the cost of the vessels

and the cost of deepening the harbors that limit the size of Atlantic liners.

Such developments generally take place slowly, otherwise failures occur—as in the case of the *Great Eastern*—and it may be many years before the airship is increased from the present maximum of 750 feet to 1,500 feet with success, but it will assuredly come. If, however, the development is subsided or assisted by government incidental failures may be faced with equanimity and very rapid development accomplished.[1] In peace time the seaplane, aeroplane, and airship will most certainly have their uses. But, except for special services of high utility, it is questionable whether they will play more than a minor part as compared with the steamship, railway, and motor transport.

*Electricity.*—The supply and use of electricity has developed rapidly in recent years. For lighting it is the rival of gas, though each has its advantages. As a means of transmitting power over long distances it has no rival, and its efficiency is so high that when generated on a large scale and distributed over large areas it is a cheap and reliable source of power for working factories, tramways, suburban railways, and innumerable other purposes, including metallurgical and chemical processes. It is rapidly superseding locally generated steam-power, and is a rival to the small and moderate-sized gas and oil engine. It has made practicable the use of water-power through the generation of electricity in bulk at the natural falls, from which the power is transmitted to the consumers, sometimes at great distances.

Fifteen years ago electricity was generated chiefly by large reciprocating steam engines, direct coupled to dynamos or alternators, but of late years steam turbines have in most instances replaced them, and are now exclusively used in large generating stations, because of their smaller

[1] The literature on this subject includes an article which appeared in *Engineering* on January 3, 1919.

cost and greater economy in fuel. The size of the turbines may vary from a few thousand horse-power up to about 50,000 horse-power. At the end of last year the central electric stations in the United Kingdom contained plant aggregating 2¾ million kilowatts, 79 per cent. of which was driven by steam turbines.

Much discussion has taken place as to the most economical size of generating stations, their number, the size of the generating units, and the size of the area to be supplied. On the one hand, a comparatively small number of very large or super-stations, instead of a large number of moderate-sized stations dotted over the area, results in a small decrease in the cost of production of the electricity, because in the super-stations larger and slightly more economical engines are employed, while the larger stations permit of higher organization and more elaborate labor-saving appliances. Further, if in the future the recovery of the by-products of coal should become a practical realization as part of the process in the manufacture of the electric current, the larger super-stations present greater facilities than the smaller stations. On the other hand, super-stations involve the transmission of the electricity over greater distances, and consequently greater capital expenditure and cost of maintenance of mains and transmission apparatus, and greater electrical transmission losses, while the larger generating unit takes longer to overhaul or repair, and consequently a larger percentage of spare plant is necessary.

The greatest element in reducing the cost of electricity is the provision of a good load factor; in other words, the utilization of the generating plant and mains to the greatest extent during the twenty-four hours of each day throughout the year. This is a far more important consideration than the size of the station, and it is secured to the best advantage in most cases by a widespread network of mains, supplying a diversity of consumers and uses, each requiring current at different times of the day.

The total load of each station being thus an average of the individual loads of a number of consumers is, in general, far less fluctuating than in the case of small generating and distributing systems, which supply principally one class of consumer, a state of affairs that exists in London, for instance, at the present time. It is true that there may be exceptional cases, such as at Kilmarnock, where a good load factor may be found in a small area, but in this case the consumers are chiefly mills, which require current for many hours daily.

There is no golden rule to secure cheap electricity. The most favorable size, locality, and number of generating stations in each area can only be arrived at by a close study of the local conditions, but there is no doubt that, generally speaking, to secure cheap electricity a widespread network of mains is in most cases a very important, if not an essential, factor.

The electrification of tramways and suburban railways has been an undoubted success where the volume of traffic has justified a frequent service, and it has been remarkable that where suburban lines have been worked by frequent and fast electrical trains there has resulted a great growth of passenger traffic. The electrification of main line railways would no doubt result in a saving of coal; at the same time, the economical success would largely depend on the broader question as to whether the volume of the traffic would suffice to pay the working expenses, and provide a satisfactory return on the capital.

Municipal and company generating stations have been nearly doubled in capacity during the war to meet the demand from munition works, steel works, chemical works, and for many other purposes. The provision of this increased supply was an enormous help in the production of adequate munitions. At the commencement of the war there were few steel electric furnaces in the country; at the end of last year 117 were at work, producing

20,000 tons of steel per month, consisting chiefly of high-grade ferro alloys used in munitions.

### *The Future*

The nations who have exerted the most influence in the war have been those who have developed to the greatest extent of their resources, their manufactures, and their commerce. As in the war, so in civilization of mankind. But, viewing the present trend of developments in harnessing water-power and using up the fuel resources of the world for the use and convenience of man, one cannot but realize that, failing new and unexpected discoveries in science, such as the harnessing of the latent molecular and atomic energy in matters, as foreshadowed by Clerk Maxwell, Kelvin, Rutherford, and others, the great position of England cannot be maintained for an indefinite period. At some time more or less remote—long before the exhaustion of our coal—the population will gradually migrate to those countries where the natural sources of energy are the most abundant.

*Water-power and Coal.*—The amount of available water-power in the British Isles is very small as compared with the total in other countries. According to the latest estimates, the total in the British Isles is under 1½ million horse-power, whereas Canada alone possesses over 20 millions, of which over 2 millions have already been harnessed. In the rest of the British Empire there are upwards of 30 millions and in the remainder of the world at least 150 millions, so that England herself possesses less than 1 per cent. of the water-power of the world. Further, it has been estimated that she possesses only 2½ per cent. of the whole coal of the world. To this question I would wish to direct our attention for a few minutes.

I have said that England owes her modern greatness to the early development of her coal. Upon it she must continue to depend almost exclusively for her heat and source

of power, including that required for propelling her vast mercantile marine. Nevertheless, she is using up her resources in coal much more rapidly than most other countries are consuming theirs, and long before any near approach to exhaustion is reached her richer seams will have become impoverished, and the cost of mining so much increased that, given cheap transport, it might pay her better to import coal from richer fields of almost limitless extent belonging to foreign countries, and workable at a much lower cost than her own.

Let us endeavor to arrive at some approximate estimate of the economic value of the principal sources of power. The present average value of the royalties on coal in England is about 6*d*. per ton, but to this must be added the profit derived from mining operations after paying royalties and providing for interest on the capital expended and for its redemption as wasting capital. After consultation with several leading experts in these matters, I have come to the conclusion that about 1*s*. per ton represents the pre-war market value of coal in the seams in England.

It must, however, be remembered that, in addition, coal has a considerable value as a national asset, for on it depends the prosperity of the great industrial interests of the country, which contribute a large portion of the wealth and revenue. From this point of view the present value of unmined coal seems not to have been sufficiently appreciated in the past, and that in the future it should be better appraised at its true value to the nation.

This question may be viewed from another aspect by making a comparison of the cost of producing a given amount of electrical power from coal and from water-power. Assuming that one horse-power of electrical energy maintained for one year had a pre-war value of 5*l*. ($25), and that it requires about eight tons of average coal to produce it, we arrive at the price of 6*s*. 3*d*. ($1.55) per ton—*i.e.*, crediting the coal with half the cost. The

capital required to mine eight tons of coal a year in England is difficult to estimate, but it may be taken approximately to be 5*l.*, and the capital for plant and machinery to convert it into electricity at 10*l.*, making a total of 15*l.* In the case of water-power the average capital cost on the above basis is 40*l.*, including water rights (though in exceptionally favored districts much lower costs are recorded).

From these figures it appears that the average capital required to produce electrical power from coal is less than one-half the amount that is required in the case of water-power. The running costs, however, in connection with water-power are much less than those in respect of coal. Another interesting consideration is that the cost of harnessing all the water-power of the world would be about 8,000 millions, or equal to the cost of the war to England.

Dowling has estimated the total coal of the world as over seven million million tons, and whether we appraise it at 1*s.* or more per ton its present and prospective value is prodigious. For instance, at 6*s.* 3*d.* per ton it amounts to nearly one hundred times the cost of the war to all the belligerents.

In some foreign countries the capital costs of mining are far below the figures I have taken, and, as coal is transportable over long distances and, generally speaking, electricity is not so at present, therefore it seems probable that capital will in the immediate future flow in increasing quantity to mining operations in foreign countries rather than to the development of the more difficult and costly water-power schemes. When, however, capital becomes more plentiful the lower running costs of water-power will prevail, with the result that it will then be rapidly developed.

As to the possible new sources of power, I have already mentioned molecular energy, but there is another alternative which appears to merit attention.

*Bore Hole.*—In my address to Section G in 1904 I discussed the question of sinking a shaft to a depth of twelve miles, which is about ten times the depth of any shaft in existence. The estimated cost was 5,000,000*l.*, and the time required about eighty-five years.

The method of cooling the air-locks to limit the barometric pressure on the miners and other precautions were described, and the project appeared feasible. One essential factor has, however, been queried by some persons: Would the rock at the great depth crush in and destroy the shaft? Subsequent to my address, I wrote a letter to *Nature,* suggesting that the question might be tested experimentally. Professor Frank D. Adams, of McGill University, Montreal, acting on the suggestion, has since carried out exhaustive experiments, published in the *Journal of Geology* for February, 1912, showing that in limestone a depth of fifteen miles is probably practicable, and that in granite a depth of thirty miles might be reached.

Little is at present known of the earth's interior, except by inference from a study of its surface, upturned strata, shallow shafts, the velocity of transmission of seismic disturbances, its rigidity and specific gravity, and it seems reasonable to suggest that some attempt should be made to sink a shaft as deep as may be found practicable and at some locality selected by geologists as the most likely to afford useful information.

When we consider that the estimated cost of sinking a shaft to a depth of twelve miles, at present-day prices, is not much more than the cost of one day of the war to Great Britain alone, the expense seems trivial as compared with the possible knowledge that might be gained by an investigation into this unexplored region of the earth. It might, indeed, prove of inestimable value to Science, and also throw additional light on the internal constitution of the earth in relation to minerals of high specific gravity.

In Italy, at Lardarello, bore holes have been sunk, which

discharge large volumes of high-pressure steam, which is being utilized to generate about 10,000 horse-power by turbines. At Solfatara, near Naples, a similar project is on foot to supply power to the great works in the district. It seems, indeed, probable that in volcanic regions a very large amount of power may be, in the future, obtained directly or indirectly by boring into the earth, and that the whole subject merits the most careful consideration.

While on the subject of obtaining power, may I digress for a few moments and describe an interesting phenomenon of a somewhat converse nature—*viz.* that of intense pressure produced by moderate forces closing up cavities in water.

A Committee was appointed by the Admiralty in 1916 to investigate the cause of the rapid erosion of the propellers of some of the ships doing arduous duties. This was the first time that the problem had been systematically considered. The Committee found that the erosion was due to the intense blows struck upon the blades of the propellers by the nuclei of vacuous cavities closing up against them. Though the pressure bringing the water together was only that of the atmosphere, yet it was proved that at the nucleus 20,000 atmospheres might be produced.

The phenomenon may be described as being analagous to the well-known fact that nearly all the energy of the arm that swings it is concentrated in the tag of a whip. It was shown that when water flowed into a conical tube which had been evacuated a pressure of over 140 tons per square inch was recorded at the apex, which was capable of eroding brass, steel, and in time even the hardest steel. The phenomenon may occur under some conditions in rivers and waterfalls where the velocity exceeds 50 feet per second, and it is probably as great a source of erosion as by the washing down of boulders and pebbles. Then again, when waves beat on a rocky shore, under some conditions, intense hydraulic pressures will occur,

quite sufficient of themselves to crush the rock and to open out narrow fissures into caves.

*Research.*—The whole question of the future resources of the Empire is, I venture to think, one which demands the serious attention of all scientists. It should be attacked in a comprehensive manner, and with that insistence which has been so notable in connection with the efforts of British investigators in the past. In such a task, some people might suggest, we need encouragement and assistance from the Government of the country. Surely we have it. As many here know, a great experimental step towards the practical realization of Solomon's House as prefigured by Francis Bacon in the *New Atlantis* is being made by the Government at the present time. The inception, constitution, and methods of procedure of the Department, which was constituted in 1915, were fully described by Sir Frank Heath in his paper to the Royal Society of Arts last February, and it was there stated by Lord Crewe that, so far as he knew, this was the only country in which a Government Department of Research existed.[3]

It is obvious that the work of a Department of this kind must be one of gradual development with small beginnings, in order that it may be sound and lasting. The work commenced by assisting a number of researches conducted by scientific and professional societies which were languishing as a result of the war, and grants were also made to the National Physical Laboratory and to the Central School of Pottery at Stoke-on-Trent. The grants for investigation and research for the year 1916-17 totalled 11,055*l.* ($55,000), and for the present year are anticipated to be 93,570*l.* The total income of the National Physical Laboratory in 1913-14 was 43,713*l.*, and

[3] The Italian Government are now, however, establishing a National Council for Research, and a Bill is before the French Chamber for the establishment of a National Office of Scientific, Industrial, and Agricultural Research and Inventions.

owing to the great enlargement of the Laboratory the total estimate of the Research Department for this service during the current year is 154,650*l.*

Another important part of the work of the Department has been to foster and to aid financially Associations of the trades for the purpose of research. Nine of these Associations are already at work; eight more are approved, and will probably be at work within the next two months; and another twelve are in the earlier stage of formation. There are also signs of increased research by individual factories. Whether this is due to the indirect influence of the Research Department or to a change in public opinion and a more general recognition of the importance of scientific industrial research it is difficult to say.

The possibility of the uncontrolled use on the part of a nation of the power which Science has placed within its reach is so great a menace to civilization[4] that the ardent wish of all reasonable people is to possess some radical means of prevention through the establishment of some form of wide and powerful control. Has not Science forged the remedy, by making the world a smaller arena for the activities of civilization, by reducing distance in terms of time? Alliances and unions, which have successfully controlled and stimulated republics of heterogeneous races during the last century, will therefore have become possible on a wider and grander scale, thus uniting all civilized nations in a great League to maintain order, security, and freedom for every individual and for every State and nation liberty to devote their energies to the controlling of the great forces of Nature for the use and convenience of man, instead of applying them to the killing of each other.

[4] For instance, it might some day be discovered how to liberate instantaneously the energy in radium, and radium contains two and one-half million times the energy of the same weight of T.N.T.

Many of us remember the President's Banner at the Manchester Meeting in 1915, where Science is allegorically represented by a sorrowful figure covering her eyes from the sight of the guns in the foreground. This year Science is represented in her more joyful mien, encouraging the arts and industries. It is sincerely to be hoped that the future will justify our present optimism.

# METHODS OF GAS WARFARE

(Report of a lecture delivered before the Washington Academy of Sciences on Jan. 17, 1918)

BY

S. J. M. AULD, D.S.M.

*British Military Mission*

I happened to be present at the first gas attack and saw the whole gas business from the beginning. The first attack was made in April, 1915. A deserter had come into the Ypres salient a week before the attack was made, and had told us the whole story. They were preparing to poison us with gas, and had cylinders installed in their trenches. No one believed him at all, and no notice was taken of it.

Then came the first gas attack, and the whole course of the war changed. That first attack, of course, was made against men who were entirely unprepared—absolutely unprotected. You have read quite as much about the actual attack and the battle as I could tell you, but the accounts are still remarkably meager. The fellows who could have told most about it didn't come back. The Germans have claimed that we had 6,000 killed and as many taken prisoners. They left a battlefield such as had never been seen before in warfare, ancient or modern, and one that has had no compeer in the whole war except on the Russian front.

What the Germans expected to accomplish by it I am not sure. Presumably they intended to win the war, and they might conceivably have won it then and there if they had foreseen the tremendous effect of the attack. It is certain that they expected no immediate retaliation, as they had provided no protection for their own men. They made a clear and unobstructed gap in the lines, which was only closed by the Canadians, who rallied on the left and advanced, in part through the gas cloud itself.

The method first used by the Germans, and retained ever since, is fairly simple, but requires great preparation beforehand. A hole is dug in the bottom of the trench close underneath the parapet, and a gas cylinder is buried in the hole. It is an ordinary cylinder, like that used for oxygen or hydrogen. It is then covered first with a quilt of moss, containing potassium carbonate solution, and then with sand bags. When the attack is to be made the sand bags and protecting cover are taken off the cylinder, and each cylinder is connected with a lead pipe which is bent over the top of the parapet. A sand bag is laid on the nozzle to prevent the back "kick" of the outrushing gas from throwing the pipe back into the trench. Our own methods are practically identical with those first used by the Germans.

The success of a cloud gas attack depends on thorough preparation beforehand. The attackers must know the country, the layout of the trenches, and the direction and velocity of the wind with certainty. Favorable conditions are limited practically to wind velocities between 12 and 4 miles an hour. A wind of more than 12 miles an hour disperses the gas cloud very rapidly. An upward current of air is the worst foe of gas. The weight of the gas is not an important factor in carrying it along, for it mixes rapidly with air to form the moving "cloud." The time occupied by a gas attack is too short to permit of much diffusion of the gas out of the original mixture.

The gas attack must be planned very carefully. If the

trench line is very irregular it is likely that gas will flow into a portion of one's own trenches. The limits of safety in wind direction are thus determined by the direction of the lines of the trenches. The Germans use a 40° angle of safety; that means that on a given straight portion of the front the wind direction must lie between the two directions which make angles of 40° with the neighboring sections of the front. The most suitable type of country is where the ground slopes gently away from where the gas is being discharged. The Germans made one mistake in believing that hilly or wooded country would not do. This was refuted by the French, who made a successful gas attack in hilly and wooded country in the Vosges, as admitted in a captured German report. If the country is flat like that about Ypres, and the wind direction is right, there is very little difficulty about making an attack, especially if the enemy does not know anything about it. The element of surprise is important.

German gas attacks are made by two Regiments of Pioneers, with highly technical officers, including engineers, meteorologists, and chemists. They brought their first cylinders into the line without our knowing anything about it, except from the deserter's report which was not believed. The element of surprise was greatly lessened when we began to know what to look for and to recognize the sounds incident to the preparation of a gas attack.

The first attack was made with chlorine. If a gas attack is to be made with gas clouds, the number of gases available is limited. The gas must be easily compressible, easily made in large quantities, and should be considerably heavier than air. If to this is added the necessity of its being very toxic and of low chemical reactivity, the choice is practically reduced to two gases: chlorine and phosgene. Chlorine is to gas warfare what nitric acid is to high explosives. Pure chlorine did not satisfy quite all the requirements, as it is very active chemically and there-

fore easily absorbed. Many men in the first attack who had sufficient presence of mind saved themselves by burying their faces in the earth, or by stuffing their mufflers in their mouths and wrapping them around their faces.

There were several gas attacks of almost exactly the same kind early in 1915. There was no gas between the end of May, 1915, and December, 1915, and by that time adequate protection had been provided.

The first protection was primitive. It consisted largely of respirators made by women in England in response to an appeal by Kitchener. They were pads of cotton wool wrapped in muslin and soaked in solutions of sodium carbonate and thiosulfate; sometimes they were soaked only in water. A new type appeared almost every week. One simple type consisted of a pad of cotton waste wrapped up in muslin together with a separate wad of cotton waste. These were kept in boxes in the trenches, and on the word "gas" six or eight men would make a dive for the box, stuff some waste into their mouths, then fasten on the pad and stuff the waste into the space around the nose and mouth. But this got unpopular after a bit, when it was discovered that the same bits of waste were not always used by the same men. During the early part of 1915 this was the only protection used.

Then came the helmet made of a flannel bag soaked in thiosulfate and carbonate, with a mica window in it. A modified form of this device with different chemicals is still used in the British army as a reserve protection. It is put over the head and tucked into the jacket, and is fool-proof as long as well tucked down. This stood up very well against chlorine.

In 1915 we got word from our Intelligence Department of a striking kind. It consisted of notes of some very secret lectures given in Germany to a number of the senior officers. These lectures detailed materials to be used, and one of them was phosgene, a gas which is very insidious and difficult to protect against. We had to hurry

up to find protection against it. The outcome was a helmet saturated with sodium phenate. The concentration of gases when used in a cloud is small, and 1 to 1,000 by volume is relatively very strong. The helmet easily gave protection against phosgene at a normal concentration of 1 part in 10,000. That helmet was used when the next attack came in Flanders, on the 19th of December. This attack was in many ways an entirely new departure and marked a new era in gas warfare.

There are three things that really matter in gas warfare, and these were all emphasized in the attack of December. They are: (1) increased concentration; (2) surprise in tactics; (3) the use of unexpected new materials.

Continued efforts have been made on both sides to increase the concentration. The first gas attack, in April, 1915, lasted about one and a half hours. The attack in May lasted three hours. The attack in December was over in thirty minutes. Thus, assuming the number of cylinders to be the same (one cylinder for every meter of front in which they were operating), the last attack realized just three times the concentration of the first, and six times the concentration obtained in May. Other cloud gas attacks followed, and the time was steadily reduced; the last attacks gave only ten to fifteen minutes for each discharge. We believe that the cylinders are now put in at the rate of three for every two meters of front, and may even be doubled banked.

The element of surprise came in an attack by night. The meteorological conditions are much better at night than during the day. The best two hours out of the twenty-four, when steady and downward currents exist, are the hour between sunset and dark and the hour between dawn and sunrise. Gas attacks have therefore been frequently made just in the gloaming or early morning, between lights. This took away one of the easy methods of spotting gas, that of seeing it, and we had

to depend upon the hissing noises made by the escaping gas, and upon the sense of smell.

Another element of surprise was the sending out of more than one cloud in an attack. After the first cloud the men would think it was all over, but ten minutes or half an hour later there would come another cloud on exactly the same front. These tactics were very successful in at least one case, namely, the attack near Hulluch in 1916. Some of the troops discarded their helmets after the first wave and were caught on the second, which was very much stronger than the first.

Efforts were also made to effect surprise by silencing the gas. But silencers reduced the rate of escape so greatly that the loss of efficiency from low concentration more than made up for the gain in suddenness. Another method was to mix the gas up with smoke, or to alternate gas and smoke, so that it would be difficult to tell where the gas began and the smoke ended.

The last attack made on the British by this means was in August, 1916. Since that time the Germans have used gas three times on the West Front against the French, and have also used it against the Italians and the Russians. It has been practically given up against the British, although the method is by no means dead.

The last attack was a slight set-back in the progress of gas defense. The casualties had been brought down to a minimum, and, as shown by the fact that the percentage of deaths was high, protection was complete in all cases where used, casualties being due to unpreparedness in some form. The attack in question was brought on under difficult conditions for the defenders, as it was made on new troops during a relief when twice as many men were in the trenches as normally. Furthermore, they had to wear helmets while carrying their complete outfit for the relief. This was the second time the Germans caught us in a relief, whether through information or luck we cannot say.

The protection that had been devised against phosgene proved effective at the time, but provision was made to meet increased concentration of phosgene. We never had any actual evidence during the attack that phosgene was being used, as no samples were actually taken from the cloud, but cylinders of phosgene were captured later. Glass vacuum tubes, about 10 by 30 cm., with a tip that could be broken off and then closed by a phasticine-lined glass cap, were distributed, but the only one that came back was an unopened tube found in a hedge, and marked by the finder "Dangerous; may contain cholera germs." In a gas attack everybody keeps quiet or else has a job on hand, and conditions are not conducive to the taking of gas samples. The original types of vacuum tube were smaller than those now used.

There was a long search for materials that would absorb phosgene, as there are few substances that react readily with it. The successful suggestion came from Russia. The substance now used very extensively by all is hexamethylenetetramine (urotropine) $(CH_2)_6N_4$, which reacts very rapidly with phosgene. Used in conjunction with sodium phenate, it will protect against phosgene at a concentration of 1 : 1000 for a considerable period. An excess of sodium hydroxide is used with the sodium phenate, and a valve is provided in the helmet for the escape of exhaled air. The valve was originally devised so that the hydroxide would not be too rapidly carbonated, but it was found in addition that there is a great difference in ease of breathing and comfort if a valve is placed in the mask. The helmet is put on over the head, grasped with left hand around the neck and tucked into the jacket. This form is still used in reserve.

By this time gas shells were beginning to be used in large numbers, and it became evident that protection by a fabric could not be depended on with certainty. The box type of respirator was the next development. Respirators have to fulfill two requirements which are quite opposed

to one another. In the first place they should be sufficiently large and elaborate to give full protection against any concentration of any gas, whereas military exigency requires that they be light and comfortable. It is necessary to strike a balance between these two. Upon a proper balance depends the usefulness of the respirator. Oxygen apparatus will not do on account of its weight and its limited life. Two hours' life is excessive for that type. The side that can first force the other to use oxygen respirators for protection has probably won the war.

The concentrations of gas usually met with are really very low. As has been said, a high concentration for a gas cloud is 1 part in 1,000, whereas concentrations of two or three per cent. can be met by respirators depending on chemical reactivity. One such respirator is a box of chemicals connected by a flexible tube with a face-piece fitting around the contours of the face, and provided with a mouthpiece and nosepiece.

As regards the chemicals used there is no secret, for the Germans have many of the same things. Active absorbent charcoal is one of the main reliances, and is another suggestion that we owe to the Russians. Wood charcoal was used in one of their devices and was effective, but most of the Russian soldiers had no protection at all.

We wanted to protect against chlorine, acids and acid-forming gases, phosgene, etc., and at one time were fearful of meeting large quantities of hydrocyanic (prussic) acid (HCN). At one period every prisoner taken talked about the use of prussic acid, saying that the Kaiser had decided to end the war and had given permission to use prussic acid. Protection was evidently needed against it. The three things that then seemed most important were: (1) chlorine and phosgene; (2) prussic acid; (3) lachrymators. Charcoal and alkaline permanganate will protect against nearly everything used, even up to concentrations of ten per cent. for short periods.

The German apparatus, developed about the same time, is of different pattern, and is still employed. It consists of a small drum, attached directly to the front of the face-piece, and weighs less than the British respirator but must be changed more frequently. It has no mouthpiece. The chemicals are in three layers: first an inside layer of pumice with hexamethylenetetramine, in the middle a layer of charcoal (sometimes blood charcoal), and outside baked earth soaked in potassium carbonate solution and coated with fine powdered charcoal.

As regards the future of the gas cloud, it may be looked upon as almost finished. There are so many conditions that have to be fulfilled in connection with it that its use is limited. It is very unlikely that the enemy will be able to spring another complete surprise with a gas cloud.

The case is different with gas shells. The gas shells are the most important of all methods of using gas on the Western Front, and are still in course of development. The enemy started using them soon after the first cloud attack. He began with the celebrated "tear" shells. A concentration of one part in a million of some of these lachrymators makes the eyes water severely. The original tear shells contained almost pure xylyl bromide or benzyl bromide, made by brominating the higher fractions of coal-tar distillates.

The German did his bromination rather badly. As you know, it should be done very carefully or much dibromide is produced, which is solid and inactive. Some of the shells contained as much as 20 per cent. dibromide, enough to make the liquid pasty and inactive. The shells used contain a lead lining, and have a partition across the shoulder, above which comes the T. N. T. and the fuse. These shells had little effect on the British, but one attack on the French, accompanied by a very heavy bombardment with tear shells, put them out badly. The eyes of the men were affected, and many of the men were even anesthetized by the gas, and were taken prisoner.

Our first big experience was an attack at Vermelles. The Germans put down a heavy barrage of these shells and made an infantry attack. The concentration was great, the gas went through the helmets, and the men even vomited inside their helmets. But it is difficult to put down a gas barrage, and there is danger that it will not be a technical success. In the instance cited certain roads were not cut off sufficiently, so that reinforcements got up. This attack, however, opened our eyes to the fact that, as in the case of gas clouds, concentration would be developed so as to make it high enough to produce the required effect under any circumstances.

When the Germans started using highly poisonous shells, which was at the Somme in 1916, they did not attend to this sufficiently, although enormous numbers of shell were used. The substance used was trichloromethyl-chloroformate, but not in great strength. It had no decided reaction on the eyes, hence the men were often caught.

The quantity of gas that can be sent over in shells is small. The average weight in a shell is not more than six pounds, whereas the German gas cylinders contain 40 pounds of gas. To put over the same amount of gas as with gas clouds, say in five minutes per thousand yards of front, would require a prohibitive number of guns and shells. It becomes necessary to put the shells on definite targets, and this, fortunately, the Germans did not realize at the Somme, although they have found it out since.

The use of gas out of a projectile has a number of advantages over its use in a gas cloud. First, it is not so dependent on the wind. Again, the gunners have their ordinary job of shelling, and there is no such elaborate and unwelcome organization to put into the front trenches as is necessary for the cloud. Third, the targets are picked with all the accuracy of artillery fire. Fourth, the gas shells succeed with targets that are not accessible to

high explosives or to gas clouds. Take, for instance, a field howitzer, dug into a pit with a certain amount of overhead cover for the men, who come in from behind the gun. The men are safe from splinters, and only a direct hit will put the gun out of action. But the gas will go in where the shell would not. It is certain to gas some of the men inside the emplacement. The crew of the gun must go on firing with gas masks on, and with depleted numbers. Thus it nearly puts the gun out of commission, reducing the number of shots say from two rounds a minute to a round in two minutes, and may even silence it entirely. Another example is a position on a hillside with dugouts at the back, just over the crest, or with a sunken road behind the slope. Almost absolute protection is afforded by the dugouts. The French tried three times to take such a position after preparation with high explosives, and each assault failed. Then they tried gas shells, and succeeded. The gas flows rapidly into such a dugout, especially if it has two or more doors.

Among the effective materials used by the Germans for gas shells were mono- and tri-chloromethyl-chloroformate. Prussic acid never appeared; the Germans rate it lower than phosgene in toxicity, and the reports concerning it were obviously meant merely to produce fear and distract the provisions for protection.

During the last five months the actual materials and the tactics used by the Germans have undergone a complete change. The lachrymator shells are less depended upon than formerly for "neutralization," but are still a source of annoyance. Mere annoyance, however, may be an effective method of neutralizing infantry. For instance, where large amounts of supplies and ammunition are being brought up there are always cross-roads where there is confusion and interference of traffic. A few gas shells placed there make every man put on his mask, and if it is a dark night and the roads are muddy the resulting confusion can be only faintly imagined. It may thus be

possible to neutralize a part of the infantry by cutting down their supplies and ammunition.

The use of a gas shell to force a man to put on his mask is practically neutralization. If at the same time you can hurt him, so much the better. Hence the change in gas-shell tactics, which consists in replacing the purely lachrymatory substance by one that is also poisonous.

One substance used for this method of simultaneously harassing and seriously injuring was dichloro-diethylsulfide (mustard gas). Its use was begun in July of last year at Ypres, and it was largely used again at Nieuport and Armentieres. A heavy bombardment of mustard-gas shells of all calibers was put on these towns, as many as 50,000 shells being fired in one night. The effects of mustard gas are those of a "super-lachrymator." It has a distinctive smell, rather like garlic than mustard. It has no immediate effect on the eyes, beyond a slight irritation. After several hours the eyes begin to swell and inflame and practically blister, causing intense pain, the nose discharges freely, and severe coughing and even vomiting ensue. Direct contact with the spray causes severe blistering of the skin, and the concentrated vapor penetrates through the clothing. The respirators of course do not protect against this blistering. The cases that went to the hospitals, however, were generally eye or lung cases, and blistering alone took back very few men. Many casualties were caused by the habit that some of the men had fallen into of letting the upper part of the mask hang down so as not to interfere with seeing. The Germans scored heavily in the use of this gas at first. It was another example of the element of surprise in using a new substance that produces new and unusual symptoms in the victims.

Up to the present time there had been no material brought out on either side that can be depended on to go through the other fellow's respirator. The casualties are due to surprise or to lack of training in the use of masks.

The mask must be put on and adjusted within six seconds, which requires a considerable amount of preliminary training, if it is to be done under field conditions.

Among other surprises on the part of the Germans were phenylcarbylamine chloride, a lachrymator, and diphenylchloroarsine, or "sneezing gas." The latter is mixed in with high explosive shells or with other gas shells, or with shrapnel. It was intended to make a man sneeze so badly that when he puts on his mask he is not able to keep it on. The sneezing gas has, however, not been a very great success.

All bombardments now are of this mixed character. The shells used are marked with differently colored crosses, and definite programs are laid down for the use of the artillerymen.

As regards the future of gas shells, it should be emphasized that the "gas shell" is not necessarily a gas shell at all, but a liquid or solid shell, and it opens up the whole sphere of organic chemistry to be drawn upon for materials. The material placed inside the shell is transformed into vapor or fine droplets by the explosion and a proper adjustment between the bursting charge and the poisonous substance is necessary. Both sides are busy trying to find something that the others have not used, and both are trying to find a "colorless, odorless, and invisible" gas that is highly poisonous. It is within the realm of possibilities that the war will be finished, literally, in the chemical laboratory.

The Germans have not altered their type of respirator for some time, and it is not now equal in efficiency to the British or American respirator. The German respirator, even in its latest form, will break down at a concentration of 0.3 per cent. of certain substances. The German design has given more weight to military exigency, as against perfect protection, than has the British. Another thing that weighs against changes in design is the fact that the German, already handicapped by the lack of certain mate-

rials, must manufacture 40,000,000 respirators a year in order to supply his Austrian, Bulgarian, and Turkish allies, as well as his own army.

In the British and American armies the respirator must always be carried with the equipment when within 12 miles of the front. Between 12 and 5 miles a man may remove the respirator box in order to sleep, but within 5 miles he must wear it constantly. Within 2 miles it must be won constantly in the "alert" position (slung and tied in front). When the alarm is given he must get the respirator on within six seconds. The American respirator is identical with the British. The French have a fabric mask made in several layers, the inner provided with a nickel salt to stop HCN, then a layer with hexamethylenetetramine; it has no valve and is hot to wear. The French also use a box respirator, consisting of a metal box slung on the back, with a tube connecting to the face mask; the latter is of good Para rubber and is provided with a valve. One disadvantage of this form is the danger of tearing the single rubber sheet. The German mask now contains no rubber except one washer; the elastics consist of springs inside a fabric, and the mask itself is of leather. It hardens and cracks after being wet, and is too dependent upon being well fitted to the face when made.

The following compounds have been used by the Germans in gas clouds or in shells:

1. Allyl-iso-thiocyanate (Allyl mustard oil), $C_3H_5NCS$ (shell).
2. Benzyl bromide, $C_6H_5CH_2Br$ (shell).
3. Bromo-acetone, $CH_2Br.CO.CH_3$ (hand grenades).
4. Bromated methyl-ethyl-ketone (bromo-ketone), $CH_2BrCOC_2H_5$ or $CH_3.CO.CHBr.CH_3$ (shell). Dibromo-ketone, $CH_3COCHBr.CH_2Br$ (shell).
5. Bromine, $Br_2$ (hand grenades).
6. Chloro-acetone, $CH_2Cl.COCH_3$ (hand grenades).
7. Chlorine, $Cl_2$ (cloud).

8. Chloromethyl-chloroformate (Palite), $ClCOOCH_2Cl$ (shell).

9. Nitro-trichloro-methane (Chloropicrin or nitro-chloroform), $CCl_3NO_2$ (shell).

10. Chlorosulfonic acid, $SO_3.H.Cl$ (hand grenades and "smoke pots").

11. Dichloro-diethylsulfide (mustard gas), $(CH_2Cl-CH_2)_2S$ (shell).

12. Dimethyl sulfate, $(CH_3)_2SO_4$ (hand grenades).

13. Diphenyl-chloro-arsine, $(C_6H_5)_2AsCl$ (shell).

14. Dichloromethyl ether, $(CH_2Cl)_2O$ (shell).

15. Methyl-chlorosulfonate, $CH_3ClSO_3$ (hand grenades).

16. Phenyl-carbylamine chloride, $C_6H_5NCCl_2$ (shell).

17. Phosgene (carbonyl chloride), $COCl_2$ (cloud and shell).

18. Sulfur trioxide, $SO_3$ (hand grenades and shell).

19. Trichloromethyl-chloroformate (Diphosgene, superpalite), $ClCOOCCl_3$ (shell).

20. Xylyl bromide (tolyl bromide), $CH_3C_6H_4CH_2Br$. (shell).

# WHAT ARE ENZYMES?

BY

BENJAMIN HARROW

The word enzyme comes from a Greek word meaning "in yeast" (*en,* in; *zyme,* leaven). Perhaps the most acceptable definition in the light of recent scientific research is to say that it is a substance showing the properties of a catalyst and produced as a result of cellular activity.

But what is a catalyst? The reader will recall his first very simple experiment in the preparation of oxygen. Here the learned instructor tells the bewildered youth that if you put a little potassium chlorate in a test tube and heat this very strongly, a gas is evolved which is later identified as oxygen. Now by merely adding a small quantity of a dirty black-looking powder, called manganese dioxide, to the potassium chlorate, the oxygen is evolved much more rapidly and at a much lower temperature. But this is not all. A careful examination at the end of the reaction shows that the manganese dioxide has not changed in any way: we have the same substance, and the same amount of substance, at the end of the reaction as at the beginning. Many such substances are known to chemists. They all have this peculiarity: that they *accelerate* chemical reactions, and that a relatively small—at times insignificant—quantity of the catalyst suffices to bring about the chemical change.

In cells we find substances of this type, but thus far these cellular catalysts, unlike the manganese dioxide, and like proteins, have never been produced outside of the cell.

When we consider that life is possible only because of continued cellular activity, and when we bear in mind that this activity is largely the result of chemical changes brought about by these enzymes, the paramount importance of these substances becomes manifest.

Alcoholic fermentation in yeast, the souring of milk, processes of putrefaction, and various other examples of changes in organic materials with, often enough, the accompanying liberation of bubbles of gas, had long been known. The epoch-making researches of Pasteur had shown that fermentations and putrefactions were inaugurated by the presence of living organisms. Then later extracts from the saliva and the gastric mucosa of the stomach were obtained which also had the power of bringing about chemical changes in carbohydrates and proteins. This led to the classification of ferments into those which, like yeast and certain bacteria, acted because of certain vital processes (organized ferments), and those which, like the extracts from the saliva and stomach, were presumably "non-living unorganized substances of a chemical nature" (unorganized ferments). Kühne designated the latter "enzymes." This classification was generally accepted, and the "vitalists" held absolute sway until Emil Buchner, in 1897, overthrew the whole theory by a series of researches which, in their influence, were only second in importance to those of Pasteur in an earlier generation. One of Buchner's classical experiments consisted in grinding yeast cells with sand and infusorial earth, and then subjecting the finely pulverized material to a pressure of 300 atmospheres—a pressure far more than enough to destroy yeast, or any other cells. The liquid so obtained had all the fermentative properties of the living yeast cell. Obviously, then, the living cell could not be responsible for the fermentation. On the other hand, this experiment did suggest that cellular activity gives rise to some substance which, once produced, exerts its influence whether the cell is alive or dead. All subse-

quent experiments have but strengthened the conviction that cells do produce these substances, and that the chemical changes are due *not* to the living organisms, but to the *lifeless* substances (enzymes) to which these organisms give rise.

Minute in quantity, and tenaciously adhering to substances present, particularly protein, the isolation of an enzyme in the pure state has become one of the most difficult problems in physiological chemistry. Yet any elementary student in the subject finds little difficulty in performing simple experiments which convince him either of its presence or of its absence. How are they done?

The method consists essentially in making use of the so-called "specificity" of enzymes. To use Fischer's simile, just as one key fits one lock, so any one enzyme will act on only a certain type of substance. Take, for example, the enzyme found in saliva, ptyalin: it readily acts on the carbohydrate, starch, but has absolutely no action on protein. Again, take the pepsin of the stomach: this enzyme breaks down proteins, but is without result on carbohydrates. These instances may be multiplied indefinitely.

Some enzymes show their specificity to an even more marked degree. In the yeast cell, for example, we find one, sucrase,[1] which acts only on cane sugar (sucrose); but on no other sugar or carbohydrate. A simple little experiment demonstrates this beyond question. A yeast cake is ground up very intimately with a little sand and water, and the mass filtered. A small portion of the filtrate is added to a solution of cane sugar, the mixture placed in an incubator kept at 38° C., and allowed to remain there for about 30 minutes or so. At the end of that time the mixture, if heated with Fehling's solution,[2]

[1] The ending "ase" denotes enzyme.

[2] This is the well-known alkaline copper solution used by all medical men to test for sugar in the urine. The sugar in the urine is not, as might be supposed, ordinary cane sugar, but

will yield a red-brick precipitate—a result which could not be obtained either with the cane sugar, or with the enzyme solution alone. No other carbohydrate solution —or protein, or fat solution, for that matter—can take the place of the cane sugar; our enzyme will be without effect. If we take our original yeast extract, and first heat it to, say, the boiling point of water, then cool it, and from here on repeat the experiment as before, no grape sugar is obtained. If instead of heating the enzyme solution, we cool it, the action is considerably delayed.

Some of the yeast extract may be poured into an excess of alcohol, the precipitate separated by filtration, and redissolved in water. This solution will show all the properties of the yeast extract.

Evidently, then, the watery extract of yeast contains something which has the power of breaking down cane sugar. This something is exceedingly sensitive to heat, rather less so to cold, and is precipitated—together with other substances (as could be shown)—by alcohol. The last three properties are characteristic not only of sucrase, but of all enzymes to a greater or less degree. That a minute quantity of enzyme can act upon an exceedingly large quantity of substrate is also readily demonstrable. The laws of catalysis hold firm.

One other fact about enzymes is most important. Graham, as far back as 1861, found that certain substances (cane sugar, salt, etc.) in solution, when placed in a dialyzer consisting of a parchment bag, which in its turn was surrounded by water, would diffuse through the bag, whereas others (proteins, gum, starch, etc.) would not. The diffusible ones he named crystalloids, those non-diffusible, colloids. If some of our original yeast extract were placed in such a parchment bag, none of the enzyme

grape sugar. Fehling's solution reacts with the latter, but not with the former.

The cane sugar is split or "hydrolyzed," by the sucrase, one of the products being grape sugar.

would find its way into the surrounding layer of water. Enzymes, like the proteins, are *colloids*.

The fact that enzymes show colloidal properties, and the fact that they are invariably associated with proteins, made it seem probable that when ultimately isolated in the pure condition, they would be found to be proteins. Attempts to obtain pure enzymes have been many. The general method of procedure in almost all cases consists in first extracting with water [3]—as already explained—or submitting the mass to much pressure (Buchner), if the enzymes are "intracellular."

Having obtained a solution, the next step is often that of dialysis (Graham). Diffusible bodies, particularly inorganic substances, are thereby separated. Three of the classical investigators in this branch, Osborne, Peckelharing, and Fraenkel, have all employed this method.

Now usually comes precipitation. Some substance—alcohol, acetone, or ammonium sulphate—is added in which the enzyme is insoluble. The precipitate so obtained contains many impurities (proteins, certain carbohydrates, etc.). To purify it, it is redissolved, re-dialyzed, and reprecipitated many times. On occasion, a biological procedure, first suggested by Effront, and put into practice by Fraenkel, may be used. This consists in fermenting the impure precipitate with yeast. The carbohydrate and protein are thereby used up, but according to Fraenkel, the enzyme is not touched.

The laboriousness of such an operation may best be gathered from a specific example. Let us take an experiment from the work of Professor Sherman, of Columbia, an active investigator. Here is his method for preparing a starch-splitting enzyme from the pancreas: Mix thoroughly 20 grammes of pancreative powder—a commercial preparation—with 200 cubic centimeters of 50 per cent. alcohol at 15-20° C. [S. finds that much of the contained

[3] Often containing alcohol, toluene, or chloroform (as preservatives).

protein is left behind by the use of this 50 per cent. alcohol.] Allow this preparation to stand 5-10 minutes, then filter, keeping the temperature below 20° C. (This takes from 1 to 2 hours.) Pour the filtrate into 7 times its volume of a mixture of 1 part of alcohol to 4 parts ether (more protein and other impurities are here separated). Within 10-15 minutes the enzyme (including certain impurities) separates as an oily solution. Decant the supernatant liquid. Dissolve the precipitate in the smallest amount of pure water at a temperature of 10-15 degrees Centigrade and reprecipitate at once by pouring into 5 volumes of absolute alcohol. Allow it to settle, keeping temperature low; filter, dissolve in 200-250 cubic centimeters of 50 per cent. alcohol containing 5 grammes of maltose. Pour the solution into a collodion sack of 500 cubic centimeters capacity, and dialyze against 2,000 cubic centimeters of 50 per cent. alcohol at not above 20° C. and preferably not below 15° C. Replace dialyzate twice: after 15 hours and a second period of 8-9 hours with fresh 50 per cent. alcohol. Continue dialysis 40-42 hours. Filter. Pour clear filtrate into an equal volume of a mixture of alcohol and ether (equal parts). Filter in the cold, and place the precipitate in a vacuum desiccator.[4] The powder obtained is so active that it can digest 20,000 times its own weight of starch. And still we are not at all certain that this is an enzyme uncontaminated with foreign bodies!

Of the three or four representative workers in attempts to isolate a pure enzyme, the substances obtained by Professor Sherman and Dr. Osborne (of the Connecticut experiment station) showed decided protein characteristics; whereas the two German investigators, Lentner and Fraenkel, both agree in proclaiming their products as carbohydrate in nature. How near or how far from the truth is either group? To begin with, no proof that any

[4] A vessel (containing a hygroscopic substance to take up moisture) from which the air has been exhausted.

of these products is 100 per cent. pure has been advanced, and the chemist through bitter experience knows the danger in discussing the composition of impure substances. Another fact to be kept in mind is that, often enough, the purer the enzyme, the less active does it become. In several of these cases it has been shown that a loss in activity goes hand in hand with a proportional loss in the phosphoric acid content of the substance. This gives rise to the possibility—expounded further on—that the enzyme is not a chemical individual, but consists of at least two substances: (*a*) a something which has the power of acting only when activated—in this instance—by (*b*) phosphoric acid. And yet, if arguing by analogy is at all permissible, it may be maintained that since all the inorganic catalysts are distinct chemical individuals, why not enzymes?

Of course, all this does not at all exclude the possibility that different enzymes may have different structures and the conflicting results of investigators may be due to this fact. Some of the men worked on amylases (starch-splitting enzymes), others on lipases (fat-splitting), others still on proteases (protein-splitting). Why assume that such diverse substances should all have the identical composition? It may be, as Professor Armstrong has suggested, that the enzyme in constitution is similar to the substance on which it acts.

Extremely suggestive as the basis for much present-day activity has been the work of Professor Gabriel Bertrand, of the Sorbonne, Paris. Most of this has been on laccase, an oxidizing enzyme first found in the milky latex of the tree *Rhus vernicifera,* and since then in many plants. The production of the beautiful Japanese lacquer from the latex of *Rhus vernicifera* was shown to be due to the activation of the atmospheric oxygen by the laccase (hence its name). Bertrand was able to prove that the activity of the laccase was connected with the manganese present, for by repeated precipitation with alcohol, he di-

vided his laccase preparations into three fractions of different manganese content, each with an activity distinctly proportional to the amount of manganese present. As further proof of the importance of this manganese, he was able to show that a minute addition of a salt of manganese (manganese sulphate) increased the activity of the laccase, whereas other metals had no such effect. This led him to the dual conception of an enzyme, also advocated by Armstrong: one of the constituents is capable of producing, to a slight degree, on its own account, the chemical reaction associated with the particular enzyme in question, but requires its activity to be augmented by the presence of another substance—inactive in itself—before its action becomes appreciable. The former may consist of acid, alkali, calcium or magnesium salt, etc. The latter component is more complex, usually protein-like (egg-white, for example), and colloidal.

Bertrand's views—perhaps, also, Fischer's colossal work on the synthesis of proteins from amino acids—has led the school of enzyme chemistry to shift its ground considerably. Why these laborious, and always futile attempts to isolate a pure enzyme from the cell? Why not attempt to synthesize one from simple inorganic and organic materials? Trillat, in 1904, prepared a mixture of traces of manganese chloride and egg albumen which showed the reaction of laccase and other oxidases (oxidizing enzymes): it blued guaiacum, its action was prevented by heat and acid, and it could be precipitated by alcohol, and redissolved in water without losing its oxidizing powers—characteristic properties of *all* enzymes. Wolf with his colloidal iron compounds, and Euler and Bolin with their calcium salts of organic acids (citric, malic, etc.), and many others, have produced strong evidence in favor of the view that many of the enzymes, at least many of the so-called oxidases, are relatively simple substances.

Along somewhat modified lines is the work of Panzer,

who claims that various carbohydrates show distinct diastatic (carbohydrate-splitting) activity when heated with hydrochloric acid gas, and then ammonia; and that of Woker, whose findings, at present rather disputed, would tend to the belief that formaldehyde (the "formalin" of commerce) may, under certain conditions, act in place of diastase in hydrolyzing starch.

Some very far-reaching possibilities are suggested by the studies on the lipases (fat-splitting enzymes) of castor and soya beans by Dr. Falk, of the Harriman Research Laboratory. Every worker in the field is aware how very easily enzymes are inactivated or destroyed by heat or the presence of relatively small quantities of certain foreign bodies, such as acids and bases. The inactivation of the lipases of the beans could be brought about not only by these means, but also by neutral salts, alcohol, acetone, etc. Dr. Falk conceived the idea that this inactivation was due to an internal rearrangement of certain of the atoms in the molecule of the enzyme. Many cases of such tautomeric changes—of rearrangement within the molecule—are known to organic chemists, and are often brought about by the action of mild chemical agents. Dr. Falk's hypothesis is to the effect that the grouping involved is to be found in all proteins, and hence, probably, in enzymes. If inactivation means the rearrangement of a group from configuration 1 to that of 2, activation, or change from 2 back to 1, may be brought about by the action of dilute alkali—often used to bring about these changes in configuration. Actual experiments on the action of alkali on proteins (themselves quite inactive) have endowed these substances with fat-splitting power.

Whilst, therefore, we are far from a comprehensive knowledge of the chemical configuration of an enzyme, studies on the production of artificial enzymes, and on the possible rearrangements of certain groups within the molecule, may throw much light on a very perplexing problem.

# NATURAL DEATH AND THE DURATION OF LIFE

BY

JACQUES LOEB

*The Rockefeller Institute for Medical Research*

## I

THE efforts to prolong life have resulted in a diminution of the chances of premature death. Nations with adequately developed facilities for medical research and an efficient public health service have practically eliminated smallpox and typhoid, yellow fever and malaria, and have conquered rabies, diphtheria, tetanus, and cerebrospinal meningitis. If this development continues to receive the support it deserves, the time is bound to come when each human being can be guaranteed with a fair degree of probability a full duration of life. But why must we die?

The French encyclopedists of the eighteenth century defined life as that which resists death. What they meant by this definition was the fact that as soon as death sets in, the body begins to disintegrate. They argued correctly that the forces of disintegration were inherent in the living body but were held in check during life. Recent progress in physical chemistry permits us to state that the spontaneous disintegration of the body which sets in with death (at the proper temperature and proper degree of moisture) is a process of digestion, comparable

to that which the meat we eat undergoes in our stomach and intestine. The essential feature of digestion is in this case the transformation of the solid meat into soluble products by two ferments, pepsin, which exists in the stomach, and trypsin, which exists in the intestine. The successive treatment of meat by the two ferments results in the breaking-up of the large insoluble molecules into the small soluble molecules of amino acids which are absorbed by the blood and carried to the cells of the body where they are utilized to build up new solid cell matter.

These two ferments, pepsin and trypsin, exist not only in the digestive organs, but in many, and possibly in all living cells, and the question arises, why they do not constantly digest and thus destroy our body while life lasts. A tentative answer to this question has been given by Dernby, who has been able to show that the coöperation of both ferments is required in the same cell for the work of destruction, and that this coöperation of both ferments becomes possible only at a certain degree of acidity, which cannot be reached in the living body on account of the constant removal of acid through respiration and oxidation. When respiration ceases, the degree of acidity necessary for the digestive action of both ferments in the same cell is reached, leading to gradual digestion and liquefaction of the tissues which characterizes the disintegration of the dead body.

This is not the only cause of disintegration, since the dead body becomes also the prey of the destructive action of microorganisms from the air and in the intestine. During life these same microorganisms are powerless in their attack on the cells protected by a normal membrane, but after death this membrane is destroyed and the action of microorganisms can superimpose itself on that of digestion. It is also probable that the normal secretions of the mucous membranes during life have a protective effect.

Death, then, in a human being means the permanent

cessation of respiration. We know that this result can be brought about by mechanical violence, by poison, and by disease, and, since nobody can escape all these agencies, doubts have arisen whether we do not all die from injury or disease, and whether such a thing as natural death really exists. If there were no natural death it should be possible to prolong life indefinitely if a complete protection against disease and accidents could be secured. It is impossible to make such an experiment in a human being, since our intestine and our respiratory tract can not be kept free from microorganisms. The problem has, however, been solved for certain insects. A Russian author, Bogdanow, invented a method of obtaining the common house-fly free from all microorganisms, by putting the newly laid eggs for a number of minutes into a solution of bichloride of mercury of sufficient concentration. Most eggs were killed in the process, but some survived and these were free from microorganisms at their surface. By keeping the eggs on sterilized meat and in sterile flasks, the maggots leaving the egg could find their food and develop into flies. A French author, Guyénot, continuing the experiments on the fruit fly, raised 80 successive aseptic generations, and Northrop and the writer have raised thus far 87 aseptic successive generations of the fruit fly on aseptic yeast. In these experiments all possibility of infection, all chances of accidental or violent death were excluded. To make sure that these flies are absolutely free from microorganisms, their dead bodies are transferred to culture media such as are used for the growth of bacteria. If a common fruit fly is put on such a culture medium, in 24 hours a rapid growth of microorganisms develops, while the culture medium on which our aseptic flies were put remained free from all growth for years (or rather permanently). Aseptic fruit flies, free from infectious disease and supplied with proper food will, therefore, not escape death. These experiments, then, indicate that higher organisms must die from

internal causes even if all chance of infection and all accidents are excluded.

## II

These aseptic flies served as a means for testing an idea concerning the duration of life which presented itself, namely, that old age and natural death are due either to the gradual production in the body of a sufficient quantity of harmful or toxic substances, or to the gradual destruction of substances in the body required to keep it in youthful vigor, or to both. On this basis the natural duration of life would be in reality the time required to complete a chemical reaction or a series of chemical reactions, resulting in the production of toxic compounds in a quantity sufficient to kill, or resulting in the destruction of necessary compounds. Metchnikoff had called attention to the fact that toxic substances were formed in the intestine under the influence of microorganisms. The intestine of aseptic flies is free from microorganisms, so that the source for the shortening of life pointed out by Metchnikoff need not be considered in this case. The toxic substances formed might be substances formed in one or several organs of the body during their normal activity. Modern physical chemistry furnishes the means of testing such an idea. The period of time required to complete a chemical reaction diminishes rapidly when the temperature is raised and increases rapidly when the temperature is lowered. Experiments show that the time required for the completion of a chemical reaction is doubled or trebled when the temperature is lowered by 10° centigrade. This influence of temperature upon the rate of processes of nature seems to be typical for chemical reactions. If, therefore, the duration of life is the time required for the completion of certain chemical reactions in the body we might expect that the duration of life will be doubled or trebled when we lower the temperature ten

degrees centigrade. Such experiments can be carried out only in organisms where accidental death by infection is excluded and our aseptic fruit flies satisfied this condition. These experiments were made by Dr. Northrop and the writer, and consisted in putting a number of newly laid eggs of aseptic flies on an abundance of sterilized yeast (which is their natural food) in a flask plugged with cotton. These flasks were put into incubators the temperature of which was kept constant within 0.2 of a degree centigrade. The temperatures selected for the purpose were 10, 15, 20, 25, 27.5, and 30° C. It is not possible to go into the numerous precautions which it was necessary to take and the many technical difficulties involved in this investigation. The result of a large number of experiments was that the duration of life of such aseptic flies was a definite one for each temperature, which means that all the flies died at practically the same age when kept at the same temperature. Thus, for instance, the total average duration of life of such flies was 21.15 days at 30° C. The overwhelming majority died at that age, but a few died a little earlier and a few a little later. When the number of flies of a culture which die on successive days is plotted in terms of percentage of the original number of flies, we get that curve of death rates usually given in life insurance statistics. But this curve is very steep in our case owing to the fact that the majority of flies die at about the same time for a given constant temperature. The following table gives the average duration of life of the fly in days for different temperatures.

TABLE I

| Temperature, °C. | Average Duration of Life of the Fly from Egg to Death, Days |
|---|---|
| 30 | 21.15 |
| 25 | 38.5 |
| 20 | 54.3 |
| 15 | 123.3 |
| 10 | $177.5 + x$ |

This table shows that the influence of temperature on the duration of life of the fly is the same as the influence of temperature on the velocity of a chemical reaction, inasmuch as a lowering of the temperature by ten degrees results in an increase in the duration of life by two or three hundred per cent., and the same figure would be obtained if we investigated the effect of temperature upon the time required to complete a chemical reaction. At 30° C. the flies live on an average 21.15 days and at 20° C. they will live on an average 54.3 days or a little over twice as long. At 25° they live 38.5 days and at 15° C. 123.9 days or about three times as long. The fruit fly is a tropical organism and 30° C. is not far from the optimal temperature. By lowering their temperature twenty degrees we prolong the duration of their life by nine hundred per cent. We cannot lower the temperature below 10° since the flies suffer in the chrysalid stage when the temperature becomes 10° or less. While these are thus far the only experiments on the duration of life of higher organisms carried out with the necessary scientific precaution, there are many casual observations mentioned in the literature which suggest that lowering the temperature prolongs the duration of life of lower animals in general.

The body temperature of a normal human being is constant, namely about 37.5° C. and this temperature remains the same in the tropics and in the arctic regions. Human beings and most mammals differ in this respect from insects whose temperature is as a rule practically that of their surroundings. If it were possible to reduce the temperature of human beings and if the influence of temperature on the duration of life were the same as that in the fruit fly, a reduction of our temperature from 37.5 to about 16° would lengthen the duration of our life to that of Methusaleh; and if we could keep the temperature of our blood permanently at 7.5° C., our average life would (on the same assumption) be lengthened from

three score and ten to about 27 times that length, *i.e.*, to about nineteen hundred years. Unfortunately our body does not tolerate any considerable lowering of its temperature and if it did, life at so low a temperature would probably become very monotonous and uninteresting since in all probability sensations of pleasure as well as pain, of joy and of sadness, would be at a very low level.

The experiments on aseptic flies therefore lend support to the idea that the duration of our life is the time required for the completion of a chemical reaction or a series of chemical reactions. If these reactions consist in the gradual accumulation of harmful products in our body, or in the gradual destruction of substances required for a youthful condition, we understand why senile decay and death are the natural result of life.

III

Unicellular organisms, like bacteria, algæ or infusorians, seem to be immortal. They reach a certain size, divide into two, each half growing again to full size and dividing again, and so on. In this case we may say that it is practically the same individual which continues to live in the successive generations. Small pieces of a cancerous tumor can be transplanted successfully to other individuals and these pieces grow again to a large size. This process can also be repeated indefinitely, and it is the same cancer cell which continues to live in these successive transplantations, as it is the same bacterium which continues to live in successive generations. In this way it has been shown that cancers in mice may outlive many times the natural life of a mouse, in fact they seem to live indefinitely. Cancer cells may therefore be called immortal as was pointed out by Leo Loeb many years ago.

It seems that this is true also for certain normal cells like connective tissue cells. Carrel has isolated connective tissue cells from the heart of a chick embryo and

cultures of these cells living on the extracts from chick embryos have been kept alive now for seven years.

All this points to the idea that death is not inherent in the individual cell, but is only the fate of more complicated organisms in which different types of cells or tissues are dependent upon each other. In this case it seems to happen that one or certain types of cells produce a substance or substances which gradually become harmful to a vital organ like the respiratory center of the medulla, or that certain tissues consume or destroy substances which are needed for the life of some vital organ. The mischief of death of complex organisms may then be traced to the activity of a black sheep in the society of tissues and organs which constitute a complicated multicellular organism.

## IV

While in human beings there is no sharp limit between youth and maturity, in many insects and amphibians this limit is marked by a sudden metamorphosis in the shape of their body. The frog hatches from the egg as a tadpole without legs and with a long tail. After a certain length of time legs begin to grow, the tail disappears, the form of the head and mouth change, the skin looks different, and the tadpole is transformed into a frog. It is possible that some of the changes underlying metamorphosis are due to changes in the circulation of the blood. Gudernatsch made the remarkable discovery that this metamorphosis, which in our climate usually occurs during the third or fourth month of the life of the tadpole, can be brought about at will even in the youngest tadpoles, by feeding them with thyroid gland, no matter from which animal. By feeding very young tadpoles with this substance, frogs not larger than a fly could be produced. Allen added the observation that if a young tadpole is deprived of its thyroid gland, it is unable ever to become a frog; and that it remains a tadpole which can reach,

however, a long life and continue to grow beyond the usual size of the tadpole. When, however, such superannuated tadpoles are fed with thyroid they promptly undergo metamorphosis. These observations cleared up an old biological puzzle. Salamanders also go through a metamorphosis which is, however, less striking than that of the tadpole of a frog. In the salamander the metamorphosis consists chiefly in the throwing off of the gills, and in changes in skin and tail. In Mexico a salamander occurs which through its whole life maintains its tadpole form, namely the axolotl. Attempts to induce the axolotl to metamorphose failed until after Gudernatsch's discovery an investigator fed the axolotl thyroid gland, and this brought about metamorphosis. The thyroid gland stores the traces of iodine taken up in our food and it seemed possible that the iodine contained in the thyroid was the active principle causing metamorphosis in tadpoles. This was confirmed by Swingle who succeeded in inducing metamorphosis in tadpoles by feeding them with traces of inorganic iodine. According to our present knowledge, the duration of the tadpole stage seems to be the time required to store the necessary amount of certain compounds, one of which contains iodine.

Insects, like the fruit fly, hatch from the egg as maggots which grow at the expense of the food they take up and which, at a certain age, metamorphose into a chrysalid; and from this chrysalid at a given time will rise the winged fly. Feeding of thyroid to the maggots of the fruit fly will not accelerate their metamorphosis, and we can not tell whether in this case metamorphosis is due to the accumulation or formation of a definite compound in the body, though this may well be the case. The idea presented itself whether the duration of the larval or maggot stage was not also determined by the temperature (provided the food supply was adequate). We measured, therefore, the influence of temperature upon the duration of the larval state in aseptic fruit flies—*i.e.*, from

the time the egg was laid until the maggot was transformed into a chrysalid. The influence was practically identical with that of temperature on the total duration of life. Thus the larval period lasted 5.8 days at 25° C. and 17.8 days at 15° C., a ratio of about 1 : 3. The total duration of life of aseptic flies is 38.5 days at 25° and 123.9 days at 15° C., also a ratio of about 1 : 3. We are, therefore, justified in making the statement that the influence of temperature upon the duration of the larval period or the youth of aseptic flies is practically identical with the influence of temperature on the total duration of life.

Experiments by Uhlenhuth on the influence of temperature on metamorphosis in salamanders have shown that it is similar to that observed in flies. Salamanders kept at 25° metamorphosed when they were 11 weeks old, while salamanders kept at 15°, under otherwise identical conditions, metamorphosed when they were 22 weeks old. All these data suggest the possibility that the duration of life and the duration of the larval period or of youth are in reality times required for the completion of definite chemical reactions. The cessation of respiration leading to the termination of life and the alterations in circulation leading to metamorphosis or termination of youth are critical points; and it seems possible that these points are reached when a certain toxic substance is formed in adequate quantity in the body, or when a necessary substance is destroyed or sufficiently diminished in quantity, or when both conditions are fulfilled.

We can prolong or shorten the period of youth in amphibians not only by modifying the temperature but by withdrawing or offering the specific substance which causes metamorphosis, namely iodine or thyroid material. There is no end to the substances capable of hastening death. Shall we ever find a substance which will prolong the duration of life? At present we can neither deny nor affirm the possibility.

# THE PHYSIOLOGY OF THE AVIATOR

(Address before the Harvey Society, New York City, March 22, 1919)

BY

YANDELL HENDERSON

*Professor of Physiology, Yale University*

DOUBTLESS you have all read the delightful historical accounts by the late Admiral Mahan of the great naval battles of the eighteenth century, when France and England struggled for the mastery of the sea. You will recall the stress laid on the weather gauge, or windward position. If the wind blew from the eastward, as does the "northeast trade" among the Caribbean Islands where a great part of the struggle occurred, whichever admiral was able so to maneuver as to be to the east of his enemy obtained a great, and often a decisive, advantage. He could choose the time and mode of attack, while his antagonist was compelled to remain on the defensive, unable either to force the fighting or to escape it.

In modern naval warfare the position of the sun in relation to the enemy's fleet affects the accuracy of aim. The speed of the ships is of importance equalling that of their gunfire. But there is no element of position which quite corresponds to that of the weather gauge for a fleet under sail.

In the battles of the ships of the air, however, there is

again a condition which corresponds quite closely to the tactical advantage of maneuvering between the wind and the enemy. In this case it is not a direction in the plane of the horizon, except so far as light is important; but it is the direction at right angles, vertical to this plane. It is the upper position—the advantage obtained by him who can climb above his enemy, and, choosing the moment of attack, can swoop down upon him from above.

With this as one of the fundamental conditions of aerial warfare, it was inevitable that in the development of the battle plane there should be the utmost effort to produce machines of continually greater speed and, its correlative, climbing power. Likewise in the air, the greatest practicable altitude has meant for the flying man at once an advantage over his enemy and a reduction of his own chance of being hit by anti-aircraft fire from the enemy's guns on the ground.

Accordingly, from the comparatively low altitude at which the aerial fighting of the first year of the war usually occurred, the struggle rose, as more and more powerful airplanes were constructed by both sides, until at the end of the war it was quite common for battle planes to ascend to altitudes of 15,000 to 18,000 feet—three miles up, higher than the summits of the Rocky Mountains or the Alps.

Along with this development there occurred with increasing frequency among the aviators a condition of so-called "air-staleness." It is a condition closely similar to, perhaps identical with, the "over-training" or staleness, the physical and nervous impairment of athletes in a football team or college crew. In the last year of the war this condition had become so common that, as reported to us by some observers, the majority of the more experienced aviators in the British service were incapacitated to ascend to the necessary altitude, and many could no longer fly at all. It was to make good this most serious military deficiency that the enlistment and training of aviators

were undertaken by the American Air Service on the enormous scale that they were. It was for the purpose of testing our airmen initially, and of keeping tab on their physical condition thereafter, that the work at the Mineola laboratory, of which probably you have heard, was undertaken.

It is work which lies in a field of physiology in which before the war not half a dozen men in America, and not many more in Europe, were interested, and for them it was a field of what is called "pure" science. To-day it promises contributions of practical value not only to aviation, but to problems in medicine, climatology, athletics and hygiene.

We will turn then to the problem of the aviator and the methods of human engineering which have been developed for its solution. But first, it will be advisable to review briefly what is known concerning the immediate effects of low barometric pressure and the functional readjustments involved in acclimatization to elevated regions; that is, life at great altitudes.

Paul Bert,[1] the brilliant French physiologist, was the first to demonstrate, in 1878, that the effects of lowered barometric pressure or altitude are wholly dependent on the decreased pressure of oxygen. He carried out experiments upon men and animals both with artificial gas mixtures and reduced barometric pressure in a steel chamber.

He showed that in pure oxygen at 21 per cent. of atmospheric pressure life goes on in practically the same manner as in air, which contains 21 per cent. of oxygen, at the ordinary pressure. So also the breathing of an artificial gas mixture containing only 10.5 per cent. of oxygen has the same untoward effects at sea level that breathing pure air has at an altitude of about 20,000 feet, where the barometer is reduced by one half.

These considerations are fundamental for the differentiation of the disorders induced by rarefied air—so-called

[1] Paul Bert, *La Pression Barometrique*, Paris, 1878.

mountain sickness—from the conditions resulting from work in compressed air—so-called caisson disease. It is clear that it is from the former, and not at all from the latter, that aviators suffer; but, as the two disorders are sometimes confused, a few words regarding the latter are in place here.

Caisson disease—known also as the "bends," "diver's palsy," and by other names—depends upon the fact that, under the high pressure necessary for diving, tunneling, and other work below water, the nitrogen of the air dissolves in the blood and in the other fluids and tissues of the body in amounts proportional to the pressure. This in itself does no harm, and has in fact no effect upon the body, until the subject comes out of the pressure lock or caisson, or rises from the depth of the sea where he has been working. Then the nitrogen which has been dissolved begins to diffuse out of the body. This also does no harm and has no effect unless the pressure under which the man has been working is so high, and the lowering of the external pressure is so rapid, that the dissolved nitrogen separates in the form of bubbles. Such bubbles may form in the blood, in the synovial fluid of the joints, and even in the brain. They induce intense pain, and even paralysis and death. In order that bubbles may be formed it is essential, however, that the pressure with which the tissues are in equilibrium should have been lowered considerably more than half its absolute amount in a few seconds.

In the present state of the art of flying it is scarcely possible for an aviator to rise to a height of more than 20,000 feet, where the barometer would be less than half of that at sea level, in a period sufficiently short to allow bubbles of nitrogen to form in this way. The disorders from which aviators suffer are, therefore, of a different class from those to which workers in compressed air are exposed.

When the study of the effects of lowered barometric

pressure was begun, it was supposed that the circulation might be primarily disturbed. The blood in the arteries of a healthy man is under such a pressure that, if a glass tube were inserted vertically into one of the arteries of his neck, and the blood were allowed to flow up the tube, the column of blood would come to rest at a height of 4 or 5 feet above his heart, corresponding to pressures of 120 to 150 mm. mercury. Knowing that the air pressure is reduced at great altitudes, some of the earlier writers made the mistake of supposing that such a column of blood would rise higher, and the blood vessels would be under a greater strain, and more likely to burst therefore, at a great altitude than at sea level. That which they looked for they found. One writer has left a lurid description of how, while crossing a pass in the Andes, he got off his mule and walked for a time to rest the animal. On the least exertion his breathing became oppressed, "his eyes bulged and his lips burst." The odd part of this is that in reality the blood vessels are under no greater strain at a high altitude than at sea level. When the air pressure upon the exterior of the body and in the lungs is reduced, a part of the gas—at least the nitrogen dissolved in the blood—rapidly diffuses out through the lungs, so that the gas pressure within and without the blood vessels are again equal just as at sea level. The idea is still prevalent that hemorrhages occur under low barometric pressures. However, among thousands of people whom I had an opportunity to observe on Pike's Peak during a five-weeks' stay at the summit, I saw not a single nose bleed, except one which was caused by the forcible application of a hard object to the organ in question.

The only direct effects of changes of pressure are those which are felt in the ears, and occasionally in the sinuses connected with the nose. The ear drums are connected with the throat and contain air at the prevailing pressure. If the pressure is lowered this air expands, and

forces its way out through the Eustachian tubes into the throat. If the outside pressure is increased, it sometimes happens, particularly when the subject has a cold and the Eustachian tubes are inflamed, that air does not pass readily into the middle ear. Accordingly the tympanic membranes are forced inward by the pressure; and this may cause acute pain. Workers in compressed air are accustomed, while going "into the air," *i.e.*, into pressure, to hold their noses and blow at frequent intervals as a means for expanding the ear drums. Aviators even during very rapid descents are generally relieved by merely swallowing.

To sum up all that has been said thus far, the influence of low barometric pressure is not mechanical but chemical. Life is often compared to a flame; but there are marked differences, depending upon the peculiar affinity of the blood for oxygen. A man may breathe quite comfortably in an atmosphere in which a candle is extinguished. The candle will burn with only slightly diminished brightness at an altitude at which a man collapses. The candle is affected by the proportions of oxygen and nitrogen. The living organism depends solely upon the absolute amount of oxygen—its so-called partial pressure.

Unlike the flame, a man may become acclimatized to a change of atmosphere in the course of a few days or weeks. He is thus adjusted to the mean barometric pressure under which he lives. Every healthy person is so adjusted, New Yorkers to a mean barometric pressure of 760 mm. no less than the inhabitants of Denver or Cripple Creek to their altitudes. Even your tall buildings could probably be shown to exert a slight climatic effect upon the tenants of the upper stories. The study of the processes involved in such acclimatization affords us one of the most promising means of analyzing some of the fundamental problems of life. In fact, is not the gaseous interchange of protoplasm, the carbon and oxygen

metabolism of the cell, the central fact of life? Is not the mode of regulation of the interior environment of the body—the constants of the "humors"—the prime problem of the "vegetative" side of physiology?

Among the ill effects of lack of oxygen we may distinguish three more or less distinct conditions. They are comparable, in terms of more common disorders, to acute disease in contrast with chronic conditions of various degrees. Thus any one suddenly exposed to acute deprivation of oxygen, as is the balloonist or the aviator in very lofty ascents, shows one set of symptoms. If the exposure is less acute, as in the case of one taking up residence on a high mountain, the effects develop gradually; he passes through the stages of mountain sickness, a condition much like sea sickness, to a state of acclimatization and renewed health. If, however, the ascent or the flight is for only two or three hours, a period too short for any degree of acclimatization to develop, and this strain on the oxygen-needing organs is repeated daily, as is the case with the aviator of the upper air, the condition of "air staleness" is likely sooner or later to result. It is the effect of repeated slight oxygen deficiency on an individual who does not become acclimatized. It is, I believe, closely related to those effects of repeated overexertion and oxygen shortage which appear in the overtrained athlete.

The classic description of collapse from oxygen deficiency is that written by Tissandier,[2] the sole survivor of a fatal balloon ascent in 1875.

> I now come to the fateful moments when we were overcome by the terrible action of reduced pressure. At 7,000 meters (Bar. 320 mm.) we were all below in the car. . . . Torpor had seized me. My hands were cold and I wished to put on my fur gloves; but without my being aware of it, the action of taking

[2] Quoted from Paul Bert, *op. cit.*, p. 1061.

them from my pocket required an effort which I was unable to make. At this height I wrote, nevertheless, in my notebook almost mechanically, and reproduce literally the following words, though I have no very clear recollection of writing them. They are written very illegibly by a hand rendered very shaky by the cold: My hands are frozen. I am well. We are well. Haze on the horizon, with small rounded cirrus. We are raising. Crocé is panting. We breathe oxygen. Sivel shuts his eyes. Crocé also shuts his eyes. I empty aspirator. 1.20 P.M.,—11°, Bar. 320. Sivel is dozing. 1.25—11°, Bar. = 300. Sivel throws ballast. Sivel throws ballast. (The last words are scarcely legible.) . . . I had taken care to keep absolutely still, without suspecting that I had already perhaps lost the use of my limbs. At about 7,500 meters (Bar. 300 mm.) the condition of torpor which comes over one is extraordinary. Body and mind become feebler little by little, gradually and insensibly. There is no suffering. On the contrary one feels an inward joy. There is no thought of the dangerous position; one rises and is glad to be rising. The vertigo of high altitudes is not an empty word; but so far as I can judge from my own impressions this vertigo appears at the last moment, and immediately precedes extinction, sudden, unexpected and irresistible. . . . I soon felt myself so weak that I could not even turn my head to look at my companions. I wished to take hold of the oxygen tube, but found that I could not move my arms. My mind was still clear, however, and I watched the aneroid with my eyes fixed on the needle, which soon pointed to 290 mm. and then to 280. I wished to call out that we were now at 8,000 meters; but my tongue was paralyzed. All at once I shut my eyes and fell down powerless, and lost all further memory. It was about 1.30.

In this ascent the balloon continued to rise until a minimum pressure, registered automatically, of 263 mm. was reached. When Tissandier recovered consciousness Sivel and Crocé-Spinelli were dead. They were all provided with oxygen, ready to breath; but all were paralyzed before they could raise the tubes to their lips. Tissandier's notes are characteristic of the mental condition when oxygen-want is becoming dangerous.

In marked contrast to this condition is that of men who, gradually ascending into the mountains, day by day become acclimatized without realizing that any change has occurred. The record for the greatest altitude attained by mountaineers is held by the Duke of Abruzzi and his party in the Himalayas. They reached an altitude of 24,000 feet, where the atmospheric pressure is only two-fifths of that at sea level, or practically the same as that at which Tissandier's companions lost consciousness. At this tremendous altitude the Duke and his Swiss guides were not only free from discomfort, but were able to perform the exertion of cutting steps in ice and climbing. Dr. Filippi, the physician who accompanied them, in discussing this matter says that the fact of their immunity admits of but one interpretation:

> Rarefaction of the air under ordinary conditions of the high mountains to the limits reached by man at the present day (307 mm.) does not produce mountain sickness.[3]

In this statement, however, he is certainly mistaken, for the observations of others show conclusively that the sudden exposure of unacclimatized men to an altitude considerably less than that reached by this party would either produce collapse like that of Tissandier's companions, or if long continued would result in mountain sick-

[3] Quoted from Douglas, Haldane, Henderson and Schneider, *Physiological Observations on Pikes Peak, Phil. Trans.*, 1913, B. 203, p. 310.

ness. The latter effect especially is one which was the subject of careful study by an expedition of which I was a member, and which during the summer of 1911 spent five weeks at the summit of Pike's Peak, Colorado, altitude, 14,100 feet, Bar. 450 mm. We were there enabled to make observations upon hundreds of tourists who ascended the Peak, and who were acclimatized at most to the altitude of Colorado Springs or Manitou at the foot of the mountain. We saw a number of cases of collapse —fainting—from oxygen deficiency as shown by the striking cyanosis.

In the majority of cases, however, tourists who spent no more than the regulation half hour at the summit of the Peak, and then descended, experienced no acute ill effects. Headache and some degree of nausea were common even among these persons, however—often developing slowly for some hours after their descent. On the other hand, among persons who remained over night, and were thus exposed for several hours to deficiency of oxygen, the classic symptoms of mountain sickness occurred; and few escaped. Their second day at the summit was marked usually by extreme discomfort—headache, nausea, vomiting, dizziness and extraordinary instability of temper—symptoms which were strikingly exacerbated by even the smallest use of alcohol.

Our immediate party passed through these conditions and after two or three days, or in one case nearly a week, re-attained practically normal health. A definite functional readjustment had occurred. To illustrate and emphasize the nature of this readjustment I will quote a recent experiment[4] of my friend the leader of the Pike's Peak expedition, Dr. J. S. Haldrane.

He has equipped his laboratory at Oxford with a small lead-lined chamber in which a man can be hermetically closed. The carbonic acid which he exhales is continually absorbed by alkali, so that no accumulation occurs, while

[4] Personal communication.

the oxygen is progressively decreased by the breathing of the man himself. Dr. Haldane found that after a day or two in this chamber he had reduced the oxygen to an extent comparable to Pike's Peak. At the same time there had evidently occurred in himself a gradual process of adjustment, for he felt quite well. At this stage he invited another person to come into the chamber with him, and he had the satisfaction of observing the immediate development of blueness and the other symptoms of oxygen collapse in his companion.

Evidently acclimatization is a very real phenomenon and of the utmost importance to any one exposed to a lowered tension of oxygen.

As we observed it in ourselves during our stay on Pike's Peak acclimatization consists in three chief alterations: (1) increased number of red corpuscles in the blood; (2) some change in the lungs or blood (Haldane considers it the secretion of oxygen inward by the pulmonary tissue) which aids the absorption of oxygen, and (3) a lowering of the $CO_2$ in the alveolar air of the lungs. This lowering of the $CO_2$ in the lungs is bound up with increased volume of breathing. It is the concomitant of a decreased alkaline reserve in the blood just as in nephritis and diabetes. Acclimatization in this respect consists therefore in the development of a condition which would nowadays be called acidosis.

All of these changes are of a quantitative character. Miss FitzGerald [5] has supplemented the results obtained on Pike's Peak by an extensive series of careful observations on the inhabitants of towns of closely graded altitude from sea level up to that of the highest inhabited place in our western country. She has thus shown that the mean hemoglobin and the mean alveolar $CO_2$ of the inhabitants of any town are functions of the mean barometric pressure of the place.

[5] FitzGerald, M. P., *Phil. Trans.*, 1913, B. 203, p. 351, and *Proc. Royal Soc.*, 1914, B. 88, 248.

I shall not discuss pulmonary oxygen secretion now, because the problem is still extremely obscure; nor the increased production of red blood corpuscles, which is a slow process requiring weeks for completion, and playing no considerable part in the matter particularly before us.

We will fix our attention upon the fact that both the alveolar $CO_2$ of the pulmonary air and the alkaline reserve of the blood are reduced in accurate adjustment to any altitude, or oxygen tension, to which a man is subjected for a few days or even a few hours. This functional readjustment is, I believe, of great significance in relation to aviation, since it involves a larger volume of breathing per unit mass $CO_2$ eliminated: it thus compensates in part for the rarefaction of the air.

But how is it brought about? And why are the changes of breathing gradual, when the changes of altitude and oxygen tension are abrupt? The answer lies in part at least in the mode of development, and the nature of that acidosis of altitude to which I have referred. It is scarcely necessary to remind you that, as L. J. Henderson has shown, the balance of acids and bases in the blood, its $C_H$, depends upon the maintenance of a certain ratio between the dissolved carbonic acid, $H_2CO_3$ and sodium bicarbonate, $NaHCO_3$, or as Van Slyke terms it, the alkaline reserve. On the basis of this conception the prevalent view of acidosis is that, when acids other than carbonic are produced in the body, the bicarbonate is in part neutralized. The alkaline reserve is thus lowered, and the carbonic acid of the blood being now in relative excess, an increased volume of breathing is caused as an effort at compensation.

Recent investigations[6] by Dr. H. W. Haggard and myself show that an exactly opposite process is likewise possible. We find that whenever respiration is excited to

[6] Henderson and Haggard, *Jour. Biol. Chem.*, 1918, pp. 333 345, 355, 365.

more than ordinary activity, and the carbonic acid of the blood is thus reduced below the normal amount, a compensatory fall of the alkaline reserve occurs. The body is evidently endowed with the ability to keep the ratio of $H_2CO_3$ to $NaHCO_3$ normal, not only by eliminating $CO_2$ when the alkali is neutralized, but also by the passage of sodium out of the blood into the tissue fluid (or by some equivalent process) to reduce the alkaline reserve. A loss of $CO_2$ during over-active breathing is thus balanced. If it were not balanced a state of alkalosis would occur, which would inhibit and induce a fatal apnoea.

It is really in this way I believe that some of those conditions arise which nowadays are called "acidosis." If so they are not truly acidosis, or rather the process producing them is not acidosis, although the resultant condition gives some of the most characteristic tests of this condition. It is on the contrary a state, or rather a process, which Mosso was the first to recognize, although obscurely, and which he termed "acapnia" an excessive elimination of $CO_2$. Recent papers [7] from my laboratory have shown that a sudden and acute acapnia induces profound functional disturbances, including circulatory failure.

It is one of the well-known facts in physiology that deficiency of oxygen, or anoxemia, causes an "acidosis." Recent and as yet unpublished work of Dr. Haggard and myself indicates that the process involved is almost diametrically the opposite of that which has heretofore been supposed to occur, and that the result is not a true acidosis. Under low oxygen, instead of the blood becoming at first more acid with a compensatory blowing off of $CO_2$, what actually occurs is that, as the first step, the anoxemia induces excessive breathing. This lowers the $CO_2$ of the blood, rendering it abnormally alkaline; and

[7] Henderson and Harvey, *Amer. Jour. Physiol.*, 1918, 46, p. 533, and Henderson, Prince and Haggard, *Jour. Pharmac. Exper. Therap.*, 1918, 11, p. 189.

alkali passes out of the blood to compensate what would otherwise be a condition of alkalosis.

We regard the current explanation, based on the production of lactic acid, as needing reversal.

The application of this idea to the changes of breathing and of the blood alkali in acclimatization clears up some of the points which heretofore have been obscure. Thus on Pike's Peak we saw that persons whose breathing under the stimulant of oxygen deficiency increased quickly to the amount normal for the altitude suffered correspondingly little, while those whose respiratory center was relatively insensitive to this influence suffered severely. The one type readily developed the acapnia and in consequence the pseudo-acidosis which the altitude requires. The other did not.

Here let me pause a moment to bring these conceptions into some degree of harmony with fundamental doctrines regarding respiration. For more than a century, in fact ever since the days of Lavoisier, the argument has been active whether our breathing is controlled by oxygen need or by the output of $CO_2$. For the past thirty years, and especially during the last ten or twelve, the theory of regulation by $CO_2$, or in its later form by C, has held the field. Indeed it is established now—almost beyond the possibility of contradiction, it would seem—that during any brief period of time, and under conditions to which the individual is accustomed, the amount of $CO_2$ produced in the tissues of the body, through its influence on the $C_H$ of the blood, is the factor controlling the volume of air breathed. Its effects are immediate.

But when we view the matter more broadly it is clear that this is by no means the whole story. The oxygen tension of the air is the influence which determines just how sensitive the respiratory center is to excitement by $CO_2$. But the effects of any change of oxygen tension are slow in developing, requiring in some persons, as we saw on Pike's Peak, hours to begin and several days to

become complete. In fact there are many perfectly healthy persons who, if caused to breathe progressively lowered tensions of oxygen down to 6 or 7 per cent. in the course of half an hour, feel nothing. Their breathing shows no considerable augmentation. They simply lose consciousness, and if left alone they would die, without any apparent effort on the part of respiration to compensate for the deficiency of oxygen. In such persons the stimulant of oxygen deficiency exerts only a slowly developing influence upon the sensitiveness of the respiratory center to the stimulus of $CO_2$. They can become acclimatized to great altitude only at the cost of prolonged mountain sickness. Evidently they are not suited to be aviators.

In very sensitive subjects, on the contrary, the period of readjustment is much shorter. It is a matter not of days but of hours, and the functional alterations begin to develop almost immediately even under slight oxygen deficiency. The upper air is for those men whose organization readily responds with vigorous compensatory reaction.

With this inadequate sketch of present scientific knowledge regarding life at great altitudes as a background, we may turn to the application of this knowledge to the problems of human engineering in the aviation service of our army during the war. In September, 1917, I was appointed chairman of the Medical Research Board of the Air Service and was asked to lay out a plan for the development of a method of testing the ability of aviators to withstand altitude.

You will readily guess the line along which one would attack such a problem. It consisted in the development of an apparatus from which the man under test breathes air of a progressively falling tension of oxygen. The particular form which we use is called a rebreathing apparatus. It consists of a steel tank holding about 100 liters of air, connected with a small spirometer to record

the breathing, and a cartridge containing alkali to absorb the $CO_2$ which the subject exhales. Breathing the air in this apparatus through a mouthpiece and rubber tubing the subject consumes the oxygen which it contains, and thus produced for himself the progressively lower and lower tensions of oxygen which are the physiological equivalent of altitude. To control and test the accuracy of the results with the rebreathing apparatus we installed in our laboratory at Mineola a steel chamber, in which six or eight men together can sit comfortably, and from which the air can be exhausted by a power driven pump down to any desired barometric pressure.

Such apparatus was, however, only the beginning. The practical problem was to determine the functional changes —pulse rate, arterial pressure, heart sounds, muscular coördination and psychic condition occurring in the good, the average and the poor candidates for the air service, and then to systematize and introduce these standards on a very large scale at the flying fields in this country and in France.

That this program was successfully carried through, and was approaching completion when the armistice was signed, was due chiefly on the scientific side to the brilliant work of my colleagues Majors E. C. Schneider, J. L. Whitney, Knight Dunlap and Captain H. F. Pierce, and on the administrative side to the splendid coöperation of Colonel W. H. Wilmer and Lieutenant-Colonel E. G. Seibert.

We have recently published a group of papers,[8] brief but fairly comprehensive in their technical details, and I shall not now repeat what has there been said, but shall confine myself to a few salient points. One of these is a final and striking demonstration of our main thesis. Schneider and Whitney went into the steel chamber and

[8] Y. Henderson, E. G. Seibert, E. C. Schneider, J. L. Whitney, K. Dunlap, W. H. Wilmer, C. Berens, E. R. Lewis and S. Paton, *Journal American Medical Association*, 1918, Vol. 71, pp. 1382-1400.

the air was pumped out of it until the barometer stood at only 180 mm., 23 per cent. of the pressure outside: the equivalent of an altitude of 35,000 feet. Throughout the test they were supplied with oxygen from a cylinder through tubes and mouth-pieces. They experienced no discomfort except from flatus: the gases of the stomach and intestine of course expanded nearly five-fold.

In comparison with this observation is to be placed the recent record ascent by Captain Lang and Lieutenant Blowes in England to a height of 30,500 feet. They were supplied with oxygen apparatus; but a defect developed in the tube supplying Lieutenant Blowes and he lost consciousness. Captain Lang seems to have suffered only from cold.

From this it might appear that the simplest way to solve the problem of lofty ascents would be by means of oxygen apparatus. The Germans evidently made use of such apparatus, for it was found in the wreck of one of the German planes shot down over London. The British also had such apparatus, but it was difficult to manufacture, wasteful in operation, and in other respects left much to be desired. In fact the devising of such apparatus and its adaptation to the peculiar requirements of the human wearer are a problem which can be solved only by the close coöperation of a physiologist and a mechanical engineer. Mr. W. E. Gibbs, of the Bureau of Mines, with whom I had coöperated in developing mine rescue oxygen apparatus, took up this problem and produced a device which should prove valuable. Unfortunately the common tendency to favor ideas and apparatus coming to us from Europe operated against the adoption of the better American device.

It is doubtful, however, whether any apparatus of this sort will ever quite take the place of physical vigor and capacity to resist oxygen deficiency on the part of the aviator himself. Imagine him, when fighting for his life above the clouds, handicapped by goggles over his eyes,

wireless telephone receivers on his ears, a combined telephone transmitter and oxygen inhaler over his mouth, and a padded helmet on his head!

The importance of determining the aviator's inherent power of resistance to oxygen deficiency, if he is to be even for a few moments without an oxygen inhaler, is demonstrated by the results of the routine examinations made with the rebreathing apparatus in the laboratory. These results show that 15 to 20 per cent. of all the men who pass an ordinary medical examination are unfit to ascend to the altitudes now required of every military aviator. On the other hand these tests pick out a small group of 5 to 10 per cent., who, without apparent immediate physical deterioration, withstand oxygen deficiency corresponding to altitudes of 20,000 feet or more.

It is particularly interesting to note that when the rebreathing test is pushed beyond the limit that the man can endure, be it the equivalent of only 10,000 or 25,000, two different physiological types with all gradations between them are revealed. The fainting type collapses from circulatory failure and requires an hour or two to recover. Often the heart appears distinctly dilated. The other and better type, on the contrary, goes to the equivalent of a tremendous altitude on the rebreathing apparatus and loses consciousness, becoming glassy-eyed and more or less rigid, but without fainting. When normal air is administered such men quickly recover.

Perhaps I ought to say at least a few words regarding the other aspects of the work at Mineola: for example the valuable psychological investigations and the controversy over the rotation tests, which have figured so largely in our medical journals of late. It seemed best, however, to confine myself this evening to my own special field. Nevertheless I cannot suppress a public expression here of my sympathy for the brave and able scientific men in the psychological group at Mineola, who insisted on investigating the validity of the rotation tests. I am sure

that you will feel as I do, when I tell you that they were threatened with punishment for insubordination when they refused to recognize that a regulation of the army, which prescribes the duration of nystagmus after the rotation test, necessarily makes this a physiological fact.

I would gladly devote a few minutes also to pointing out some of the lessons to be drawn from the rather unusually good opportunities which fell to my lot to observe the mingling of science and militarism. The chief lesson can be put in a single phrase: They do not mix. The War Gas Investigations, which formed the nucleus on which the Chemical Warfare Service finally developed, and the Medical Aviation Investigations, of which I have spoken this evening, were both successful largely because at first they were developed under civilian control, under that splendid scientific arm of the government, the Bureau of Mines and its able director. It is a wise provision of our government by which the Secretary and Assistant Secretaries of War are always civilians. It would also be wise for the general staff in any future war to keep scientific men on a scientific status instead of practically forcing them into uniform.

We all hope that we are done with war, and with soldiers—at least for a generation. We can, however, derive certain broad lessons applicable to the conditions of peace from the experiences and intense activities of war, when almost unlimited funds were obtainable for research and the experiences ordinarily scattered over years were crowded into a few months. One of these lessons is that scientific men need to develop the capacity to become the heads of large enterprises without ceasing to be scientific, without degenerating, as is too often the case, into the super-clerk, who seems to be the American ideal of the high executive official. It is not enough for the scientific man to become the expert adviser to the unscientific administrator. If the latter has the responsibility he will use his power as he, and not as the scientific man, sees

fit. To this rule I have known only one splendid exception.

For the most part among us the great prizes go to the man who works up through clerical rather than through expert lines. We must find some way to change this. The path of science must lead to the top, and at the top must still be science. To achieve this ideal, the scientist must show generosity toward colleagues and subordinates, an enthusiastic recognition of their merit and an abnegation of self-aggrandizement, no less than skill in plan and energy in execution. It is essential also that he should develop methods for conserving time and strength by assigning clerical work to clerks instead of becoming a clerk himself, in order that he may keep mind and desk clear for the really important things.

The Chemical Warfare Service was a success largely because the chief of the Research Division followed these principles as the spontaneous promptings of science and patriotism.[9] Medical research in aviation was productive just so long as it pursued a similar course.

He who charts this course, so that others may follow it through the pathless seas of the future, will make a great contribution to science, education, government, and indeed to nearly every phase of trained activity in America.

[9] *Cf.* G. A. Burrell, *Journal of Industrial and Engineering Chemistry,* 1918, Vol. II., p. 93.

# TWENTY-FIVE YEARS OF BACTERIOLOGY: A FRAGMENT OF MEDICAL RESEARCH

(Address of the President of the American Association for the Advancement of Science, Chicago, 1920)

BY

SIMON FLEXNER

*Rockefeller Institute*

## IMMUNITY

JUST a quarter of a century ago, that is in 1895, the announcement was made at the 67th meeting of the German Society of Naturalists and Physicians that diphtheria, one of the most severe and fatal diseases of mankind, had been conquered by means of an antitoxin. This great event is a landmark, not alone in the history of medicine, but also in the history of the world, and it provides a high peak of achievement from which the growth of bacteriology may be viewed. In order that we may follow the growth with understanding, it is necessary, at first, to cast a glance backward before we begin on the narrative, the aim of which is to bring us to the state of knowledge of bacteriology existing in our own day.

Since disease is so universal a phenomenon and communicability from individual to individual so obvious an incident of its epidemic prevalence, the conception of a

*contagium vivim* or *animatum* and hence of an invisible form of life as the initiator of the condition, can be traced far back in the written records of human events. And yet it was not until about 1850 that a microscopic body, which we would now call a bacterium, was actually detected in the blood of a sick animal. The anthrax bacillus, as it has since been named, which is now recognized as the inciting microbe of splenic fever, was destined to play a leading part in the development of the future science of bacteriology, but at this early period its full meaning was not perceived. When, however, in 1863 Davaine succeeded in communicating splenic fever to a healthy animal by the direct inoculation of blood containing the anthrax bacillus, the science of bacteriology may be said to have been born.

The dates are significant to one who wishes to follow the march of events which brought the greatest master of all, Pasteur, into the field of microbiology and led him on to the study of the infectious diseases, first of animals and then of man. For on looking backward we find that coincidental with Davaine's epochal experiments, Pasteur was already engaged on those studies of fermentation and putrefaction which were not only to set our conception of those processes on a secure biological foundation, but as an important side effect were to demolish, once and forever, the elaborately constructed but insecurely based doctrine of the spontaneous generation of microscopic forms of life.

For Pasteur it was but a step, although for us one of the highest importance, from the studies in fermentation and putrefaction to those on the infectious diseases in which, indeed, the great triumphs he achieved consist far less in the detection of new kinds of microbes to which the various contagious diseases might be described, than in his fundamental discoveries in immunology, or the science of the specific prevention of disease.

This work in the field of immunology, first opened to

experimental investigation by him, is the aspect of Pasteur's labors to which I wish especially to direct your attention, since it forms the connecting bond between the earliest and thus the oldest, and the present and thus the latest discoveries in a field in which medical science has come to secure some of its most notable successes. There can be no doubt that the discovery in 1880 of the artificial immunity to fowl cholera came not as a direct incident, but rather as an accidental circumstance to the experiments being pursued. In after years Pasteur loved to point out the importance of the "prepared mind" as a requisite of the investigator, in order that he may seize hold of and utilize in respect to a question propounded by experiment what, viewed superficially, appears to be only an indirect and misleading answer. The advances leading rapidly from the artificially induced immunity in fowl cholera to the dramatic and historically and economically important immunity in anthrax and to the humanly important immunity in rabies, involved no strictly new conceptions on Pasteur's part. They consisted merely of the carrying forward of the ideas, often ingeniously modified, derived from the study of the sources of the condition of immunity in fowl cholera.

But should we inquire to what order of events already known this phenomenon of artificial immunity belongs, we should say at once probably to the order having to do with the Jennerian vaccination against smallpox. As every one knows, vaccination against smallpox consists in the utilization of human smallpox material which has become modified by passing through the cow, in which it sets up the condition named cowpox. When this modified microbic virus of the disease is returned to man, a mild form of smallpox is induced, which suffices through a term of years to protect the individual vaccinated, so-called, from infection with the more active or virulent smallpox virus.

The significance of the new observations was grasped

by Pasteur and related to Jennerian vaccination. His great discovery then consisted in the determination that pathogenic or disease-producing microbes may be modified otherwise than by passing through foreign and relatively insusceptible animal species, and that such simple agencies as long cultivation *in vitro* (fowl cholera), high temperatures and therefore non-optimal conditions of growth (anthrax), and partial drying of the animal material carrying the microbe (rabies), would suffice so to modify and attenuate the respective microbes that upon inoculation they set up not the severe, but only mild states of infection, from which not only does recovery ensue, but the restored animal is enduringly protected from the ordinary and often fatal attacks of a disease.

Looking backward from our present higher position of vantage, we may discern certain minor imperfections in this fundamental work on artificial immunity. For example, it would now appear that the so-called attenuated cultures of the bacillus of fowl cholera, used for purposes of immunization, were not so much attenuated as actually dead, and that the material inoculated consisted of a mixture of dead bacilli and their metabolic and disintegrative products. In other words, it seems that Pasteur without perceiving it had discovered not only a principle of wide applicability in inducing artificial immunity, but a general method of utilizing dead bacteria as vaccines, and one which in more recent times has been widely resorted to in preventing outbreaks of typhoid fever, cholera, and some other diseases.

In 1882 antirabic inoculation was perfected. Pasteur had, of course, reflected deeply on the sources of the immune state and in explanation of it he inclined to the view that the basis of the phenomenon was a nutritive condition. He conceived that in the course of that form of microbic development within the body which came to a spontaneous end and left the individual protected, certain essential foodstuffs were consumed, in virtue of which

the same variety of microbe could not later gain another foothold. Time has not upheld this simple conception; but when it was formulated the subject matter of bacteriology was still too fragmentary and scanty to point to the deeper underlying chemical and biological processes involved. Indeed, nearly ten years elapsed until Behring's discovery of antitoxic immunity brought about a revolution in the prevailing ideas and opened up new and fascinating vistas of research.

We have now reached the period at which the German school of bacteriology, led by Robert Koch, has arisen beside the French. Koch's career in science was meteoric. From an inconspicuous country practitioner he became, in the period beginning about 1880, the outstanding world figure in bacteriology. But his greatest work was completed in relatively few years, although that of his pupils has continued up to and is still potent at the present day. It is informing to reflect that just as Davaine made the first signal advance in the experimental inoculation of disease with the anthrax bacillus, and Pasteur the first dramatic demonstration of the practicability of protective inoculation with bacterial cultures also with that bacillus, Koch rose into fame through the study of its life history by direct observation under the microscope. But Koch's greater contribution to bacteriology consisted of a method of cultivation so perfected that pure growths of bacterial species were readily obtainable. The consequence was that in a very brief period of years a whole host of pathogenic bacteria or incitants of diseases of man and animals was secured, among which were the highly important bacilli of tuberculosis, cholera, typhoid fever, diphtheria, tetanus, dysentery, plague, meningitis and many others.

Up to the period we are now considering, all the diseases of microbic origin thus far investigated successfully belonged to the class in which the bacteria invaded the blood and the internal organs. But now we are about to learn of another kind of disease induced by a class of

bacteria which are peculiar in that they do not migrate throughout the body but remain fixed in a special tissue or part, where they multiply and secrete a poison which finds its way first into the lymph, then into the blood and the organs generally. This latter class of microbes produces its effects to which we give the name of disease, and of which diphtheria and tetanus are examples, through the operation of a poison, peculiar to each, and in each instance attacking by preference certain definite organs or parts of them. Thus the poison elaborated by the diphtheria bacillus selects especially the lymphatic organs, heart and nervous system for its action, and the tetanic poison the nerve cells governing muscular contraction.

We have now returned by a route somewhat circuitous perhaps to the point from which we started, namely diphtheria and its antidote. But in the course of the journey we have taken, new points of view have been gained which, as will appear, are to transform entirely the outlook upon the problems that bacteriologists set themselves to solve.

Behring and Kitasato chose the task of inducing in animals immunity, to diphtheria on the one hand and to tetanus on the other. This was a logical undertaking and one clearly in the spirit of the times. Both men had a strong interest in the quest. The one (Behring) was deeply engaged in the investigation of the chemical disinfectants and conceived ideas of modifying bacterial growth through these agents, as Pasteur had succeeded in accomplishing with physical means. The other (Kitasato) had succeeded where his predecessor and the discoverer of the tetanus bacillus, Nicolaier, had failed in obtaining pure cultures of that microbe. Moreover, the restricted local development of the two bacilli and their generally poisonous or toxic effects aroused in them an eager interest intensified by the epochal discovery just made by Roux and Yersin that the toxin of the diphtheria bacillus was readily separable from the bacilli producing it and could be

obtained by precipitation in, it is true, an impure state but one in which its poisonous action was preserved. Indeed, so appalling did its poisonous effect prove to be that these investigators could not imagine any other non-living substance than an enzyme which could exhibit such active properties.

The isolation of the diphtheria toxin, quickly to be followed by the similar isolation of the tetanus toxin, was an event of capital importance and reacted at once vigorously on the chemical aspects of bacteriology just struggling into the light. The immediate effect of the study of the new poisons, called toxalbumins, was to discredit a whole series of pure, crystalline basic substances obtained not long before from a wide variety of bacteria, to which the name of ptomaines had been given. Many of the ptomaines were possessed of poisonous properties; but what was disconcerting was that very diverse bacteria might yield identical chemical compounds which, therefore, lacked the property of specificity, an essential quality of bacterial activity. The toxalbumins, on the other hand, which even to this day have not been secured in a chemically pure state, exhibit in perfect degree the property of specificity and display all the power for evil and all the potential possibilities for good which their original and respective bacilli possess; and although no method of chemical identification of their special nature is available, yet their pathological effects and immunological activities serve readily and accurately to distinguish one from the other and to indicate their origin.

The rendering of animals immune to diphtheria, on the one hand and to tetanus on the other, proved a difficult but not impossible task. The method adopted was to admix disinfectant chemicals, of which the one finally selected was iodin trichlorid, with the bacilli to be injected under the skin of animals, or with the contents of the culture flasks at the end of the incubation period. Obviously, the intent was to moderate the poisonous action

of the inoculated material, in the hope that a mild and not fatal infection would be induced from which recovery would follow leaving the treated animal immune.

The experiments were sometimes successful, and as such seem merely to illustrate a variation of the Pasteurian method of inducing immunity which, as we saw, was not distinct in principle from the Jennerian vaccination. But the break with the past was none the less imminent, for Behring's next act was not to speculate on the theory of immunity but to perform a decisive experiment. It is to be kept in mind that in the poisons or toxalbumins of diphtheria and tetanus, we possess the essentially active ingredients of the respective bacilli and that the body attacked does not succumb to the invading bacilli but to the action of the toxins. Hence, Behring turned to the blood of the immune animals and tested it for neutralizing power against the poisons, and discovered antitoxin; he injected the blood of an immune into the body of a normal animal prior to inoculation and discovered passive immunization; and finally, he injected the blood of an immune animal into animals previously inoculated with the bacilli of diphtheria and tetanus, and discovered serum therapy. The day for speculation on what constituted the immune state had now definitely passed, and the time had arrived for subjecting the phenomenon to experimental study.

The fluids or "humors" of the body, to employ a term made respectable by age, as represented by the serum of the blood, had been shown to carry the immunity principles, but what part did the cells of the body play in the process? Both fluids and cells were now submitted to rigid and ingenious scrutiny, and about them an immense literature has grown up. Soon the students in the field divided into two camps, namely, one led by Ehrlich, defending the humoral doctrine, the other led by Metchnikoff, urging the cellular or phagocytic doctrine. The conflicts which raged about these concepts were always animated and sometimes even bitter; but the ultimate effect

was to extend rather than to retard and confound knowledge. We are moving now in more peaceful times, the heat of the earlier conflicts having largely subsided, and it may be stated that neither the one nor the other doctrine finally triumphed, but that the humors or fluids of the body on the one hand and the cells on the other have come to be recognized as the active participating factors in the immunity process, the one complementing the other. Where the phenomenon is one purely of the neutralization of a poison or toxin, the fluid portion of the blood suffices; where also the process is relatively the simple one of acting on and dissolving a bacterial cell, there also the fluid may suffice, although an essential element in the process may have been supplied by the white blood cells at the moment of their withdrawal from the body. But where the bacteria are not readily disintegrated and dissolved, there the phagocytes of the blood and tissues come into play and, through their power of engulfing these particles, operate as one of the body's main defenses against infection.

The unraveling of the intricacies of the immune state, following upon the work of Behring, has brought about a sudden and unprecedented enlargement of the scope of bacteriology, as well as supplied a wealth of new facts of which many have permanently enriched practical medicine and opened new territory to profitable exploration. It may suffice at this point merely to mention certain of the devices for diagnosis and means of preventing or of treating disease, which are the immediate heritage of studies in the field of immunity, of which many have come not as direct fruits, but as invaluable by-products of the search. In this manner have been secured the Widal test for typhoid fever, the Wassermann and allied reactions, the hypersensitive or Schick test for diphtheria susceptibility, the hypersensitive reaction as now applied to the detecting of the offending agency in hay fever and allied states, the refinements of bacterial vaccination in

the prevention and sometimes in the treatment of disease, and so-called specific serum therapy. Moreover, these studies have placed in the hands of the bacteriologist a powerful instrument for detecting, through immunity reactions carried out in test tubes, or the animal body, new varieties of pathogenic or disease-producing bacteria and of investigating more closely and sorting out groups of pathogenic microbes not hitherto subject to analysis. Finally, the immunity reactions, as they are generically named, have been found not to be restricted to bacterial cells and poisons, but to apply to a wide variety of cells and their products. For it should be recalled that in the decade immediately succeeding the discovery of antitoxin, agglutinins, precipitins, bacteriolysins, cytotoxins, hemolysins, complements, chemotaxis, anaphylaxis, and the minutiae of phagocytosis were discovered and became the objects of animated and often feverish and sometimes controversial but always profitable investigation.

It happened also and quite naturally and logically that this should be the heyday of hypotheses concerning the biological basis of immunity and the manner in which interaction takes place between toxin and antitoxin inside as well as outside the body, and of the englobing of bacteria and other bodies by the blood and tissue cells, as well as the nature of the combinations and permutations and reactions between the more complex bacteria and cells in course of their immunological transformations. And thus there came to be elaborated the side-chain hypothesis of Ehrlich, which vied with the phagocytic theory of Metchnikoff as well as with the adsorption theory of Bordet and the physico-chemical theory of Arrhenius. And if in our busy lives of to-day we think less of receptors and amboceptors, of complements and complementoids, haptophores, and toxophores, and limit ourselves somewhat more closely, perhaps even a little too exclusively, to the observed fact itself, yet it is well that we do not forget how great at the time was the stimulus to

research and how rich the booty which accrued from those labors tinged with the radiance of the real scientific imagination of an Ehrlich, a Metchnikoff, and a Bordet.

Not all the high expectations of practical benefit to follow from these discoveries have been realized, but sometimes the very failures have been turned to account in opening up new, or illuminating old, avenues of progress. In this connection it is instructive to recall the early pronouncement of Behring made two years after the discovery of antitoxin, and while he was under the influence doubtless of that great contribution:

"The present state of the immunity question," he says, "may be defined as follows: Thus far no generally applicable explanation for natural immunity has been forthcoming. But of the artificially produced immunity it may be said that the precise study of a number of examples has so far advanced our knowledge that we may assert with confidence that the immune state arises from a peculiarity of the blood and, indeed, of its cell-free portion; in no instance in which a sufficiently high grade of immunity has been attained in an animal species, easily susceptible to the infection in question, has the blood withdrawn from the body failed to show evidences of the presence of the immunity-conferring substances."

In this statement will be perceived the extreme humoral view of the origin of immunity, which subsequent investigators failed to uphold. But he continues in a prophetic vein, unfortunately likewise destined not to be wholly fulfilled.

"With the achieving of this standpoint the next step in the winning of specific curative agents for the infectious diseases is clearly outlined: all that is required is the induction in a susceptible animal species of a high degree of artificial immunity, and then to test the blood for the presence of protective and healing substances."

Time has exposed the fallacy of this over-confident

attitude and taught the distinction between the two varieties of infectious disease and their corresponding immune states, according as their main effects and symptoms arise from the toxalbumins or poisons we have been considering, or the intimate presence within the organs of the microbes themselves. The former variety chances indeed to be in the minority, and hence it has come about that the diseases to be successfully combated by antitoxins are few in number, while those in which the microbes penetrate deeply into the body and which poison its tissues by means of so-called endotoxin, are far more numerous. The latter class includes such important diseases as tuberculosis, typhoid fever, meningitis, plague, cholera, the septicemias, and still others. And yet the failures have been only partial, and success has been and is still being won against odds which were once considered insuperable.

What is striking is the capriciousness with which the microbes themselves or their endotoxins lend themselves to the making of therapeutically effective serums, as contrasted with the ease and certainty of action in this respect of the toxalbumins. All the latter seem capable of yielding abundant antitoxins, and this independently of their precise source, since it happens that toxalbumins resembling those of bacterial origin exist also in the higher plants—as in the castor and jequirity beans—and in the venoms of reptiles and insects. On the other hand, it has not thus far been found practicable to fashion curative serums for tuberculosis, typhoid fever, plague, cholera, etc., while success has been achieved in the instance of epidemic meningitis, and very hopeful results have recently been attained in the case of pneumonia.

In meningitis the success is linked with the recognition of a second principle of action, namely the advantage to be derived from what may be called the local specific treatment of a disease, or the bringing of the healing serum into direct and intimate relation with the seat of

the infection itself. Since in epidemic meningitis it is the membranes surrounding the brain and spinal cord and those more delicate ones lining the cavities of the ventricles of the brain which are the seat of infection, it has been found easily possible, through a simple and safe procedure, to inject the serum into the cavity of the spinal meninges, whence it is quickly distributed over all the membranes of the brain and cord. It may be of interest to remark that it is not practicable to reach the inflamed membranes with the serum by way of the blood, since nature, in order to protect the sensitive nerve tissues from injury by any chance deleterious substance in this fluid, has interposed an impenetrable barrier, the choroid plexus, between the circulation and the cerebrospinal fluid which bathes and sustains the nervous organs, and which is itself elaborated from the blood by this plexus with an accuracy of selectiveness highly remarkable.

In pneumonia again a beginning success has been achieved through a finer discrimination of specific kinds among the pneumococci, the inciting microbes of the disease. This distinction is independent of ordinary physiological and cultural characters displayed by the bacteria, which do not serve to bring out the underlying specific properties of each, and has been accomplished by means of the so-called immunity tests carried out in test tubes or in the animal body. The gain to practical medicine from the detection of the fundamental differences subsisting between the three main types of pneumococci existing in this country has been very great. Already a curative serum for one of the specific types of pneumonia has been secured, and through its application many lives have been saved; while beginnings have been made in respect to vaccination against the disease when, as sometimes happens in institutions and in communities, epidemics prevail and claim many victims, as occurred in the Army training camps during the measles epidemic of 1917-18.

Thus we have learned that the immunity reactions, or the effects on bacteria and their poisons, of the fluid and cells of the body as modified by the process of artificial immunization, provide more delicate and precise means of discriminating bacterial species than the qualities of form, growth appearances and physiological activities, and more accurate methods of distinguishing poisons than the most refined chemical analyses; and we shall learn a little later in connection with the distinct but related hypersensitive or anaphylactic state, that the prepared and sensitized animal body responds to infinitesimal amounts of protein matter according to its specific origin, in a manner not otherwise determinable and far beyond the most delicate laboratory test which the chemist has invented. The animal body thus artificially prepared, or as sometimes happens naturally sensitive, acquires an appreciation of the inner constitution of the protein molecule, classifying it, as it were, not only according to its ordinary chemical nature, but according to its species origin.

The immunity reactions we have considered are not artificial creations, since as we now know, they are the very processes which nature employs in her unaided efforts to abate infections, and when need be, to adopt the body to foreign proteins. The spontaneous recovery from infectious disease, by which is meant merely that the body by its own power overcomes the microbes and their poisons, depends upon the setting into motion of the series of operations through which immunity responses in fluids and cells are insured, precisely as has been described in the event of an artificial immunization. Hence in our efforts at serum therapy we aim merely to aid "nature," by introducing, as it were, into the beset body the finished immunity products artificially produced in healthy animals; and in protection by vaccination, success is assured only to the extent to which the healthy body has been compelled to prepare the specific immunity substances and to hold them ready at hand to combat the entrance through

its outer gateway of, for instance, such microbes as those inciting typhoid fever and smallpox.

That it is through the prowess of the body itself, and not the skill and art of the physician, that recovery from infectious disease takes place, had already become evident to the ablest physicians of nearly one hundred years ago. It is true that they could form no real conception of the manner in which the cure was brought about, but in admitting the existence of a class of maladies which Jacob Bigelow in 1835 called the "self-limiting diseases" [1] this innate faculty of the organism to overcome infection was recognized. It may be of even more than historical interest to reprint here the pregnant paragraph in which Bigelow expresses this view:

> This deficiency of the healing art (he is now writing of the advances in knowledge of the structure and functions of the human body in contrast to the lagging behind of the science of therapeutics, or the branch of knowledge by the application of which physicians are expected to remove diseases) is not justly attributable to any want of sagacity or diligence on the part of the medical profession. It belongs rather to the inherent difficulties of the case and is, after abating the effect of errors and accidents, to be ascribed to the apparent fact that certain morbid processes in the human body have a definite and necessary career, from which they are not to be diverted by any known agents, with which it is in our power to oppose them. To these morbid affections, the duration of which, and frequently the event also, are beyond the control of our present remedial means, I have, on the present occasion, applied the name of the *self-limited diseases;* and it will be the object of this discourse to endeavor to show the ex-

[1] Jacob Bigelow, *Discourse on Self-limited Diseases,* Boston, 1835.

istence of such a class, and to inquire how far certain individual diseases may be considered as belonging to it.

### ANAPHYLAXIS

Allusion has several times been made to the hypersensitive state which is often regarded as the opposite of the immune condition. Because the latter is conceived as protective and hence is spoken of as being prophylactic, the former in turn has been named anaphylactic. The obvious distinction between the two conditions is simply defined by the statement that while the immunized animal shows a greater degree of resistance to a second inoculation of the materials used for immunization, the anaphylactized animal on the contrary shows a heightened susceptibility.

The history of anaphylaxis illustrates the manner in which the rapidly growing knowledge of immunity reacted on the appreciation of this condition. It now appears that the physiologist Magendi, who flourished in the first quarter of the nineteenth century, first noted that an animal which had borne without apparent effect one injection of a quite harmless protein such as egg white, reacted severely to a second injection of the same kind of material given after an interval of days. No further contemporary attention seems to have been given to this isolated incident, and it was not until 1894 that the speaker chanced again upon the phenomenon. He was engaged upon a study of the pathologic action of the toxalbumins, and his attention was attracted by recent experiments on the similar globulicidal (or red blood corpuscle destructive) action of certain alien blood serums, such for example as the serum of the dog for the red globules of the rabbit. Since animals could be rendered immune to the toxalbumins, the attempt was made to make rabbits immune to dog's serum, but without success. On the contrary, it was found that animals which had withstood one

dose of dog's serum succumbed to a second dose given after the lapse of some days or weeks, even when this dose was sublethal for a control animal.

Again the observation fell on stony soil, as indeed subsequent ones were destined to do a few years later and, as it now appears, chiefly because knowledge of and interest in the general subject of immunity had not progressed far enough at that period to present to the contemplation of the "prepared mind," to use Pasteur's phrase, the sharply contrasted hypersensitive state.

But the time for the systematic investigation of the phenomenon was approaching, for between 1902 and 1904, Richet and his pupils had their attention arrested by an extraordinary incident, as it then seemed. In undertaking to effect immunization with certain poisonous proteins of animals, they found that instead of inducing resistance, they induced hypersensibility. To this latter condition they applied the name Anaphylaxis. Although as it subsequently turned out, the idea involved misconception of the nature of the process, yet these studies stand forth illuminatingly as recognizing for the first time the dependence of the hypersensitive state upon a preceding injection of a given protein substance and the necessity of an incubation period covering a number of days between the injection, in order that the sensitive condition might be ushered in. That the sensitizing effect was of the nature of a general biological reaction of the animal body to the parental introduction of natural proteins into the body, without reference to their primarily poisonous character, came to be appreciated a little later as the result of observations made on rabbits and guinea pigs injected and then reinjected with horse serum, as well as with other innocuous proteins. In order to arouse the reaction of immunity in the animal body, some degree of primary poisoning of the cells, as with bacteria, their metabolic products and similar substances originating in other varieties of living beings, must be accomplished;

while the sensitive state arises from the interaction of the animal body with any native protein substance whatever which finds its way directly or indirectly into the blood.

From the many investigations which now ensued, it appeared that while many kinds of warm-blooded animals are subject to the condition, yet the most striking, because most uniform and dramatic effects are yielded by the guinea pig, which has since become, as it were, the "classical" animal for observing and studying anaphylaxis. The reason for this choice arises from the circumstance that in the guinea pig a sensitization of the smooth muscle fibers occurs, so that in reinjection of the original protein, among other effects, a contraction of the lining membrane of the bronchi takes place, which by closing their lumina and excluding air, quickly causes death from asphyxiation. Moreover, the guinea pig has proved exquisitely responsive to sensitization, so that minute quantities, measured even in fractions of milligrams, of pure native proteins suffice to induce a specific hypersensitive condition, whence it has followed that the prepared guinea pig has been found suitable for the investigation of the ultimate chemical relationships, not otherwise observable, which subsist between native proteins.

Profoundly different as ar. the obvious features of the anaphylactic and immune reactions, yet certain of the fundamental conditions governing both coincide. It will be recalled that in arousing immunity in animals by artificial means, certain new substances of the general nature of antipodes, or as technically named, antibodies, are made to arise in the blood of the treated animal; and it now appears that in the course of sensitization of animals, antibodies to the proteins injected also develop. In both instances the material originally injected, whether primarily poisonous or not, if active, belongs to a class now called antigens, that is generators of antibodies. The expression of the immunity reaction, in its simplest terms,

consists of a chemical or physico-chemical union between the original antigen and the manufactured antibody, taking place in the body or in a test tube, through which the primarily poisonous antigen is rendered innocuous. In other words, the immune antigen-antibody complex is a harmless compound.

In a similar manner the sensitizing antigen and induced antibody unite in anaphylaxis, but the product of the union is essentially different from the one just considered, in that it is highly injurious, and the effect of the antigen-antibody complex is not to protect, but to poison the animal. The basic distinction between the immune and the anaphylactic condition, as described, is further enforced when we recall that the original toxic protein used to immunize is detoxicated in the course of the immune reaction and the original non-toxic protein used to sensitize is endowed with the property of intense toxicity in course of the latter reaction.

As in the instance of the immune state, a still undecided controversy is going on as to whether the hypersensitive condition depends upon humoral or upon cellular factors. There is no doubt that the anaphylactic antibody exists free in the blood, and hence that a normal animal can be rendered passively sensitive by the infusion of blood derived from a sensitized animal. It is equally true that the anaphylactic response is in part a cellular one, as in the instance mentioned of the bronchial musculature stimulated to contraction. By appropriate experiments it can be shown that organs containing smooth muscle taken from sensitive animals, exhibit the equivalent of the anaphylactic reaction even outside the living body; and also that coincidentally with the appearance of the "shock" of the reaction in the guinea pig, the blood becomes incoagulable.

Hypersensitiveness may exist independently of purposive artificial sensitization, and some of the most important examples of that condition have been observed

in man. Because of their size, perhaps for other reasons, human beings even when sensitive react to the parenteral injection of native proteins less severely than the smaller animal species. And yet lamentable instances, if very few in number, of serious or even fatal anaphlyactic effects have been observed in man. These have occurred especially in connection with the therapeutic employment of curative serums derived from the horse. The greatest danger from this source is at the time of the first injection, for while severe effects do sometimes follow upon a second or subsequent injection, they have never been attended by fatal consequences. Luckily, means are known for anticipating these even infrequent accidents, and of guarding against their dangers without at the same time depriving those in need of the benefits of serum protection or therapy.

Beside the active state of sensitization another is known which may be termed negative. Thus it has been found that when a sensitive animal is given an injection of a protein which produces a certain degree of anaphylactic effect, but not a fatal outburst, the treated animal can for a time be rendered insensitive. And thus human beings who are sensitive, say to horse serum, may be desensitized by means of successive small inoculations of the diluted serum, and while in the refractory state thus induced receive without risk larger injections of the serum.

On the other hand, lesser states of anaphylaxis in man are by no means infrequent. To them belong the rashes of "serum sickness" following the injection of curative serums which while annoying are not dangerous, and the very disagreeable manifestations of hay fever and its allied conditions, now attributed to the action of vegetable materials, pollens chiefly, upon the sensitized mucous membranes of the nose and throat. Recent studies by Auer have shown that animals sensitized with harmless proteins, such as horse serum, develop severe local inflammations when from any local cause an extrusion of

the antigen-containing fluid of the blood is enabled to penetrate the extravascular tissues; and on the basis of this observed fact he has suggested that functional disturbances of many organs of the body in sensitive human subjects may be brought about in a similar manner.

In a related field the hypersensitive reaction has been employed to aid in the diagnosis of important diseases of man and animals. It is apparent from what has been stated of the site of the fatal anaphylactic shock in the guinea pig, and as stated a moment ago of the sensitiveness of tissue cells in general to the circulating anaphylactic antigen, that a visible local reaction might be obtainable by introducing the protein to which the animal or person is sensitive into a visible portion of the body, as say the skin. In this way sensitiveness is looked for before serum injections are given, tuberculin is employed to disclose hidden foci of active tuberculosis, luetin is used to expose evidences of latent syphilis, and, in a modified manner, the Schick test is applied to determine whether exposed children do or do not carry in their blood, spontaneously as one might say, sufficient diphtheria antitoxin to afford them security without a protective serum injection. And beside the benefits accruing to human therapy directly from the working out of the meaning of anaphylaxis are to be placed those improvements introduced into veterinary practice, from which human preventive medicine also has derived great gain, namely, the application of the tuberculin test in clearing milch herds of actively tubercular cattle, and of mallein to the controlling of glanders among horses.

## Filterables

As we move from the contemplation of one achievement to another in bacteriology, we rarely pause to reflect how far circumstances almost accidental have favored the gains. The working out of the biological basis of fer-

mentation and putrefaction, and a little later of the microbic origin of disease, is obviously bound up with the perfection of the compound microscope, and the usefulness of that instrument for the purpose is as obviously bound up with the ultimate size of bacteria and related organisms. And yet without the fortunate conjunction of an optical device and the degree of magnitude of living objects, we should still be groping in outer darkness in the search for the origin of disease, and still struggling with the phantoms of spontaneous generation. But the great men who proved the connection between microscopic life and the biological processes mentioned, including the source of the infectious diseases, did more than describe the phenomena revealed by the microscope and otherwise. They established methods with principles so clearly enunciated and rigidly based that it has been found possible to penetrate into an inhabited territory in which thus far the most powerful microscope has not always enabled us to discern the living forms.

Thanks to their labors we know now, first, that the faculty of setting up disease in successive individuals is a property only of matter which can itself increase indefinitely, and all matter thus constituted is possessed of life; and second, that certain disease-producing parasites can be separated mechanically from the soluble products of their growth, by passage through earthenware filters, in which the interstices or pores are smaller even than the size of the microbes themselves. By varying the density or porosity of these filters, we arrive at a way of roughly estimating the size of the microbic cells.

Thus it came about that in 1898 two German bacteriologists, Loeffler and Frosch, who were engaged on the study of the very highly communicable foot and mouth disease of cattle, discovered that after diluting the contents of the unbroken vesicles which arise in that disease, with 20 to 40 times their volume of water and passing them through such earthenware filters, the filtrate not only

would induce the disease on inoculation, but that the same series of events followed the dilution and inoculation of the vesicular contents of the experimental variety of disease through an indefinite series. Obviously the filtrate contained a living element which came to be called a virus, just as is the small-pox germ, for in neither instance, and notwithstanding laborious endeavors, has the living organism itself ever been seen under the microscope.

We now recognize a class of microbes or viruses which are so minute as to be regarded as ultramicroscopic, and yet so active as to be capable of setting up disease in animals and man. The precise limits of the class have yet to be defined. When we consider that there remain still to be detected the microbic incitants of some of the most contagious as well as common of diseases, our minds readily seize hold of the possibility of their being of this nature. Thus the microbes responsible for such contagious maladies as measles, scarlet fever, and chicken-pox, and those inducing small-pox and rabies are not known, and not a little obscurity still surrounds the etiology, as we say, or immediate origin of epidemic influenza.

Inasmuch as the filterable microorganisms or viruses, or filter passers as the British prefer to call them, are known alone through their disease-producing propensities, no one can say whether, as is true of the bacteria, innumerable kinds exist in nature, among which relatively a small number has acquired parasitic or pathogenic qualities. Of the less than a dozen diseases known or on good grounds considered to be induced by filterable microorganisms, two attack human beings, namely poliomyelitis or infantile paralysis, and trench fever; and a third, yellow fever, which until very recently was believed to belong also in this category, has now been relegated to another class, with respect to which special devices suffice to bring into view its microbic incitant.

There exists, therefore, a degree of uncertainty in this field of research for which allowance must be made, since

it may well happen that suddenly through a fortunate series of experiments or the opening up of new methods, a parasite hitherto regarded as invisible may be brought into microscopic view. Should, for example, complete evidence be brought forward to relate the Rickettsia bodies to certain specific infectious diseases transmitted especially by insects, as by the wood tick in Rocky Mountain spotted fever, and lice in trench and typhus fever, then another group will have been transferred from among the ultramicroscopic to the visible parasites. A similar situation exists regarding the globoid bodies of poliomyelitis, the disease of man most convincingly established as induced by a filterable microorganism. By means of a highly specialized method of cultivation applicable especially to the class of spiral microbes, or spirochetæ, Dr. Noguchi and the speaker isolated from the nervous organs of cases of poliomylitis, globular bodies so minute as to be just at the limit of visibility under the highest power of the microscope. With cultures of these bodies they induced experimental poliomyelitis in the monkey; but the culture method itself is so intricate that thus far few bacteriologists have been able to repeat the work, which, therefore, still awaits final confirmation.

Since the recent pandemic of influenza and the assault made upon the so-called *influenza* bacillus of Pfeiffer, isolated first in Germany during the influenza epidemic of 1889-1890, the inciting microbe of that disease has been sought among the filterables. The announcement of the finding of such a parasite in the nasopharyngeal secretions by Nicolle and Lebailly of Paris in the autumn of 1918, aroused high hopes which subsequent investigations have not served to sustain. The problem was approached in a somewhat different manner by two workers —Olitsky and Gates, at the Rockefeller Institute. Their studies embraced two periods, the epidemics of 1918-1919 and 1920, and the intervening (interepidemic) period, the latter serving as a control for the former. The es-

sence of their investigations consisted in injecting through the trachea into the lungs of rabbits saline nasopharyngeal washings derived within the first 24 to 36 hours after the appearance of symptoms from influenza patients and observing the effects (*a*) upon the blood and (*b*) upon the lungs. The striking changes, in the successful experiments, relate to the white corpuscles of the circulating blood which suffer a numerical depression affecting chiefly the mononuclear type of cells, and to the lungs in which multiple hemorrhages and edema, but not pneumonia, arise. The effects are correlated: where no lung lesions are found no blood alterations occur. These objective phenomena are induced by filtered materials free of all ordinary bacteria (ærobic and anærobic) and they have not been secured otherwise than with materials derived from early cases of epidemic influenza; but when present, the rabbits affected very readily become subject to the action of various other bacteria (streptococci, pneumococci, staphylococci, influenza bacilli), to which they are otherwise resistant, but which then settle in the lungs and excite fatal pneumonic affections. The unassisted action of the influenzal material is not fatal; only when an ordinary bacterial lung infection is superadded does death follow. All who are familiar with the effects in man of pure influenza and then of influenza complicated with pneumonia of pneumococcal, streptococcal, etc., origin will appreciate this distinction.

What also characterizes the class of diseases incited by the true filterable parasites in their high degree of specificity and the enduring immunity which follows recovery from an attack. This is true among animals, for instance, of hog cholera and foot and mouth disease, and in man of poliomyelitis. This specificity is shown by the difficulty or impossibility of implanting the virus on specifically remote animals. In poliomyelitis, for example, only monkeys are subject to experimental infection, in hog cholera and foot and mouth disease, only swine and cattle. Bear-

ing in mind Behring's dictum that to produce a therapeutic serum, it is essential to immunize highly susceptible animals, it becomes evident why success has not crowned the many undertakings to prepare an antipoliomyelitis serum in the horse or other large animal, and why it is only by the use of swine themselves that an anti-hog-cholera serum has been secured.

The investigation of this class of excessively minute or filterable parasites casts a sharp ray of light into a neighboring field of biological research which at the time aroused hopes of further rapid progress but which the intervening time and effort have not realized.

Perhaps no subject in experimental pathology has been pursued with more thought and energy than the one to which the name of cancer research is applied. The reasons are obvious. The nature of the source of the cancerous tumors is still shrouded in essential darkness. It is, of course, known that cancer sometimes follows upon prolonged irritation and inflammation of tissues variously excited. But what the immediate impulse is that calls forth the cancerous state is unknown. And yet advances have come from the study of the spontaneous and transplantable cancers in mice, rats and some other animals. A long series of biological conditions governing the growth and recession of the tumors have been uncovered, and by altering those conditions, on the one hand growth can be promoted, and on the other, retarded. In this way, Murphy and his co-workers have accounted for the influence of the action of the X-ray in affecting cancer growth; and by observing the correlative effects on the lymphoid structures of the body, which are very sensitive to the rays, and the changes corresponding to them in the circulating blood, they have so altered the scale as almost at will either to abolish or stimulate the development of mouse cancers.

But these experimental results and others of a class in which the defensive forces of the body can be marshalled

against the implanted cancer cells, throw no real light upon the series of events underlying the origin of cancer. The light referred to was shed by the studies of Rous, of the Rockefeller Institute, upon a sarcoma, or fleshy cancer, of the domestic fowl. This cancer, which arises at times spontaneously in fowl, is subject to successful implantation in other fowl. The specificity is accurate; it will not grow in other birds and grows best in the variety of fowl in an individual of which it originally appeared. Its growth is first local, as is cancer in man, and later metastatic, or, appearing at a distance and starting from microscopic masses of cells derived from the original tumor and carried by the circulation to remote parts of the body. The altogether new and unprecedented fact about this tumor, which has, however, not yet been found to be true of the cancers of mammals, is that it may be induced by the injection into the susceptible variety of fowls, of a cell-free filtered extract of the tumor. In other words, Rous has accomplished for this tumor what bacteriologists had effected for a certain refractory group of the infectious and communicable diseases, namely, relating it to a form of life not imagined by the founders of bacteriology, but which their discoveries in the field of the living microscopic, as opposed to the ultramicroscopic, universe brought within range of recent biological research.

## SPIROCHETES

The vicissitudes of bacteriological science, like those of other sciences, have depended upon time and method, and sometimes the one and sometimes the other has served to promote discovery. When by a happy conjunction of circumstances, time and method happen to conjoin, then advances almost startling in nature may take place.

It is in this way that we may view the remarkable progress of events in connection with a class of special micro-

organisms or spirochetae, so called since Schaudinn's discovery in 1905 of the *pallida,* the microbic inciter of syphilis. The search for the microbe of syphilis had been unremitting since the early days of bacteriology, and not a few false claimants held the field for a brief space. Schaudinn's discovery was very soon confirmed, and has now been firmly established; and it is interesting to note that in fact it was itself a confirmation of an observation made a few years earlier by Metchnikoff and Bordet, who, however, because of the technical difficulties of the quest did not succeed in confirming their own findings. The unusual difficulties surrounding the detection of the living *pallida* in the body fluids, because of its extreme tenuity merely heighten the respect we must hold for the zoologist Schaudinn's perspicacity. Very soon staining methods were introduced to lighten the task of detecting the *pallida,* but so capriciously did they act and so baffling did the ordinary microscopic detection prove, that the great promise of the employment of the *pallida* for purposes of diagnosis and treatment was not at once realized.

None the less, a great advance in bacteriology had been achieved, and a new class of microbes potentially disease-producing was presented for study. Within a year a second spirochete, called *pertenuis,* was discovered in the lesions of yaws, a tropical disease having certain affinities with syphilis. The search for the delicate spiral organisms was not an easy one, and only the masters of bacteriological technique were likely to succeed in it. Then suddenly the labor was lightened and the road made smooth for a rapidly succeeding succession of discoveries in this field by the invention and application of the dark-field or ultramicroscope. This instrument was perfected for observing you are aware, operates by projecting powerful rays of light in directions parallel to the surface of the microscopic slide. Such a field if optically empty will be dark and not luminous; but if particles are present in it, the

rays of light will be intercepted and the particles illuminated. They in turn, and according to their size, will appear as bright objects, or when very small, give a diffuse luminosity to the field. The phenomenon is similar to the one described by Tyndall, in which a beam of light passed through a dark space containing suspended particles causes them to become visible. When the suspended matter consists not only of dispersed particles, but of microorganisms, these also become luminous, and when, as with the spirochete, they exhibit a wavy structure and independent motion, they at once arrest attention. To-day the dark-field microscope is found in every well-equipped clinic, and it has aided in adding many new species to the already considerable number of microbes known to be disease-producing.

The latest significant addition to this field is the *Leptospira icteroides,* or the jaundice-producing spiral, which Noguchi has recently detected in the blood and internal organs of cases of yellow fever. His extensive investigations carried on in Ecuador, Mexico, and Peru, as well as at the Rockefeller Institute, have rendered it highly probable that this spirochete is the microbic incitant of that severe epidemic disease.

Yellow fever, as you know, is an insect-borne disease and arises from the insertion into the blood of man of a virus carried by a particular mosquito—*Stegomyia calopus.* After the mosquito transporting the virus has bitten a healthy person, an interval of about five days elapses before his blood becomes infective, and the infectiousness endures about three days longer. During the latter period the blood serum can be passed through the finest-grained porcelain filters without losing its infectivity. On the other hand, a normal mosquito which has bitten a yellow fever patient, does not become capable of infecting other human beings until after about twelve days. Hence the insect acts not merely passively, as a needle might, as the conveyer of the virus, but it is necessary

in order to increase or otherwise modify the infective material withdrawn from the blood.

The discovery of the yellow fever spiral definitely removes the disease from the class believed to be provoked by ultramicroscopic organisms, and at the same time adds so well defined a microbe as *Leptospira icteroides* to the group of filter passers. The data so far secured regarding this spiral in relation to yellow fever fulfill the conditions arising out of Reed and Carroll's discoveries in connection with the disease in man. These are great gains for theoretical bacteriology. The rewards to practical medicine are even greater, since it has been found that *Leptospira icteroides* lends itself to the making of an active vaccine (killed organisms) and also an effective therapeutic serum. Hereafter yellow fever is to be combated (1) by removing the breeding places of the stegomyia, (2) through vaccination, and (3) by an antiserum.

The etiology, or causation, of yellow fever so long and fruitlessly sought seems to have been solved, and it may be of interest to inquire why just at this juncture? The answer is, through the conjunction of the "prepared mind" and animal experimentation. For nearly a decade Noguchi has been investigating this spiral class of microbes, in course of which he added materially to our knowledge of methods of study and of new species. He had first-hand knowledge of a related disease, infectious jaundice, transmissible to guinea pigs, which prevails endemically in Japan and sporadically elsewhere, and in which Inada had discovered a peculiar spiral organism (*Spirocheta ichterohæmorrhagiæ*). In other words, the time was ripe and Noguchi peculiarly equipped to take up again and investigate with newer methods the problem of yellow fever.

The story is still incomplete, as recent developments have shown; for just as Metchnikoff and Bordet had seen the *pallida* before Schaudinn, so it now appears Stimson of the U. S. Public Health Service had previously ob-

served the *icteroides*. He examined a series of sections of organs stained by Levaditi's method to show spiral organisms, taken from a patient having yellow fever who succumbed in New Orleans in 1907, and in the kidney found spiral forms to which he gave the name of *Spirochæta interrogans,* but the significance of which could not then be determined, and which Noguchi now identifies as the *icteroides*. Coming at this time and in this way, the observation is a welcome confirmation. Without the many data since supplied by Noguchi's experiments and studies of living cases of yellow fever, it possesses only suggestive value. The finding came too early in the development of our knowledge of the spirochete, and again the seed fell on stony ground.

There remains one further aspect of this incomplete discussion of spiral microbes in their relation to disease to be considered briefly, namely their separation into two classes according as the diseases induced by them respond to treatment on the one hand by curative serums, and on the other by so-called drugs or chemicals. It has just been stated that yellow fever can be combated by a serum of this kind, and the same is true of infectious jaundice. In this respect the two inciting microbes—*L. icteroides* and *S. ictero-hæmorrhagiæ*—behave as do certain bacteria. But the spirochete of syphilis and yaws and some others are not subject to serum influences, and hence they and the disease they induce must be attacked from another quarter, and in this instance with chemicals for which they evince an extraordinary selectiveness, as do the malarial organisms and certain parasitic trypanosomes which are of protozoal nature.

### CHEMOTHERAPY

Chemotherapy is the name applied to the branch of experimental medicine in which chemicals, or drugs, are searched for, and when necessary and possible, fashioned

to subdue a particular kind or class of infection. The beginnings of chemotherapy reach into the dim past; the science of chemotherapy is just being built up. The epochal discoveries of the curative value of cinchona bark in malaria and of mercury in syphilis, are examples of the early, and as we now say empirical working out of specific therapeutics. But in emphasizing these two triumphs of the empiric period long antedating the experimental epoch in medicine, sight should not be lost of the essential point, namely that the virtues of those remedies were established also by experiment carried out over long decades and upon man himself, for in no other way could these active drugs have been separated from the thousands of innocuous or even harmful ones applied by man at all stages of his evolution to the alleviation of suffering.

In a strict sense, curative serums are examples of chemotherapy, and the most specific ones known, since they are so exactly adapted to combat a given microbe or its toxin, and because in the end the active component is chemical in character. But as usually employed, the term is applied rather to chemicals or drugs not produced by the animal body and of definite and ascertainable ultimate composition.

The beginnings of the experimental science of chemotherapy are very recent, and hardly more than a start has been made in exploring the field. The principle on which it is based can be expressed simply: microbic parasites on invading the animal body arouse defensive activities on the part of the host, which when of sufficient intensity serve to weaken and restrain, and ultimately to overthrow and conquer the invaders. These natural defenders, as we learned earlier, consist of fluid and cellular constituents of the body, sometimes performed, sometimes only manufactured on demand, and in part especially adapted to the particular parasitic agent to be vanquished.

With this picture before them, of the manner of the body's defense against microbic invasion, bacteriologists

could appreciate that the overcoming and healing of infection is never a mere passive process, and the action of healing agents in the body does not occur, as the older therapeutics believed, precisely as would happen if the parasitic agent could be exposed to the effects of drugs, say in a test tube. Moreover, it was always evident that such effective drugs as quinine and mercury must be employed sparingly, because while they were able to injure and thus to lead to the destruction of the microbes inducing malaria and syphilis, they were likewise capable of injuring the component cells of the body itself.

The outstanding instance in which experimental chemotherapy has registered a great success is in connection with the organic compounds of arsenic, which have been adapted to the overcoming of infection induced on the one hand by spirochetes and on the other by trypanosomes. That arsenical compounds possess therapeutically active properties against these two classes of parasitic diseases —as represented on the one hand by syphilis and on the other by African sleeping sickness—is not entirely a recent discovery; but until the systematic investigations of Ehrlich were instituted, which ultimately yielded salvarsan, knowledge was fragmentary, medical practice based on it ineffective, and the road to progress obscure. Now the outlook is wholly changed, and there is going forward an active and either already successful or at least highly promising search for new drugs or chemicals, directed against both the bacterial and the protozoal parasitic microbes. This territory so newly opened to exploration in which organic chemists and pathologists should pool interests in order to move forward, is of almost infinite possibility, since the number of chemicals is nearly limitless which can be produced and so fashioned as to injure and subdue as it were the parasitic invader, and at the same time, pass over and leave little influenced the adjacent body cells. But the conditions of the search are intricate since, as just indicated, a useful drug must

exhibit high power of attack upon the protoplasm of a parasitic microbe and a low one on that of the cells of the blood and the organs, in order that the former and not the latter may be predominately affected. It is a peculiarity of chemicals as contrasted with serums that they can never be so accurately designed to their purposes as to remain entirely without effect on the cells of the host; but it is also recognized that when the drugs are effective, they do not carry on a single-handed combat, but serve best when they either assist or are assisted by the natural defensive mechanisms of the body, which also are roused into action to overpower the invader and the coöperation of which often insures protection against reinvasion, acquired at the end of, and in consequence of, the struggle.

### INFECTION AND SURVIVAL

Infection and the mastering of infection are intricate biological processes in which contending forces are brought into play one against the other, whence a struggle ensues. We have seen that the host stands ready equipped with mechanisms of defense which may be quickly mobilized, and which undergo favorable modification during infection, when as we say, it proceeds toward a favorable termination. The bacteriologist has learned within the past quarter of a century to imitate nature's method of surmounting infection by supplying certain of the defensive implements artificially wrought to be brought to her aid in time of stress and need, and the chemist is learning more and more the manner of adapting drugs to the destruction of the microbic parasites of disease for a like purpose.

All the advantage is, however, not on the side of the body, since the parasites also possess powers of modification, through which the most elaborate obstacles placed in their way by the host may be rendered futile.

These adaptations consist in the acquisition of special

properties of aggressive action or virulence, with which is associated the ability to produce and liberate substances paralyzing to the defensive processes of the host. Again, the parasites may surround themselves with a kind of mantle, protecting them from the potentially destructive effects of serum and phagocyte. Or they may undergo an internal change of constitution, through which resistance to injurious agencies not normal to the species is developed. The last condition is called "fastness" and has been observed especially among trypanosomes and spirochetes exposed within the body of the host to ineffective amounts of specific serums or chemicals.

With so many factors interplaying, it is not difficult to perceive that the problem of infection is a complex one, both as regards its occurrence and its issue. But our understanding of the conditions under which it arises has been immeasurably extended by the discovery of the insect and higher animal agencies in communicating infective agents to man, and of the part played by so-called microbe carriers, those unfortunate and innocent persons who have recovered from or merely been exposed to a communicable disease, or suffered a slight, abortive, or ambulant attack of which they are ignorant, and the discovery of the usual portals of entry into the body of pathogenic microorganisms.

Infectious diseases prevail in two more or less distinct, but at times interwoven ways, which we speak of as the sporadic and the epidemic. The former represents the ordinary manner of spread, the latter the occasional or periodic explosive outbreak or wave, such as has been experienced recently with the pandemics of poliomyelitis, influenza and lethargic encephalitis.

What has been sought in the past and is being assiduously looked for in the present is an adequate explanation of the transition from the sporadic to the epidemic type of disease. We possess already quite accurate numerical data which show the manner in which epidemics begin,

how they reach their maximum or peak, and then how they fall away again. Indeed, we now construct easily and recognize readily the epidemic curves of different epidemic diseases. But it is to be hoped that a new era is appearing in the study of epidemiology in which experiment may play a part along with observation, statistical and other. Already beginnings are being made in the attempt to define the distinction between the potentially fluctuating grades or power of infectivity and degree of virulence, taking the former to mean the natural propensity which a microbe displays in penetrating the ordinary portals leading into the body and its ability to survive and multiply there, and the latter the capacity to overcome the natural defenses when artificially inoculated. This is a field clearly approachable by experiment, using small laboratory animals, among which arise from time to time, and much as happens with man himself, destructive epidemics induced by known microbes. Finally, there is the field in which not a single species of microbe is concerned but more than one, the first preparing, the other utilizing the prepared way for its more vicious purposes. Frequent examples of the last condition are observed among the lower animals, in which, of course, the opportunities for study are superior to those existing in man; but recent experiences in this and other countries during the influenza epidemic carry conviction of this relationship, since the original disease is recognized to be not of severe nature, while the pneumonia engrafted upon it is admittedly of highly fatal character.

My purpose in reviewing some of the notable events and tendencies in bacteriology which have come to light in the past twenty-five years has been to present to your consideration the achievements in one branch of modern medicine, and to indicate the relation subsisting between medicine and the more fundamental sciences of physics, chemistry and biology. Bacteriology has depended also

for its development on its sister sciences of physiology, pharmacology and pathology, without which many of its phenomena could not be interpreted. It seems but proper to state that what has been attempted here for bacteriology could readily be equalled or even exceeded by spokesmen for those sister sciences, so surely has medicine grown scientific in recent times.

# BEFORE AND AFTER LISTER

(Two lectures before the U. S. Army Medical School, Washington, D. C., April 27 and 28, 1915)

BY

W. W. KEEN

*Emeritus Professor of Surgery*
*Jefferson Medical College,*
*Philadelphia*

## LECTURE I. "BEFORE LISTER"

ON July 1, 1861, I entered the service of the State of Massachusetts as assistant surgeon of the Fifth Massachusetts, and on July 4 was sworn into the service of the United States in the shadow of yonder capitol. On August 1 I was honorably discharged and resumed my medical studies at the Jefferson Medical College. Strange as it now seems, when assistant surgeon I was not yet a graduate in medicine. As an evidence of the loose way in which medical and military matters were then conducted, I was actually appointed without any examination whatever.

After graduating in March, 1862, I again entered the service in May, after an examination, and was ordered to the Eckington Hospital in the then outskirts of Washington. Shortly afterwards I was ordered to fit up two churches as hospitals and to have them ready in five days. It was 5 P.M. on a Saturday afternoon.

People sometimes imagine that a practising physician can be transformed into an army surgeon merely by putting a uniform on him. I was not lacking in ordinary intelligence and was willing to work, but I was utterly without training. To get those two churches ready as hospitals I had to have beds, mattresses, sheets, pillow-cases, chairs, tables, kitchen utensils, knives, forks, spoons, peppers and salts, all sorts of crockery and other necessities for a dining-room, all the drugs, appliances and instruments needed for two hundred sick and wounded men; I needed orderlies, cooks and the endless odds and ends of things which go to make up a well-organized hospital. I did not know how to get a single one of these requisites. As to drugs, I did not know whether to order six ounces or a gallon of laudanum, an ounce of two or a pound or two of opium, and I was in utter darkness as to the mode of getting any of the other things from a teaspoon to a cook. However, I inquired and as soon as I learned how, I set myself to work. For two nights I slept only about three hours each, and I had the satisfaction of reporting to Dr. Letterman at the end of three days, instead of five, that I was ready. On the fourth day I had one hundred wounded men in each hospital.[1]

I congratulate you in this more enlightened age and as students in this fine school where you are trained and drilled in matters which we had to cope with in our stumbling way, by dint of desperately hard work, without guidance, often learning only by our bitter mistakes.

We, the few surgeons still surviving those momentous four years, may well say to you *Morituri salutamus.*

I have been so very fortunate as to live during the whole period of the greatest revolution surgery has ever passed through. How strange seem these words of

[1] Keen, *Addresses and Other Papers,* 1905, p. 424.

Erichsen, the then foremost London surgeon and Lister's early chief at University College Hospital uttered in 1874, just as surgery was on the eve of its very greatest triumph.

> Surgery in its mechanical and manipulative processes, in its art in fact, is approaching, if it has not already attained to, something like finality of perfection.[2]

Anesthesia in 1846 and 1847 had robbed operations of the terror of agonizing pain. Quick, "slap-dash surgery" —a necessity before the days of anesthesia—then gave way to delicate, painstaking, artistic surgery. Antiseptics thirty years later relieved the patients from the terrors of death and gave to the surgeon restful nights and joyous days.

Hence when I received the kind invitation to address you it seemed to me that I could possibly render you some service by describing the state of surgery "Before and After Lister," since my testimony would be that of an eyewitness.

When the Apostle Paul was about to be bound and scourged you remember that he claimed immunity as a Roman. "With a great sum obtained I this freedom," explained the chief captain. "But I," said the Apostle, with justifiable pride, "was free born." "With a great sum" of the most strenuous labor the men of my generation acquired the knowledge and the skill and the immense satisfaction of the antiseptic and aseptic era—but you, you are "free born" and have entered into a rightful heritage from your fathers. "Before Lister" and "After Lister" in the surgical calendar are the equivalents of "B.C." and "A.D." of our common chronology.

Modern military surgery may be said to begin with Ambroise Paré in the middle of the sixteenth century.

[2] Wrench, *Lister's Life and Work*, p. 281.

Gunpowder, though long known, had been used in warfare to any large extent for only a few decades. The belief, shared fully by Paré himself, that such wounds were "poisoned," was universal. Treatment was directed to the destruction of the supposed poison by pouring boiling oil and hot pitch into such wounds. In the heat of his anger at the inhumanity of the new weapons he says in his preface to Book XI., "Of wounds made by gunshot and other fiery Engines and all sorts of Weapons": [3]

> I think the deviser of this deadly Engine hath this for his recompence that his name should be hidden by the darkness of perpetual ignorance as not meriting for this his most pernitious Invention Any Mention from Posterity.

Yet with a curious inconsistency he immediately gives the name of a German monk as the "deviser."

Listen to his quaint story of how he discovered that gunshot wounds were *not* poisoned. In 1536

> it chanced on a time that by reason of the multitude that were hurt I wanted this Oil ["oyl of Elders Scalding hot with a little Treacle mixed therewith"]. Now because there were some few left to be dressed I was forced . . . that I might not leave them undrest to apply a digestive made of the yolk of an egg, Oil of Roses and Turpentine. I could not sleep all that night for I was troubled in mind, and the dressing of the precedent day (which I judged unfit), troubled my thoughts; and I feared that the next day I should find them dead, or at the point of death by the poison of the wounds. . . . Therefore I rose

[3] *The Works of that Famous Chirurgeon Ambrose Parey*, translated by Th. Johnson, London, 1678, p. 270.

early in the morning. I visited my Patients and beyond expectation I found such as I had dressed with a digestive only, free from vehemency of pain, to have had a good rest and that their wounds were not inflamed . . . but . . . the others that were burnt with the Scalding Oyl were feverish tormented with much pain . . . and swoln. When I had many times tried this in divers others, I thought this much, that neither I nor any other should ever cauterize any wounded with Gunshot.[4]

But he still advocated the actual cautery for arresting hemorrhage even down to early in 1552. But later in that same year he changed his practice and thus describes his introduction of the ligature—a famous advance.

I confess here freely and with great regret that heretofore my practice has been entirely different from that which I describe at present after amputations. . . . I advise the young surgeon to abandon such cruelty and inhumanity and follow this better method. . . . Having several times seen the suture of veins and arteries for recent wounds which were attended by hemorrhage I have thought that it might be well to do the same after the amputation of a limb. Having consulted in reference to this matter with Etienne de la Rivière, Ordinary Surgeon to the King, and other surgeons sworn of Paris, and having declared my opinion to them, they advised that we should make the experiment [espreuve] on the first patient that we had, but [note his cautious uncertainty] but we would have the cautery all ready in case of any failure of the ligature. I have done this on the person of a postilion named Pirou Garbier, whose right leg I cut off . . . following a fracture.[5]

[4] Johnson's *Paré*, p. 272.
[5] Malgaigne's *Paré*, Chap. XXVI., pp. 227, 230.

At the Siege of Danvilliers[6] also in 1552 he records the amputation of the leg of a gentleman in the suite of M. de Rohan "without applying the actual cautery." In another place[7] Paré says that he was taught this new method "by the special favor of the Sacred Deity." He also refers to Galen's advocacy of the ligature. After many trials, Paré definitely adopted the ligature and "bid eternal adieu to all hot Irons and Cauteries."

He does not seem to have lost sleep over the ligature as he did sixteen years before when he abandoned the boiling oil and the hot pitch. Both were experiments on human beings. "Human vivisection" would have been the outcry of a sixteenth-century antivivisection society. But had he or some successor *not* made these experiments we should still be filling gunshot wounds with boiling oil and hot pitch and searing amputation flaps with the actual cautery. How much greater a boon to humanity it would have been if years earlier instead of experimenting in both cases on human beings first, Paré had experimented on a few animals to determine whether gunshot wounds *were* poisoned and whether the ligature or the cautery *was* the best means of arresting hemorrhage.

We can also incidentally learn how the doctrine of euthanasia was applied in Paré's time in the case of the desperately wounded by the following incident.

> In his first campaign, entering a stable where he expected to put up his own and his man's horses, Paré found four dead soldiers and three propped against the wall, their features all changed, and they neither saw, heard nor spake, and their clothes were still smouldering where the gun-powder had burnt them. As I was looking at them with pity there came an old soldier who asked me if there was any way to cure them. I said no, and then he went up to them

[6] Malgaigne's *Paré*, III., 698.

[7] Johnson's *Paré*, London, 1678, Book XII., Chap. xxiv., p. 305.

and cut their throats gently and without ill will toward them.[8]

Leaping over three and a half centuries of only moderate progress, let us next consider the state of surgery a hundred years ago. No better representative perhaps could be chosen than John Bell, the professor of surgery in Edinburgh, whose "Discourses on the Nature and Cure of Wounds" had reached a third edition in 1812, and his "Principles of Surgery" a new edition in 1826, to which his brother, Sir Charles Bell, also contributed.

In the former he states that tents or setons were much in use and the surgeons "were quite delighted with seeing prodigious quantities of matter spouting out when they drew their spigot away" (p. 299).

As to abdominal wounds he says:

> Having put it down as a prognostic, which is but too well confirmed, by much melancholy experience, that wounds of the belly are mortal, there is no reason why we should, in recording our cases, take any note of a man having died after such a wound. Death from such a wound is a daily and expected occurrence and, therefore, is not marked; but if we find that a man has escaped, are we not to record every such escape? (p. 313).

*Per contra,* to-day recovery has been achieved after 19 wounds of the abdominal viscera!

He considers wounds of the joints also as mortal, and amputations even in the most favorable circumstances did not heal under four, five or six months!

In his "Principles of Surgery" [9] he pictures the wards of a hospital as follows:

[8] Paget's *Ambroise Paré,* p. 31.

[9] John Bell's *Principles of Surgery,* new edition, with comments by Charles Bell, London, 1826, p. 86.

> You look upon limbs variously wounded, but all of them lying out, swollen, suppurating, fistulous, rotting in their own filth, having carious bones, bleeding arteries and a profusion of matter; the patients exhausted in the meanwhile, with diarrhea, fever and pain.

Again he refers to a wounded limb as "soaking in suppuration" and again, of its "lying in a slush of matter and foul poultices."

He relates the case of an officer under the care of Guérin, a celebrated French surgeon. He was wounded by a ball which had broken the fifth rib twice and traversed the entire chest. After dilating the wounds, Guérin introduced a seton ["a great strap of coarse linen"],

> which, of course, went across the breast as a bowstring crosses a bow, and this seton he continued to draw with a perseverance which is truly wonderful from the first day to the thirty-eighth day of the wound; during all of which time the patient's sufferings were dreadful (p. 458).

In fifteen days the patient was bled twenty-six times. After the removal on the thirty-third day of a splinter of bone, which had been imbedded in the lung, the patient, strange to say, recovered both from the wound and from the surgeon. It is not to be wondered at that Bell condemns such treatment. But, as we have seen, it existed in the practice of reputable surgeons.

Erysipelas, tetanus, pyemia, septicemia were rife. Hospital gangrene was endemic in many if not most hospitals, due to inevitable infection in practically every wound. Veritable epidemics were frequent. Is it any wonder that it had always been present for nearly two hundred years in the Hôtel Dieu in Paris when there were often from two to six patients (and such patients!) in one bed? Passing along the streets of Paris even during the

Crimean War[10] "one could recognize at a distance a surgical hospital owing to the stench of the human putridity it contained." In the surgical wards, "no matter how well ventilated, there was a fetid sickening odor" up to the days of Lister himself, wrote Sir Hector Cameron, Lister's house surgeon in Glasgow. Death always stalked grimly behind the surgeon.

> Secondary hemorrhage, tetanus, erysipelas, septicemia, pyemia and hospital gangrene were never all absent . . . and at times pyemia and hospital gangrene became alarmingly epidemic.[11]

After vividly describing the ravages of hospital gangrene Bell then vehemently asks:

> What, then, is the surgeon to do? Is he to try experiments with ointments and plasters while the men are dying around him? Is he to seek for washes and dressings to cure such a disease as this? Is he to expend butts of wine contending, as it were, against the elements? No! Let him bear this always in mind, that no dressings have ever been found to stop this ulcer, that no quantities of wine or bark which a man can bear have ever retarded this gangrene; let him bear in mind that this is a hospital disease, that without the circle of the infected walls the men are safe; let him, therefore, hurry them out of this house of death; let him change the wards, let him take possession of some empty house and so carry his patients into good air; let him lay them in a schoolroom, a church, on a dunghill, or in a stable; let him carry them anywhere but to their graves.[12]

[10] Wrench's *Life of Lord Lister,* p. 239.
[11] Cameron, *British Medical Jl.,* Dec. 13, 1902, p. 1844.
[12] Bell, *Principles of Surgery,* 1826, I., p. 149.

To-day we do not even know the bacteriology of this foul disease. I saw many cases of it during the Civil War, but since 1865 I have never seen a single case. There has been no opportunity to discover its germ if, as is probable, it is a germ disease. Lister made its return impossible.

But let us come down next to the period immediately before Lister's work.

You cannot do better than read that remarkable and revolutionary paper entitled "Hospitalism" by Sir James Y. Simpson, of Edinburgh, published in 1867.[13] It was a bombshell whose explosion aroused the profession as hardly any other paper in my lifetime. The controversy was bitter and widespread. Fortunately, antisepsis came close upon its heels and has forever done away with such a disgrace.

Simpson collected the statistics of the obstetrical mortality in hospitals and in homes with the following startling result.

Of 888,302 women delivered in hospitals, 30,394 died or 1 in 29—3.4 per cent.
Of 934,781 delivered at home, 4,045 died, or 1 in 212—0.47 per cent.

The reason for the greatly increased mortality in maternity hospitals—over seven times greater than in individual homes—was chiefly puerperal fever. After Oliver Wendell Holmes (1843) and Semmelweiss (1861) had attacked the evil, Pasteur finally in 1879 showed its bacteriological cause and gave it the *coup de grâce*.

The 0.47 per cent. of Simpson's home cases has been reduced to 0.15 per cent. and even 0.08 per cent. in the maternity hospitals of to-day!

But his chief assault was upon the surgeons. He analyzed the four main amputations—arm, forearm, thigh

[13] *Simpson's Works*, Vol. II., p. 345.

and leg—and excluded amputations at joints and all the minor amputations (fingers, toes, etc.).

Of 2,089 such amputations in hospitals, 855 died, or 41 per cent.

Of 2,098 in country practice, 222 died, or 10.8 per cent.

The latter were collected from 374 country practitioners, thus eliminating the personal equation. The difference was clearly due to the crowding and lack of sanitation in the hospitals of that day.

He gives two very interesting tables. The first is most instructive in showing the results in the then unsanitary state of all hospitals.

*Mortality After the Four Selected Amputations in Proportion to the Number of Beds in the Hospitals*

In the large Parisian hospitals.....62 in 100 die
In British hospitals with 300 to 600 beds.41 in 100 die
In British hospitals with 300 to 201 beds.30 in 100 die
In British hospitals with 200 to 101 beds.23 in 100 die
In British hospitals with 100 to 26 beds..18 in 100 die
In British hospitals with 25 beds or less..14 in 100 die
In isolated rooms in country practice..11 in 100 die

In the second he tabulates the mortality according to the experience of the operator.

*Death Rate After the Same Four Amputations in Accordance with the Experience of the 374 Operators*

Those who had done less than 6 amputations.....lost 1 in 7
Those who had done from 6 to 12 amputations.....lost 1 in 9
Those who had done 12 or more amputations.....lost 1 in 12

What an argument for the necessity for a year in a

hospital for the recent graduate before allowing him full liberty of action!

In France matters were as bad if not even worse. T. Holmes and Bristowe in 1861 had found that in Paris, of 102 of the four amputations in question, 67 died, a mortality of 65.7 per cent., or two out of every three. Out of 1,656 amputations in the Paris hospitals collected by Malgaigne and Trélat 803 died, 48.5 per cent., almost one in every two (Simpson, p. 291).

To-day, how entirely changed is all this. Listerism has transformed what Bell well called "Houses of Death" into "Havens of Safety." No home, however wealthy its inmate, can be as sanitary, as surgically clean or give as good results as a modern hospital.

The best evidence of the truth of this statement I can give you is the statistics of Dr. W. L. Estes,[14] of South Bethlehem, Pennsylvania. They are of especial value in that they are the statistics of the same surgeon in the same hospital and on the same class of patients. He reports the result in 724 major amputations. In 616 single amputations there were 28 deaths, a mortality rate of 4.54 per cent. Of 469 of the four selected amputations, 25 died, a mortality of 5.3 per cent. Of synchronous double, triple and one quadruple amputation, many of them complicated with other wounds and operations, there were 108, with 19 deaths, a mortality of only 18 per cent. It is very noticeable that in an earlier paper in 1894 in which he had reported the first 46 cases of synchronous double, triple and quadruple and complicated amputations, there were 13 deaths, 28.3 per cent., whereas from 1894 to 1913 in the last 62 such cases there were only six deaths, a mortality of 9.6 per cent., showing again the value of still larger experience even to an already experienced surgeon. In the second series there was no quadruple amputation.

But as officers of the Medical Corps of the Army you will be especially interested in the facts as to military

[14] *Annals of Surgery*, July, 1913.

surgery before and after Lister. Capt. Louis C. Duncan of our corps published a very interesting and comprehensive article[15] just before the present European war broke out.

He states that in Motley's "Rise of the Dutch Republic" in three volumes covering "30 years of almost constant sanguinary warfare" in the sixteenth century he "never once alludes to an army surgeon or an army hospital"! The surgeons were undoubtedly not officially attached to the army, but were in the suites of kings, princes or great nobles, as was Paré, in the same century.

To Sir James McGrigor in the Peninsular Campaign (1808-11) only fifty years before our Civil War, is given the credit by Duncan of first collecting accurate military medical statistics.

One hundred and fifty years ago 25 per cent. or more of the wounded died. In the Civil War and in the Franco-Prussian War of 1870-1 the rate had fallen to about 15 per cent., while to-day up to the present war not over 5 or 6 per cent. die of wounds.

The Crimean War will always be an example of utter inefficiency in the English and even worse in the French army. Its one bright spot is the splendid epoch-making work of a woman, Florence Nightingale, whose labors were unceasing and effective. Every war since then has seen less sickness and fewer deaths because of what she then accomplished.

Chenu, the French medical historian of that war, has made one curious and interesting calculation, partly official, partly estimated. The number of projectiles of all kinds actually fired he gives as 89,595,363. The total number of killed and wounded was 175,057. This would show that it took 512 projectiles to kill or wound one man. Such a disproportion would more than justify a cartoon during our Civil War. Two soldiers were sur-

[15] *Journal of the Military Service Institutions of the United States*, March–April, 1914.

prised by a hundred of the enemy. One proposed to the other to run for it. "No," was the cool reply, "There's no danger, for they say only one ball in 200 ever hits and there are only one hundred of those fellows."

Duncan's figures give 82,901 British soldiers sent to the Crimea, but the average strength was only 34,559, or only about 40 per cent., of effectives. The killed (2,755) and the deaths from wounds (2,019) gave a battle death rate of 69 per 1,000 per annum, while the disease death rate rose to 230 per 1,000 per annum.

In all, 300 men out of each 1,000 perished each year!

But the French statistics are still worse. While 315,000 were sent out, the average strength was less than 104,000 effectives, or only 33 per cent. The killed numbered 7,607 and the deaths from wounds 8,813. The battle death rate was 70, the disease death rate 341, per 1,000 per annum. Over 6,000 died from typhus alone.

Could there be a nobler example of the altruism of our profession—an altruism often tested and never in vain—than that shown by Drs. Richard P. Strong, Thomas W. Jackson, and many other doctors and trained nurses, and now finally by the chief of our corps—the friend of humanity—Major General William C. Gorgas in hastening, regardless of danger, to the relief of Serbia, sorely smitten by the deadly typhus fever?

Chenu's report gives a summary of the English as well as the French losses. Comparing it with Simpson's civil statistics eleven years later the mortality of the four selected amputations (arm, forearm, thigh and leg) was as follows: Of 2,089 of these four amputations in civil hospitals the mortality in Simpson's table was 41 per cent. In the Crimean War among the British there were 460 such amputations and 183 deaths, or 40 per cent. In the French army there were 5,972 such amputations with 4,023 deaths, a mortality of 67.4 per cent. In both armies

disarticulation at the hip-joint had a mortality of 100 per cent., *i.e.*, every case died. It is instructive also to compare the fate of those who had an amputation of the thigh (1,666 French cases) with a mortality of 92 per cent., and 487 cases treated conservatively, *i.e.*, without amputation, with a mortality of only 70 per cent.!

In our Civil War Duncan quotes the figures of Fox, which are "the latest revised statistics and are all larger than those of the Medical and Surgical History of the War." The average strength of the Union Armies was 806,755, and the deaths 359,528, of whom 67,058 were killed in battle and 43,012 died of wounds. This gives a battle death rate of 33 per 1,000 per annum. The disease death rate was 65 per 1,000 per annum. The case death rate from disease was only 3.4 per cent., a very low figure.

I can testify to the excellent condition of the Civil War hospitals, of which I saw many, but only in the East. When I say "excellent condition" it must be with the reserve that we knew nothing as to bacteriology, which did not exist, nor of infection, which was utterly unknown as to its causes and prevention. The general sanitary conditions, and by this I mean shelter, ventilation, cleanliness, good food, as good nursing as intelligent orderlies could give, etc., were all excellent. But the surgical conditions as we *now* know were simply dreadful. Practically every wound suppurated, and in summer I have seen many wounds swarming with squirming maggots as large as chestnut worms—disgusting, but, fortunately, not especially dangerous.

In my "Surgical Reminiscences of the Civil War"[16] I have given many statistics taken from the official Medical and Surgical History of the War, a few of which I will reproduce that you may see what blessed conditions you "free born" men have inherited. Pyemia (blood-poisoning) was one of our worst scourges. There were 2,818 cases, and of these only 71 recovered, a death rate

[16] Keen, *Addresses and Other Papers*, 1905, p. 420.

of 97.4 per cent. Few of you probably have seen even one such case. I have given a matter-of-fact description of it in my "Surgical Reminiscences," but if you wish to see it sketched by a master's hand read that most touching and beautiful of all medical stories I know—"Rab and His Friends," by dear old Dr. John Brown, of Edinburgh. He vividly paints the sudden change in the wound, the pulse, the eye, the mind, on and on, worse and worse, until "that *animula, blandula, vagula, hospes comesque* was about to flee."

Tetanus had a mortality of 89.3 per cent. Of amputations at the hip-joint 83.3 per cent. died. Trephining had a mortality of 61 per cent. Even of ligations of the femoral artery, 374 in number, 281 died, or over 75 per cent. Of 2,235 cases of secondary hemorrhage, 61.7 per cent. died. Hospital gangrene, of which there were several hundred cases, had only a mortality of about 25 per cent., because we early learned the correct though empirical treatment, viz., the application of the actual cautery, pure bromine, strong nitric acid or similar destructive agents which killed the germ, whatever it was, and arrested the disease.

The Franco-Prussian War of 1870-71 was marked by notable progress in military sanitation in the German army, yet in spite of this there were 74,205 cases of typhoid fever, almost 10 per cent. of the entire average strength (788,213) and 8,904 deaths, a mortality of 11.3 per cent.

Surgically the results were nothing to boast of. Listerism had as yet made but little progress in the profession. Carbolic acid was used to some extent, but there was no thorough antiseptic system, for the germ theory was as yet neither understood nor accepted.

Of tetanus there were 294 cases, and 268 died, a mortality of 91.1 per cent.

The total of the four selected amputations was 2,194 with 1,196 deaths, a mortality of 54.5 per cent.—over one-half.

Disarticulation at joints showed an average mortality of 56 per cent. Fifteen amputations at the hip-joint gave a mortality of 100 per cent., and resections claimed 40.2 per cent. of deaths. Even at the knee-joint Stromeyer amputated 36 times with 36 deaths and Nussbaum 34 times with 34 deaths.[17]

The French results were naturally worse, for their armies were constantly being defeated and retreating, and, especially in the latter part of the war, they consisted largely of volunteers, while the Germans were mostly veterans of the Schleswig-Holstein and Austro-Prussian wars.

Of the Boer War (1899-1901) only two features need be noticed. First, that typhoid attacked 57,684 men and killed 8,022, while the Boers only killed 7,781. Bacteria were more deadly than bullets, as Osler has said.

Secondly, the modern missile was for the first time in general use, with the result that instead of about 15 per cent. of the wounded losing their lives, only about 8.8 per cent. died. The wounds from the new missile were much less severe and healed more quickly than ever before. The first aid packet also had come to the aid of the soldier.

The Spanish American War, surgically speaking, was of little moment, as the numbers killed and wounded were too small to make the statistics of any great value, but it is gratifying to find that only 4.6 per cent. of the wounded died.

Typhoid, however, held high carnival. It caused 86.24 per cent. of all the deaths! Happily we can say that hereafter—thanks chiefly to the anti-typhoid inoculations—there will never be another such holocaust. (*Vide* Lecture 11.)

The statistics of the Russo-Japanese War also need detain us for only a moment. I shall only quote the Japanese official statistics, as given by Major Lynch, of

[17] Wrench's *Lister*, p. 236.

our army.[18] There were 47,387 killed. Of 173,425 wounded 11,500 died, a mortality of 6.7 per cent. The killed and those who died of wounds numbered in all 58,887, while the deaths from disease numbered only 27,158, a remarkable showing.

The present war naturally has yielded so far very few statistics. These can only be collected and tabulated after some years of peace. So far as I can judge, I fear that, while the mortality from disease (except perhaps from typhus, especially in Serbia) will be less than in former wars, the military conditions are such that the larger number of artillery wounds, the unavoidable delay in gathering the wounded into hospitals, the apparent absence of any truce for collecting the wounded and burying the dead, and the virulent infection from the soil may result in a large mortality rate and possibly a larger percentage than in previous wars in spite of the benefits of Listerism. But were the first-aid packet and the Listerian treatment not available the mortality ratio in this present horrible war unquestionably would be far greater than that which will be recorded.

This short résumé gives us some idea of surgical conditions preceding the great revolution inaugurated by Lister to which we will next proceed.

### LECTURE II., AFTER LISTER

Yesterday the dominant note was one of despair and defeat. To-day the dominant note shall be one of joy and victory.

Instead of hospitals reeking with pus and emptied by death, of operation after operation, when the roll was called, reporting a mortality of 40 per cent., 50, 75, 90, and even 100 per cent.—we have hospitals of immaculate whiteness and emptied by quick recovery, while the roll-call of operations reveals very few mortalities exceeding

[18] *Reports of Military Observers attached to the Armies in Manchuria during the Russo-Japanese War,* Part IV., p. 399.

10 per cent.; most of them having fallen to 5 per cent., 2 per cent., 1 per cent., and even small fractions of 1 per cent.

The story of Lister's work as recorded in his successive papers [1] is one of the most fascinating in all surgery. His earliest studies, from 1853 to 1863, were in physiology and pathology. Next he took up his researches on putrefaction (or as we should now say infection and suppuration) which led to his devising the antiseptic system. He was influenced to make these observations and experiments, which he applied with such signal success to surgical problems, by Pasteur's earlier researches. He always cheerfully acknowledged his debt to the eminent Frenchman. When a student in Paris in 1865 I knew Pouchet *fils* and was an interested spectator in the fight between Pasteur and Pouchet's father as to spontaneous generation. Lemaire's book on "Acide Phénique" (carbolic acid) was published in that same year.

Bacteriology did not exist as a science, but Pasteur, Lister and a few of the elect in the upper realms of imagination saw the "germs" or "microbes" and firmly believed them to be the cause of infection. In 1900, at the age of seventy-three, Lister restated his earlier work [2] and illuminated it by many observations, experiments and drawings made in these early years, but first published fifty years after they were made.

If you wish to know the man, his fertility in devising new and convincing experiments, and his mental acumen in interpreting them "read, mark, learn and inwardly digest" that paper and use it as a model.

Paré in his naïve way tells us that he sought various applications which might "mitigate the pains [of his patients] and happily"—mark the word *"happily"*—"bring them to suppuration." That is the "laudable pus" of the pre-Listerian days. Lister, on the contrary, believing that

[1] Lister's Collected Papers, 2 vols., Oxford, 1909.
[2] *Brit. Med. Jour.*, 1900, II., 969.

infection and suppuration were evils, and avoidable evils, sought by various means to prevent them. But he says "all my efforts [during his work in Glasgow, 1860-69] proved abortive," and then adds significantly *"as I could hardly wonder when I believed with chemists generally that putrefaction was caused by the oxygen of the air."*

They and he were deeply impressed with the absence of putrefaction in simple fractures when the air and its oxygen had no access to the fracture. In my own lectures, as I often used to express it, "The very best antiseptic dressing is an unbroken skin." In compound fractures on the other hand when the air and its oxygen *had* access to the lesion, putrefaction always took place and caused a frightful mortality.

To test this supposed noxious influence of oxygen he devised many experiments, and among them one which may be well called an "experimentum crucis." He filled four flasks one-third full of urine (a quickly putrescible liquid) and drew out the necks to tubes one-twelfth of an inch in diameter. All these tubes were *left open.* Three of these long necks he bent at various angles downwards; the fourth was left vertical upwards and also open. He then boiled all four flasks and awaited the result. The air and its oxygen had free access to the urine, being slowly drawn in during the colder night hours and driven out in the warmer daytime. Any supposed "germs" floating in the air, he reasoned, being heavier than air, could not climb up the slanting neck and fall into the liquid. In a short time the urine in the flask with the vertical open neck was decomposed, but the other three flasks, also with open necks but bent downward, *remained undecomposed for years!* [3] They were finally destroyed by a fire in the laboratory.

Could there be a more convincing proof that the oxygen

[3] For a fuller account of this interesting experiment with references see my *Animal Experimentation and Medical Progress,* pp. 204-205.

had no influence whatever in producing putrefaction, but that it was due to living matter, "germs," in the air? It was a fine instance of the "scientific use of the imagination." "Germs" had been observed from time to time, but had not been generally accepted as the *vera causa* of putrefaction. The experiment just related was tried about 1867. The commonest, all-pervading germs, the staphylococcus and streptococcus, were not identified and proved to be the chief pyogenic (pus-producing) organisms until 1881, fourteen years after Lister had seen them so clearly with his mind's eye! Even in 1898 when I published my "Surgical Complications and Sequels of Typhoid Fever" I had to prove by elaborate citations of experimental and clinical evidence that the typhoid bacillus itself could cause suppuration, and that it had actually been observed in the circulating blood—for the past ten years or more a work of supererogation.

From Glasgow Lister went to Edinburgh (1869) as the successor of his father-in-law, Syme, and continued to experiment, to practise and to publish, but only a few were convinced, among them being Syme himself.

On the continent in the early 70's Saxtorph in Copenhagen, Thiersch in Leipzig, Volkmann in Halle, Nussbaum in Munich, and Championnière in Paris were among Lister's earliest and enthusiastic disciples. In America not much attention was paid to his work until he visited Philadelphia in September, 1876, to attend the International Medical Congress held in connection with the Centennial Exhibition. He was made president of the Section on Surgery and read a paper on the antiseptic method.

At that time I heard him and became fully convinced of the truth of the "germ theory" and of the value of his antiseptic method. When I went on duty at St. Mary's Hospital, October 1, 1876, I adopted the system (and was the first surgeon in Philadelphia to do so) and have never

abandoned it. For me it changed surgery from Purgatory to Paradise.

But the reception given to his paper at our congress was anything but enthusiastic. The only surgeon who practically accepted Lister's method was that excellent St. Louis surgeon, John T. Hodgen. But so hazy were the general ideals of bacteria that in his own paper Hodgen speaks only of "germs" and "germinal matter" and had no idea of bacteriology as we know it, for the science, and even its name, did not yet exist.

In the discussion of Hodgen's paper Hewson advocated his then well-known views on the value of dry earth as an "antiseptic." Canniff of Toronto rejected *in toto* the germ theory of putrefaction. Frank Hamilton, of New York, while claiming extraordinarily good results from the open-air treatment and the warm-water treatment and other rival methods, "damned with faint praise" the antiseptic method. Kinloch, of Charleston, took the same attitude; Carpenter, of Pottsville, a Civil War surgeon, advocated chlorine in septic cases. Others sang pæans in praise of "perfect cleanliness" and said they "used both carbolic and salicylic acids, but *not* for the purpose of excluding germs." In the discussion on Lister's paper, Van Buren, of New York, doubted the safety of the spray in hernia and abdominal sections and Satterthwaite, of New York, rejected the germ theory of putrefaction.

In 1877 Girard, of the U. S. Army,[4] became the enthusiastic supporter of Listerism.

In 1880 Markoe, of New York, while admitting the fine results of Listerism, spoke of "its somewhat arrogant pretension to be the true and only gospel of the surgery of wounds." [5]

In 1882 Listerism was again discussed in the American Surgical Association. Briggs, of Nashville, endorsed Lister's method as "an epoch in surgery." Yet so limited was

[4] Circular No. 3, Surgeon General's Office, August 20, 1877.
[5] *Amer. Jour. Med. Sci.*, LXXIX., 1880, p. 305.

our knowledge of "germs" even then that warfare was waged only upon those "in the air." When these could be excluded he said "putrefaction . . . fails to occur." Yet Briggs qualifies his endorsement by saying that the

> supremacy [of the antiseptic method as contrasted with other methods of treatment] . . . cannot be demonstrated by statistics . . . and the present unsettled opinion concerning the proper status of his [Lister's] method is due in great measure to that fact.

He emphatically dissented from the germ theory, and added:

> Carbolic acid is the keystone of the Listerian wound treatment. . . . The germ theory is at fault and furnishes a very unstable foundation for a system of wound treatment.

Moore, of Rochester, N. Y., proposed to exclude the air

> by passing carbonic acid gas directly into the place where the operation is to be performed. In consequence of its being heavier than the atmosphere it preoccupies the space (!).

Campbell, of Georgia, "did not believe that bacteria . . . are the cause of that condition [suppuration]." The various men named were among our foremost American surgeons.

Lister's opponents entirely missed the great fundamental facts underlying the germ theory and Lister's antiseptic method, *viz.*, that infection in all its various forms was always of bacterial origin—a wholly novel and momentous idea. Each form of infection, *e.g.*, tetanus, tuberculosis, typhoid, etc., it was soon proved, arose in-

variably and solely from its own specific kind of germ. Whether carbolic acid or any other germicide was the best was a mere matter of detail and not of principle.

In commenting on this discussion in which one prominent speaker is said to have asserted that Listerism "is now dead"—a remark I do not find in the *Transactions—The Lancet*,[6] a belated, but then, and ever since, a real convert, truly said:

> Surely it is too late in the day to contest the truth of the germ theory.

Yet even a year later (1883) at the American Surgical Association while B. A. Watson, of Jersey City, fully accepted Listerism, other prominent surgeons of Philadelphia, New York, New Orleans, Mobile, and other cities even declared in the discussion that no surgeon in their cities or states used the method. McGraw, of Detroit; Dawson, of Cincinnati; Campbell, of Georgia; Prince, of Illinois, were "doubting Thomases," while Kinloch, of Charleston, and Nancrede, then of Philadelphia, advocated it.

But if its progress was obstructed in the United States, its foes in Great Britain were even more strenuous and for a season more successful.

In spite of the striking results in Glasgow and in Edinburgh Lister was looked at askance as "unorthodox."

In 1875 *The Lancet*[7] had said

> there is less antiseptic surgery practised in the metropolitan hospitals than ever there was.

At the Clinical Society[8] in a debate on antiseptic sur-

[6] July 1, 1882, p. 1088.
[7] October 16, 1875, p. 565.
[8] *Lancet*, October 30, 1875, p. 628.

gery in 1875, Mr. Maunder said with a fine, but, as the event showed, a too precipitate sarcasm:

> Mr. Lister expects to prevent traumatic fever and . . . suppuration.

Timothy Holmes, while professing to have used antiseptics "for some years," declared his disbelief in Mr. Lister's theory with regard to "germs." *The Lancet's* editorial on the debate said it was "evident that few of the speakers either place faith in Lister's theory or carry out his practice in full."

After eight years in Edinburgh Lister was chosen professor of surgery in King's College, London, in 1877. This was the last stand of his opponents. The *British Medical Journal,* however, heartily urged the appointment of "the great surgeon of Edinburgh."

October 1, Lister gave his first lecture. He took as his subject "Bacteriology," though not using that title for, as Stewart said, "as yet the science had not a name." [9]

Stewart [10] gives a vivid account of the dreary days during which he and the other assistants whom Lister had brought with him from Edinburgh wandered in the wards of other hospitals "heavy with the odor of suppuration" while Lister's own small wards were filled with empty beds. Instead of the Edinburgh crowds of "500 eager listeners" their "hearts were chilled by the listless air of the 12 or 20 students who lounged into lecture at King's" —only 12 or 20 students!

But a month later the tide turned.[11] A case of fractured patella was admitted and in violation of all surgical precedent, for in that septic era to open a knee-joint meant too often the loss of limb or even of life, Lister boldly

[9] The earliest instance of the use of the word "bacteriology" I have found is a quotation dated 1884 in the Oxford Dictionary.
[10] *Wrench,* p. 274 *et seq.*
[11] *Wrench,* p. 278 *et seq.*

opened the joint, but with every antiseptic precaution, and wired the two fragments together. This elicited the remark from a distinguished London surgeon:

> When this poor fellow dies, some one ought to proceed against that man for mal-practice.

But the man *got well.* Soon after this a case with an enormous malignant tumor of the thigh, which had been declined by other surgeons, came to Lister. He amputated the limb and,

> the members of the staff and students visiting this interesting patient were astonished to find him in a day or two sitting up in bed and reading a paper, being free from pain and free from fever.

A little later Paget and Hewitt both refused to operate on a lady of social importance with a large tumor of the shoulder-blade. Lister operated in the presence of Paget and Hewitt and she recovered without suppuration, fever or pain.

Yet two years later still (1879) Savory, Thomas Bryant, Tait and Spence, while claiming to practise antiseptic surgery so far as strict cleanliness was concerned, declined to subscribe to Lister's doctrines or to practise his method.

But the enthusiastic acclaim of the International Medical Congress in Amsterdam in that same year set the seal of approval of the profession at large. This may be said to be the date of the general acceptance of Lister's theory and Lister's method. London then capitulated.

In 1902, twenty-three years later, London made ample amends for its persistent early skepticism by a most generous outburst. The Royal Society, of which Lister had been president and from which he had received two medals, gave a banquet in honor of the jubilee of his doctorate. It was a most distinguished occasion and was made pre-

eminent by a most happy sentiment by Mr. Bayard the American Ambassador. Said he, addressing Lister:

> My Lord, it is not a Profession, it is not a Nation, it is Humanity itself which, with uncovered head, salutes you.

Better, far better, such a eulogium than the peerage which had been already bestowed upon him.

Having now traced so imperfectly the fortunes of the germ theory, let us see the results of Lister's labors. The first results are his own, especially in Glasgow. There the horrible conditions he has so startlingly portrayed [12] should have made his wards a charnel house.

The mortality in the other accident ward was so excessive that it had to be closed. But in Lister's ward, separated from the other only by a corridor twelve feet wide, for the nine months "in which his antiseptic system had been fairly in operation . . . not a single case of pyemia, erysipelas or hospital gangrene had occurred."

The reason for his first attempt to apply the antiseptic system to man is well stated in his very first paper on the antiseptic method in 1867.[13] He wrote:

> The frequency of disastrous consequences in compound fracture, contrasted with the complete immunity from danger to life or limb in simple fracture, is one of the most striking as well as melancholy facts in surgical practice.

Well might he say this, for while simple fractures had practically no mortality, the mortality of compound fractures was all the way from 28 to 68 per cent.! In this,

[12] *Lancet*, 1870, I., pp. 4, 40, and quoted in my *Animal Experimentation and Medical Progress*, pp. 216-218.

[13] *Lancet*, 1867, I., p. 326 *et seq.* and II., p. 95, and Lister's *Collected Papers*, II., p. 1.

his first paper, he reported in detail eleven cases, with one death, an unheard of mortality of only 9 per cent.!

Thus encouraged, he attacked with an equally happy outcome abscesses, especially that bane of surgery in those septic days, abscesses of the spine. Be it observed, too, that fifteen long years were to elapse before the tubercle bacillus, the cause of such abscesses, was discovered by Koch (1882).

From accidental wounds it was but a step to deliberately inflicted wounds, *i.e.*, surgical operations. Here, too, preventive antisepsis gave equally valuable results.

Lister, however, was more given to establishing principles and methods than to statistics, but some of his early disciples published striking proofs of the value of his method by contrasting their former results with those which followed the acceptance of the germ theory and the adoption of Lister's antiseptic treatment.

Thus Dennis [14] (1890) says that

> The time is within my own recollection when, in Bellevue Hospital, amputation was immediately performed as a routine treatment to prevent blood poisoning, upon the admittance of a compound fracture; and this operation was considered by surgeons as offering to the patient the only chance of recovery.

This but corroborates what Syme had already said in Edinburgh, that on the whole he was inclined to think

> it would be better if in every case of compound fracture of the leg amputation were done without any attempt to save the limb.[15]

Dennis in his paper reported 681 cases of compound fracture, with only 19 deaths, a mortality of only 2.8

[14] *Medical News*, April 19, 1890, p. 423.
[15] Cameron, *Brit. Med. Jour.*, Dec. 13, 1902, pp. 1844-1845.

per cent., and only one of these 19 deaths was from sepsis, or 1/7 of 1 per cent.!

In Nussbaum's insanitary hospital in Munich, which Lister visited in the summer or autumn of 1875, he states [16] that pyemia had been

> very frequent and hospital gangrene which made its appearance in 1872, had become annually a more and more frightful scourge until in 1874 it had reached the astounding proportion of 80 per cent. of all wounds that occurred in the hospital, whether accidental or inflicted by the surgeon!

After trying every possible different method of treatment and still being unable to combat hospital gangrene and pyemia, Nussbaum finally adopted Lister's full antiseptic treatment and from the beginning of 1875 they had *"not had one single case of hospital gangrene . . .* and *were doubtful whether they had had one case of pyemia";* and

> the convalescent wards—which previously had been filled and overflowing constantly—Lister saw standing one after another empty, because patients, no longer affected with hospital gangrene, recovered much more rapidly.

In Halle Volkmann [17] was operating in an extremely unhealthy hospital in small, overcrowded wards, with the toilet rooms opening directly into them and a large drain running directly underneath. It was so bad that it had been condemned to demolition. In the two years after his introduction of the antiseptic method in 1872, *no single patient suffering from compound fracture had died either from the fracture or from a necessary ampu-*

[16] *Brit. Med. Jour.*, 1875, II., p. 769, and *Lister's Works*, Vol. II., p. 248.

[17] *Lister's Works*, II., pp. 249-251, *Brit. Med. Jour.*, 1875, II., p. 769, and Lindpainter (Volkmann's assistant), *Deutsch Zeit. f. Chir.*, Oct., 1876, p. 187.

*tation, nor was there a single death from secondary hemorrhage or gangrene. No case of blood poisoning had occurred for a year and a half, though sixty amputations had been done.* Just before Lister's method had been introduced, of 17 amputations 11 had died from pyemia alone, a mortality of 65 per cent. Just after adopting Listerism the death rate of his amputations fell to 4 or 5 per cent.[18]

Hospital gangrene had been as it were "blown away" by a puff ("weggeblasen"); not a single case occurred. In Lindpainter's extensive tables of Nussbaum's cases one is struck, on glancing over them, to see how *before* the antiseptic method was adopted case after case is marked "died," "died," "died," and in the later tables, *after* its adoption, almost a uniform "recovered," "recovered," "recovered."

But the most striking testimony to the value of Lister's services to suffering humanity is not the statistics of the mortality in amputations, compound fractures, puerperal fever[19] or in any single disease or operation, but in the enormous and successful enlargement of the beneficent field of surgery. In my own early days "before Lister" the common operations were

1. Amputations.
2. Ligation of arteries.
3. Removal of external tumors.
4. Lithotomy.
5. Tracheotomy, chiefly for croup and foreign bodies.

A few resections, colostomies, trephining (when unavoidable) and herniotomies (for strangulation) were done. Ovariotomy was never done until the tumor had become so large as to threaten life, and even then operation was denounced by many as wholly unjustifiable, for it had a mortality as high as two out of every three cases. The

[18] *Lancet*, 1881, II., p. 281.

[19] See the extraordinarily interesting paper by J. Whitridge Williams, *Jour. Am. Med. Ass.*, April 22, 1911.

head, the chest, the abdomen were ticketed *"Noli me tangere"* except in the rare cases when operation was absolutely unavoidable.

I used to wonder why the students in "Rab and His Friends" rushed to the amphitheater to get the best seats to see Syme amputate a breast—a so very common operation nowadays. But then I recalled the fact that even in my student days, when anesthesia was the rule, capital operations were rare. But in the pre-anesthetic days operations were far rarer. In the *five years* preceding the introduction of ether at the Massachusetts General Hospital the *entire staff* only performed in all *184 operations* or *three operations a month.* When operations had become not only painless, but safe, then the number performed increased almost at a geometrical ratio, so that at present the numbers even of single operations by single surgeons—*e.g.,* of ovariotomies, appendectomies, goiters —mount into the thousands. What is still more gratifying, the usual death rates of most capital operations in the pre-Listerian days of one patient in four, in three, or in two, or even two out of three (!) have been changed to one in twenty, thirty, fifty, or to even less than one life lost in one hundred or even one in two hundred operations!

It is impressive—most impressive—to call the list of only the most frequent and the most important of our present operations. Were Mott, Bigelow or Pancoast—all of whom I remember well—to come to life again they would wonder whether we were not stark crazy.

The following list I have made—*currente calamo*—on the instant.

Amputations are far *less frequent.* After a single battle in the Russian campaign (1812), Larrey, Napoleon's great surgeon, performed not less than 200 amputations. To-day of 200 similar cases, sometimes even with wounds involving joints, the great majority would recover without amputation.

Formal ligations are far fewer.

External tumors of any size are now removed from all parts of the body without fear of erysipelas, which so worried Sir Astley Cooper before he operated on the king for a simple wen. The mere fact that any tumor is internal—inside the head, the chest, the abdomen, or the pelvis—has practically no influence on the decision whether it should or should not be removed.

Trephining—even for exploration—is frequent and *per se* involves slight danger, as in decompression.

Martin, of Berlin, has done over 1,000 ovariotomies, with a mortality of less than 2 per cent., and the Mayos from 1905 to 1914, inclusive (the only period for which I had the annual reports at hand), reported 609 cases with 5 deaths, or eight-tenths of 1 per cent. Colostomy and enterostomy are frequent. Many thousands of hernias have been cured by operation, with practically no mortality; and if done early in strangulation, with slight mortality.

The new surgery of the head attacks tumors even of the hypophysis, punctures the lateral and the fourth ventricles with impunity, successfully extracts foreign bodies and in some cases relieves epilepsy and mental derangements.

In the neck simple goiters even of large size are removed, with a mortality of 1 and 2 per cent.; and laryngectomy is common.

In the chest, that very citadel of life, the heart itself is sutured for gunshot and stab wounds, saving one life out of two; the esophagus is attacked for cancer and the removal of foreign bodies; large portions of the chest wall are removed for old empyemas, and the lungs can now be operated on at leisure, thanks to insufflation anesthesia.

In the abdomen, the various operations on the stomach, even to its total extirpation, are too many to name in detail; and with a success that is truly marvellous. We

play with the intestines at will, opening them for foreign bodies and for drainage of the contents, removing what we wish, anastomosing them and short circuiting their contents. Tumors of the liver unless malignant are extirpated with a very low mortality and wounds of its substance are treated with success; gall stones and gall bladders are removed every day; the spleen is anchored, sutured or removed as we find best; the pancreas is no longer inaccessible; the kidney and the ureter, like the stomach, have their own lists of operations far too long to rehearse.

In the pelvis the bladder is opened and partly or even wholly extirpated; the prostate removed; the uterus, the ovary, the tubes, the parovaria have a long list of life-saving, comfort-giving operations to their credit.

We suture and anastomose nerves; we suture and anastomose blood vessels even in the new-born, we criss-cross the circulating blood to prevent gangrene, and endo-aneurismorrhaphy has practically banished the Hunterian operation for aneurism and saved many a limb and life. We transplant skin and bones and joints, and even half joints, with success. To all these we have added the X-rays, the serum and vaccine treatment of many surgical disorders and are gradually throttling disease, sometimes at its very birth.

It almost takes one's breath away! Yet it is an incomplete and ever-lengthening list! As Mumford[20] well says:

> Daring has become conservatism; rashness has become common sense.

*Practically our ability to do all these life-saving operations is the result of the researches, the experiments, and the achievements of Lister and his followers. Had antisepsis not made all operations, including the opening of the head, the chest, the abdomen, and the pelvis, safe, we*

[20] Keen's *Surgery*, I., p. 76.

*should still be practising the very limited surgery of the 60's. Every year thousands whom now we restore to life and health would still be dying.*

What now are the prospects of Listerism in the present horrible war? I have so far used the term "antisepsis." Asepsis is a later and a natural development of antisepsis and in civil life is, of course, preferable. The underlying and enduring principle of Listerism—*the germ theory*—is the same in both. There is no fundamental antagonism, but really a fundamental agreement between the two methods.

In the present war the surgeons whose papers I have so far read are almost a unit in favor of the antiseptic rather than the aseptic treatment of the wounded. They are right in my opinion, and the reason is plain. Comparatively few of the wounded reach hospitals with uninfected wounds. Mild wounds, and even in some cases severe ones, if they can be dressed soon after being inflicted, heal readily.

Sir Anthony Bowlby's [21] striking description of the conditions in the trenches shows the difficulties very clearly:

> In this trench warfare, if a man is hit, he often falls into filthy mud and water, which may be three feet deep or more. The trench is only two and a half feet wide. It is night, you can only grope about in the dark and can do no dressing of any kind, for you can't even get any clothes off in the dark, and in so cramped a space, and you must try to get the man away to a "dressing station" half a mile distant, and thence to a field ambulance. If it is daylight, you can't get the man out of the trench at all, and he may have to be kept there for many hours, because he would certainly be killed if he were got out of the trench. And the water in the trenches is hopelessly polluted and soaks his clothes and his wound. Large

[21] *Jour. Am. Med. Ass.*, April 10, 1915, p. 1257

lacerated wounds, and especially bad bone smashes, are so contaminated that it can never be possible to render them aseptic.

There is a noteworthy difference between the results of the wounds in the case of the trench-inhabiting soldiers and the wounds of sailors. The latter escape the dangers of the soil-infected trenches.

Sailors with the most severe type of wound, ragged, irregular, with uneven surface produced by herniated muscle and retracted severed fibers, usually have recovered promptly. Soldiers suffering from slight wounds have often had them contaminated with bacilli from the soil; particularly the anaerobes.

Hypertonic salt solutions like sea water are actually remedial by promoting the flow of lymph and serum in the wounded tissues.

But in a very large number of wounded soldiers, possibly the majority, hours and sometimes even days of delay ensure infection and then the surgeon is face to face with the one overwhelming surgical problem which has so far baffled all our efforts, *viz., how to transform a septic wound into an aseptic wound and keep it so, and at the same time how to combat the toxins already diffused throughout the body, but without doing harm to the patient himself.* Cheyne,[22] Ehrlich, Wright and Carrel are all at work and it may be that the happy day when this, the most pressing and urgent problem in surgery, shall be solved, may come through this devastating war.[23]

[22] *Lancet,* Feb. 27, 1915, p. 419.

[23] In the *British Medical Journal* of April 10, 1915, a most important article by Sir Almoth E. Wright on "Wound Infections" is begun. This should be very carefully read. On pp. 735-738 of the same *Journal* for April 24, 1915, is another very important paper giving full directions for treatment. See also an interesting editorial in the *Journal American Medical Association,* May 23, 1915, p. 1765.

Meantime Souttar[24] extols plenty of fresh air or better still of oxygen (our old supposed enemies in the 60's) and says:

> Men with wounds so foul that their presence in the wards could not be permitted, were placed, suitably protected, in the open air, the wounds being left exposed to the winds of heaven, covered only with a thin piece of gauze. The results were almost magical, for in two or three days the wounds lost their odor and began to look clean, while the patient lost all signs of the poisoning which had been so marked before.

Of tetanus in our Civil War there were in the Union army in all 505 cases and 451 deaths, 89.3 per cent. In the War of 1870—1 in the German army there were 294 cases and 268 deaths, or 91.1 per cent. In the present war there have been many cases in the allied armies in the west, but I have seen no numbers or percentages. In the German army, however, Czerny[25] says that

> the greatest danger to the wounded had been tetanus. Of 60,000 wounded Bavarians, 420 developed tetanus, which proved fatal in 240 cases (57.1 per cent.). The prophylactic value of the tetanus serum had been established, but its extensive employment was not always feasible.

This is a far larger percentage of cases than in our Civil War, or the Franco-Prussian War, but the mortality is far less—probably due to the even partial employment of the serum.

During the Civil War I never saw a case of "gas gangrene" which has been so prevalent and dangerous in

[24] *Brit. Med. Jour.*, March 20, 1915, p. 504.
[25] *Brit. Med. Jour.*, March 20, 1915, p. 521.

the present war. The soil of Belgium and France, which has been cultivated and roamed over by animals for more than twenty centuries, is highly infected. Over ten different gas-producing bacteria have been found.

Sidney Rowland's experiment [26] well shows the virulent infection of the soil. Shaking up some of the soil from the trenches with some water, he injected a few drops into a guinea-pig and it was dead in eighteen hours with widely diffused gas gangrene. Soldiers have died from the disease in thirty-six hours.

Delorme has advised, as the germ is anaërobic, the injection of peroxide of hydrogen. Hartmann believes it needful to open the wounds freely and employ thorough irrigation with the peroxide [27]—a most important procedure. *Early* treatment of infected wounds even in cases of gas gangrene resulted favorably in the hands of Cazin. Of 158 cases received even up to forty-eight hours after battle all recovered in spite of their serious nature. Among those received after four or five days' transportation the mortality reached 10 and even 20 per cent.[28]

I have related the terrible mortality from typhoid in the Boer and the Spanish-American wars. The one bright spot in the present war is the conquest of typhoid. In spite of greatly increased numbers and of most unfavorable sanitary conditions in the trenches as I have shown, conditions which in former wars would have given rise to dreadful epidemics of typhoid, the following statistics in the British army officially given to Parliament on March 4, 1915,[29] show emphatically how well this scourge of every past campaign has been conquered. There had been only 606 cases in all: 247 among the partially (136) and fully (111) inoculated, with two deaths (0.81 per

[26] *Brit. Med. Jour.*, Nov. 28, 1914, p. 913.
[27] *Jour. Am. Med. Ass.*, Jan. 16, 1915, p. 259. See also Lawson and Whitehouse, *Brit. Jour. Surg.*, Jan. 9, 1915, p. 444.
[28] *Jour. Am. Med. Ass.*, Jan. 16, 1915, p. 259.
[29] *Brit. Med. Jour.*, March 13, 1915, p. 485.

cent.), and 359 among the unprotected, with 48 deaths (7.47 per cent.), over nine times as many deaths proportionately! The one reason for this splendid showing is the use of the antityphoid inoculation. If instead of its being only voluntary in the British army it had been compulsory as in our own army, the results would have been even better. And yet a blatant band of men and women both in England and our own country are doing all they can to oppose the use of this life-preserving remedy!

Let us now in conclusion take a general review of the surgical progress I have so inadequately sketched.

During the horrible days of Paré, Bell, Simpson, and our own Civil War there was still gradual improvement, but no *fundamental* change occurred for three centuries after Paré introduced the ligature and banished the boiling oil.

But about the middle of the nineteenth century, and especially in its last quarter, experimental research took the field. Everything that could be put to the test of accurate experiment in medicine and surgery was thoroughly investigated physically, physiologically, chemically, microscopically, biologically, bacteriologically. Laboratories were founded and research workers vied with each other in countless investigations. A flood of light was thrown upon every problem. And see the result in the long list I have just read to you! Medicine proper, obstetrics, all the specialties, sanitation and hygiene, furnish equally impressive calendars of progress—principally the result of experimental research.

Chief among these experimental researches were those of Pasteur (of whom I have said far too little for want of time) and of Lister. They inaugurated a wholly *new era* in surgery.

Then followed the battle for the germ theory and antiseptic surgery, ending in final victory. Meantime a new science, bacteriology, was born.

Next came the wide extension and application of the

new surgery to almost all the surgical ills that flesh is heir to. The wonderful results to both life and limb that I have recounted have naturally followed.

Even amid the disabilities and obstacles of war itself Lister's work has been a boon beyond price.

While the soldier and the scientist have been busy devising ever more frightful engines of destruction to maim and to kill, we surgeons have been equally busy devising means for saving thousands of lives and limbs in civil life, and even amid the carnage and savagery of war.

Surely our hearts should be lifted in gratitude to God for giving us such splendid powers of reasoning, experiment and research—all for the service of our fellow men.

In the five years since these lectures were delivered, the treatment of infected wounds has been revolutionized, and with the happiest results. The exact percentages have not yet been tabulated.

If seen within about the first twenty-four hours after the wound has been inflicted, the wounds were usually only "contaminated"; *i.e.*, the germs had only invaded the surface and had penetrated to a slight depth into the tissues. In this case, careful removal of all "foreign bodies," such as fragments of the missile, and especially of infected clothing carried deep into the wound, was thoroughly carried out. The wound was then widely opened down to the very bottom (débridement). This was followed by the entire removal of the layer of "contaminated" flesh to which as yet the bacteria were practically confined (épluchage). By these steps, the great bulk of the germs were removed mechanically. Moreover, this contaminated layer of tissue, owing to the injury done to it by the missile moving with enormous velocity, had had its vitality destroyed and was sure to die. Such dead and dying tissue was the most favorable food for the bacteria.

The wound could then be closed at once and immediate recovery, without fever or suppuration, followed in eighty

or ninety per cent. or even a larger percentage of the cases! The knife was the best "antiseptic."

In cases, in which by delay, the bacteria had invaded the tissues more deeply, débridement and épluchage alone were not sufficient. Then chemical disinfection, chiefly by the method of Carrel and Dakin, was employed. After a few days, or sometimes a few weeks, the bacteria would be destroyed and then the wound could be closed with success. The chemical used was bleaching powder or Sulfite of Soda in a weak solution. This fluid was distributed to every part of the wound by small rubber tubes, closed at the far end but with many small holes in the sides. By these means, the infected wound was kept constantly bathed in the antiseptic fluid and the germs were gradually destroyed.

Lister's fundamental postulate—*ridding the wounds of bacteria*—whether mechanically by the knife, or chemically by destroying them—was more firmly established than ever before.

When the Surgical History of the War is published, the wonderful results in saving life will be an astonishing story.

# THE MEASUREMENT AND UTILIZATION OF BRAIN POWER IN THE ARMY

BY

R. M. YERKES

*Chief, Section of Psychology, Office of the Surgeon-General*

*History of Psychological Service.*—The psychologists of America, of whom upward of two hundred served in the Army or Navy, have rendered conspicuously important assistance to the government in organizing an efficient fighting machine. Chief among the civilian agencies responsible for the development of this new and unexpectedly significant variety of service are the American Psychological Association and the Psychology Committee of the National Research Council. Nearly a score of committees or subcommittees of these organizations functioned during the military emergency.

Within the Army three principal groups of psychologists appear: one attached to the Office of the Adjutant General of the Army (specifically known as the Committee on Classification of Personnel in the Army), another in the Office of the Surgeon General of the Army (known as the Division of Psychology of the Medical Department), and a third in the Division of Military Aeronautics (the Psychological Section of the Medical Research Board). Although the several tasks of these groups of psychologists differed markedly, the primary purpose of each was the increase of military efficiency through im-

proved placement with respect alike to occupational and mental classifications.

Psychological service was rendered also to the following divisions or departments in addition to those named above: (1) the Morale Branch of the General Staff, (2) the Division of Military Intelligence, (3) the Committee on Education and Special Training of the War Department, and (4) the Chemical Warfare Service.[1]

Early in the emergency it became clear to psychologists in the military service that the fundamental psychological problem of the army is one of placement and that the most important service psychologists could possibly render would be to assist in so assigning every soldier that his mental (as well as physical) ability should be used to advantage. It was assumed by the psychological personnel that intelligence, alertness, the will to win, enthusiasm, faith, courage and leadership are even more important than are physical strength and endurance, and that this fact must be scientifically reckoned with wherever a strong military organization is to be built quickly. Very promptly it became the recognized purpose of army psychologists to assist in winning the war by the scientific utilization of brain power. The achievement of this purpose necessitated the preparation of special methods of mental measurement in order that recruits should be properly classified for elimination or assignment to military training.

The army, at first naturally and wisely skeptical concerning the practical values of psychological service and

[1] For the United States Navy serviceable methods of selecting, placing and training gunners, listeners and lookouts were devised and developed by Lieutenant Commander Raymond Dodge. The methods prepared by Dr. Dodge as well as certain instruments designed by him for naval use have been extensively and profitably used, and the appointment of this psychologist as Lieutenant Commander in the Naval Reserve is at once a fitting recognition of his practical service and an indication of the appreciation of his work by the officers with whom he has been associated.

inclined to anticipate research instead of service, shortly achieved a new point of view and opinion. Skepticism was replaced in some directions gradually, elsewhere rapidly, by faith in the practicability and immediate value of various kinds of psychological work and eagerness for its continuation and extension. In the end the psychological personnel of the army was completely swamped by requests, demands and orders for help. Scores of telegrams and letters from commanding officers testify to their hearty appreciation of efforts towards scientific placement within the army and their desire for the introduction or furtherance of psychological service in various departments or organizations.

Skeptics, of course, still exist and there are inevitable misunderstandings and prejudices, but the data at hand indicate that at least seventy-five per cent. of the officers of the United States Army have been won by actual demonstration of values and first hand acquaintance with psychological service to its hearty support.

It is extremely important to emphasize at the outset that this article deals with only one of the several important lines of psychological military service, that, namely, of the Division of Psychology of the Medical Department.

*Purposes of Mental Examining.*—As originally conceived, psychological service within the Medical Department was to assist medical officers, and especially neuro-psychiatric officers, in discovering and eliminating men who are mentally unfit for military duty. It appeared, prior to actual trial, that reasonably well planned methods of mental measurement should enable psychological examiners to discover mentally inferior recruits as soon as they arrived in camp and to make suitable recommendation concerning them to the medical officer. It was also believed that psychologists could assist neuro-psychiatrists in the examination of psychotic individuals. The proposed rôle of the psychologist then was that of assistant

to the army surgeon: the actual rôle, as a result of demonstration of values, was that of expert in scientific personnel work.

In interesting contrast with the original purpose of mental examining, as stated above, stands the following account of the purposes actually achieved by this service: (1) The assignment of an intelligence rating to every soldier on the basis of systematic examination; (2) the designation and selection of men whose superior intelligence indicates the desirability of advancement or special assignment; (3) the prompt selection and recommendation for development battalions of men who are so ininferior mentally as to be unsuitable for regular military training; (4) the provision of measurements of mental ability which shall enable assigning officers to build organizations of uniform mental strength or in accordance with definite specifications concerning intelligence requirements; (5) the selection of men for various types of military duty or for special assignments, as for example, to military training schools, colleges or technical schools; (6) the provision of data for the formation of special training groups within the regiment or battery in order that each man may receive instruction suited to his ability to learn; (7) the early discovery and recommendation for elimination of men whose intelligence is so inferior that they cannot be used to advantage in any line of military service.

Although it originally seemed that psychological examining naturally belonged in the Medical Department of the Army and would there prove most useful, it subsequently became evident that this is not true because the service rendered by psychological examiners is only in part medical in its relations and values. In the main its significance relates to placement and its natural affiliation is with military personnel. For practical as well as logical reasons it would doubtless have been wiser had the service of the Division of Psychology been associated

from the first with that of the Committee on Classification of Personnel in the Army, so that the psychological as well as occupational, educational and other important data might have been assembled by a single military agency and promptly rendered available for use in connection with the assignment of recruits. Thus also the organization of a special branch of the General Staff or of a Personnel Section of the Adjutant General's Office to deal with varied problems of military personnel might have been hastened and otherwise facilitated and the utilization of brain power as contrasted with man power in the ordinary sense rendered more satisfactory early in the emergency.

*Methods of Measuring Intelligence.*—The committee of psychologists originally organized to prepare and test methods of psychological examining for the army promptly decided that it would be desirable to examine *all* recruits in order to provide an intelligence rating for every soldier. This decision necessitated the development of methods which could be administered to relatively large groups and in addition the selection of procedures which could be used for the more careful examination of individuals.

Most of the methods which were recommended to the military authorities in the summer of 1917 have since that time been repeatedly revised and improved in the light of results. The procedures finally adopted and in use throughout the army during the past few months differ radically from those originally recommended. They may be described summarily as follows:

There are four principal systems or stages in the examination. First comes the procedure of segregation, by means of which the original group, which may, if examining rooms permit, include as many as five hundred men, is split into two sub-groups; (*a*) the literates, men who can speak and read English fairly well, and (*b*) the illiterates, men who are relatively unfamiliar with the

English language. These two groups must necessarily be treated somewhat differently, therefore the literates are given a group examination known as Alpha, which consists of eight markedly different tests. This examination, although it requires almost no writing on the part of the subject, does demand facility in using written and oral instructions. The illiterate group is given an examination known as Beta, which is in effect Alpha translated into pictorial form. In this examination pantomime and demonstration supplant written and oral instructions.

Each group examination requires approximately fifty minutes. Subjects who fail in Alpha are ordinarily given opportunity to improve their ratings by taking Beta, and subjects who fail in Beta are given individual examination in order that they may be more accurately and justly rated than in the group examination alone.

Any particular individual may have to take one, two or three of these types of examination, thus for example, a man of low grade literacy who happens to get into examination Alpha may also have to take Beta and some form of individual examination.

Examination papers for both Alpha and Beta are scored rapidly by the use of stencils and the resulting rating is promptly reported to the appropriate military authority.

By means of this system of examinations it is possible for an examining staff consisting of four psychologists and a force of scoring clerks to examine as many as one thousand men per day.

Every man examined by one or more of the procedures described is assigned a numerical rating and in addition a letter grade which indicate his general intellectual ability or mental alertness. The numerical rating is used only for statistical purposes, the letter grade for practical military purposes. The latter alone is reported ordinarily to military officers and recorded on the soldier's service record and qualification card.

The letter grades which are in use are defined as follows: A designates very superior intelligence; B, superior intelligence; C +, high average intelligence; C, average intelligence; C —, low average intelligence; D, inferior intelligence; D —, very inferior intelligence. The letter E has been reserved for the designation of men whose mental ability is seemingly inadequate for regular military duty.

Commissioned officers usually possess and obviously should possess A or B intelligence. Many excellent non-commissioned officers possess C or C + intelligence, but in the main this group is composed of men with C+ or B ratings. The great body of privates grades C. Men with D or D — intelligence are usually slow to learn and rarely gain promotion. Many of them, especially the D — individuals, cannot be used to advantage in a military emergency which demands rapidity of training. The results of army mental testing indicate that the majority of D — and E soldiers are below ten years mental age. A few fall as low as three or four years.

The contrast between A and D — intelligence becomes impressive when it is shown that men of A intelligence have the requisite mental ability to achieve superior records in college or professional school, whereas D — individuals are rarely able to pass beyond the third or fourth grade of an elementary school, however long they may attend.

*Reliability of Methods.*—The methods of mental examining used in the army have been found to possess reliability as well as practical value which far exceeded the expectations of the men who are responsible for them. Indeed, the success of this particular methodological undertaking is a remarkable demonstration of the "fecundity of aggregation." It is extremely unlikely that any individual working alone would have developed within reasonable time equally valuable methods of group examining. Inasmuch as reliability is of first importance,

various measures of the validity of the army mental tests are presented.

The probable error of an Alpha score is about five points. This is approximately one-eighth of the standard deviation of the scores for unselected soldiers. The reliability coefficient of examination Alpha approximates .95. This group examination correlates with other measures of mental ability as follows: (1) With officers' ratings of their men, .50 to .70 for the total Alpha score and .30 to .54 for the separate tests; (2) with Stanford-Binet measures of intelligence, .80 to .90 for the total Alpha score and .31 to .85 for the separate tests; (3) with the Trabue B and C Completion tests combined, .72 for the total score and .39 to .76 for the separate tests; (4) with Examination Beta, .80; (5) with the composite result of Alpha, Beta and Stanford-Binet examinations, .94; (6) in the case of school children results of Alpha examination correlate (*a*) with teachers' ratings .67 to .82, (*b*) with school marks .50 to .60, (*c*) with school grade location of thirteen and fourteen-year-old children .75 to .91, (*d*) with age of children .83 (for soldiers the correlation of Alpha score with age is practically zero).

The Alpha examination given with double the usual time allowance correlates approximately .97 with the regular time examination.

The following data indicate the reliability of Examination Beta: It correlates with Alpha, .80; with Stanford-Binet, .73; with the composite of Alpha, Beta and Stanford-Binet, .915. The correlation of the separate Beta tests with the Stanford-Binet ranges from .47 to .63 (average .58). Results of Beta given with double time allowance correlate with those obtained with the regular time allowance .95.

For the several forms of individual examination used in the army the principal correlations at present available are as follows:

Results obtained by repetition of Stanford-Binet ex-

amination of school children correlate .94 to .97. Results of one-half of the scale compared with the other half correlate .94 to .96. An abbreviated form of the Stanford-Binet examination consisting of two tests per year was used extensively in the army. The results of this abbreviated scale correlate .92 with those obtained by use of the complete scale.

For the Point Scale examination the measures of reliability are practically the same as for the Stanford-Binet.

A Performance Scale examination prepared especially for military use consisted of ten tests. Results for the several tests of the scale correlate with Stanford-Binet results, .48 to .78. Five of the ten tests yield a total score which correlates .84 with the Stanford-Binet score. The same five tests correlate .97 with the results of the entire scale.

*Summary of Results.*—After preliminary trial in four contonments psychological examining was extended by the War Department to the entire army, excepting only field and general officers. To supply the requisite personnel, a school for training in military psychology was established in the Medical Officers' Training Camp, Fort Oglethorpe, Georgia. Approximately one hundred officers and more than three hundred enlisted men received training at this school.

The work of mental examining was organized finally in thirty-five army training camps. A grand total of 1,726,000 men had been given psychological examination prior to January 1, 1919. Of this number, about 41,000 were commissioned officers. More than 83,000 of the enlisted men included in the total had been given individual examination in addition to the group examination for literates, for illiterates, or both.

Between April 27 and November 30, 1918, 7,749 (0.5 per cent.) men were reported for discharge by psychological examiners because of mental inferiority. The recom-

mendations for assignment to labor battalions because of low grade intelligence, number 9,871 (0.6 + per cent.). For assignment to development battalions, in order that they might be more carefully observed and given preliminary training to discover, if possible, ways of using them in the army, 9,432 (0.6 + per cent.) men were recommended.

During this same interval there were reported 4,744 men with mental age below seven years; 7,762, between seven and eight years; 14,566, between eight and nine years; 18,581, between nine and ten years. This gives a total of 45,653 men under ten years mental age. It is extremely improbable that many of these individuals were worth what it cost the government to maintain, equip and train them for military service.

The psychological rating of a man was reported promptly to the personnel adjutant and to the company commander. In addition, all low grade cases and men exhibiting peculiarities of behavior were reported also to the medical officer. The mental rating was thus made available for use in connection with rejection or discharge, the assignment of men to organizations and their selection for special tasks. The mental ratings were used in various ways by commanding officers to increase the efficiency of training and to strengthen organizations by improved placement.

It was recently stated and emphasized by psychological examiners that a man's value to the service should not be judged by his intelligence alone, but that instead temperamental characteristics, reliability, ability to lead and to "carry on" under varied conditions should be taken into account. Even after the feasibility of securing a fairly reliable measure of every soldier's intelligence or mental alertness had been demonstrated, it remained uncertain whether these measurements would correlate positively with military value to a sufficient degree to render them useful. Data which have become available during

the past year settle this question definitely by indicating a relatively high correlation between officers' judgments of military value and the intelligence rating.

The various figures herein described are presented not as a summary of the results of psychological examining in the army but instead as samples of these results, the chief value of which is to indicate their principal relationship and practical values.

*Military Applications of Mental Ratings.*—By sample distribution curves Fig. 1 indicates the value of mental ratings for the identification and segregation of different kinds of military material. The illiterate group of this figure was examined by means of Beta, all other groups by means of Alpha.

Comparison of various military groups distinguished from one another by actual attainment in the service shows that the psychological tests discriminate between these groups with definiteness. This point may be illustrated by reference to the percentages of men of different groups making A and B grades in Examination Alpha: officers, 83.0 per cent.; officers' training school candidates, 73.2 per cent.; sergeants, 53.4 per cent.; corporals, 39.7 per cent.; literate privates, 18.8 per cent. The comparison of measures of central tendency reveals equally striking differences. Moreover, within the officer group itself significant differences appear for different branches of the service.

The relation of success or failure in officers' training schools to intelligence ratings is exhibited by Fig. 2, in which it is indicated that elimination through failure in the school increases rapidly for ratings below C +. Of men rating above C +, 8.65 per cent. were eliminated; of those below C +, 52.27 per cent. The data for this figure were obtained from three schools with a total enrollment of 1,375 men.

Similarly Fig. 3 indicates the relation between success or failure in non-commissioned officers' training schools and

intelligence ratings. The elimination increases rapidly for grades below C +. Of men rating above C, only 18.49 per cent. were eliminated; of men rating below C, 62.41 per cent. The results presented in this figure were obtained from four schools with a total enrollment of 1,458 men.

Increasingly extensive and effective use has been made of the psychological rating as an aid in the selection of men for officers' training schools, non-commissioned officers' training schools and other lines of training or service which require special ability. It has been convincingly demonstrated that the data of psychological examinations can readily be used to diminish the necessary elimination during training and thus to increase the efficiency of the schools.

The extreme differences in the intellectual status of army groups are fairly indicated by Fig. 4, which presents the data for groups whose military importance cannot readily be overemphasized. Roughly, the groups in the upper half of the figure are important because of their relatively high intelligence and the mental initiative demanded for success, whereas those in the lower half of the figure are important because of poor intelligence and relative inefficiency or uselessness.

These results suggest that if military efficiency alone were to be considered, the army would undoubtedly gain largely by rejecting all D — and E men. This procedure would greatly lessen the group of disciplinary cases so troublesome and costly in the military organization and also the group which in the figure is distributed among "ten poorest privates," "men of low military value" and "unteachable men."

Numerous varieties of evidence indicate the extreme military importance of the prompt recognition of low grade men. The percentages of men ranking below the average in psychological examinations are notably large for the disciplinary group, men having difficulties in drill,

men reported as "unteachable" and men designated by their officers as "poorest" from the standpoint of military usefulness.

The comparison of negro with white recruits reveals markedly lower mental ratings for the former. A further significant difference based on geographic classification has been noted in that the northern negroes are mentally much superior to the southern.

The relation between officers' judgments of the value of their men and intelligence ratings is exhibited in somewhat different ways by Figs. 5 to 7. Thus the median scores for five groups of privates arranged in order of military value from "very poor" to "best" are presented in Fig. 5. The total number of individuals in the group is 374. The men were selected from twelve different companies, approximately thirty men in each company being ranked by an officer in serial order from "best" to "poorest." The rank order for each company was then correlated by the psychological examiner with the rank order supplied by psychological examination. In seven of the twelve companies the correlations ranged from .64 to .75. The average correlation was .536. These correlations are high, considering the large number of factors which may influence a man's value to the service.

The median score for the "very poor" group of Fig. 5 is 28 points in an examination whose maximal score is 212 points. By contrast with this, the median score of the "best" group of privates is 99 points.

The commanding officers of ten different organizations, representing various arms of the service, in a certain camp were asked to designate (1) the most efficient men in their organizations, (2) the men of average ability and (3) men so inferior that they are "barely able" to perform their duties.

The officers of these organizations had been with their men from six to twelve months and knew them exceptionally well. The total number of men rated was 965, about

equally divided among "best," "average," and "poorest." After the officers' ratings had been made, the men were given the usual psychological test. Comparison of test results with officers' ratings showed:

(*a*) That the average score of the "best" group was approximately twice as high as the average score of the "poorest" group.

(*b*) That of men testing below C —, 70 per cent. were classed as "poorest" and only 4.4 per cent. as "best."

(*c*) That of men testing above C +, 15 per cent. were classed as "poorest" and 55.5 per cent. as "best."

(*d*) That the man who tests above C + is about fourteen times as likely to be classed "best" as the man who tests below C —.

(*e*) That the per cent. classed as "best" in the various groups increased steadily from 0 per cent. in D — to 57.7 per cent. in A, while the per cent. classed as "poorest" decreased steadily from 80 per cent. in D — to 11.5 per cent. in A.

In an infantry regiment of another camp were 765 men (regulars) who had been with their officers for several months. The company commanders were asked to rate these men as 1, 2, 3, 4 or 5 according to "practical soldier value," 1 being highest and 5 lowest. The men were then tested, with the following results:

(*a*) Of 76 men who earned the grade A or B, none was rated "5" and only 9 were rated "3" or "4."

(*b*) Of 238 "D" and "D —" men, only one received the rating "1," and only 7 received a rating of "2."

(*c*) Psychological ratings and ratings of company commanders were identical in 49.5 per cent. of all cases. There was agreement within one step in 88.4 per cent. of cases, and disagreement of more than two steps in only .7 per cent. of cases.

Fig. 6 exhibits a striking contrast in the intelligence status and distribution of "best" and "poorest" privates. The personal judgment data for this figure were obtained

from sixty company commanders who were requested to designate their ten "best" and their ten "poorest" privates. Of the "poorest," 57.5 per cent. graded D or D—; less than 3 per cent. graded A or B. The results suggest that intelligence is likely to prove the most important single factor in determining a man's value to the military service.

In one training camp excellent opportunity was offered to compare a group of soldiers selected on the basis of low military value with a complete draft quota. In the "low value" group there were 147 men, in the complete draft quota 12,341 men. The distributions of intelligence ratings for these two military groups appear as Fig. 7, from which it is clear that if all men with intelligence ratings below C— had been eliminated, the "low value" group would have been reduced by at least half.

In a certain training camp 221 inapt soldiers, belonging to a negro regiment of Pioneer Infantry, were referred by their commanding officer for special psychological examination. Nearly one-half (109) of these men were found to have mental ages of seven years or less. *The army nevertheless had been attempting to train these men for military service.* In justice to the Psychological Service it should be stated that these negroes had been transferred from camps where there were no psychological examiners. For this reason they had not been examined before being assigned to an organization for regular training.

In another instance some 306 soldiers from organizations about to be sent overseas were designated by their commanding officers as unfit for foreign service. They were referred for psychological examination with the result that 90 per cent. were discovered to be ten years or less in mental age, and 80 per cent. nine years or less.

It has been discovered that when soldiers are assigned to training units without regard to intelligence, extreme inequalities in the mental strength of companies and regi-

ments appear. This fact is strikingly exhibited by Figs. 8 and 9, of which the former shows the proportions of high grade and of illiterate or foreign soldiers in the various companies of an infantry regiment. Compare, for example, the intelligence status of C and E companies. The former happens to have received only 3 per cent. of A and B men along with 38 per cent. of illiterates and foreigners, the latter received by contrast 29 per cent. of high grade men with only 9 per cent. of men who are as a rule difficult to train. It is needless to attempt to emphasize the military importance of this condition. The tasks of the officers of these two companies are wholly incomparable, but more serious even than the inequalities in response to training are the risks of weak points in the army chain as a result of such random or unintelligent assignment.

Naturally enough the officers of the army were quick to appreciate the disadvantages of a method of assigning recruits which permits such extreme inequalities in mental strength to appear and persist. They promptly demanded the reorganization of improperly constituted units and assignment in accordance with intelligence specifications so that the danger of weak links in the chain and of extreme difference in rapidity of training should be minimized.

That serious inequalities existed in regiments as well as in smaller units prior to assignment on the basis of intelligence is proved by the data of Fig. 9, which records the differences found in four infantry regiments and three regiments of field artillery.

Following the demonstration of the value of psychological ratings in connection with assignment, the experiment was tried in various camps of classifying men in accordance with intelligence for facilitation of training. To this end A and B grade men were placed in one training group, C +, C and C — men in another, and D and D — men in a third. The three groups were then instructed and drilled

in accordance with their ability to learn. Thus delay in the progress of high grade men was avoided and the low grade soldiers were given special instruction in accordance with their needs and capacity.

The marked differences in the mental strength of groups in different officers' training schools are shown by Fig. 10. For the eighteen schools of this figure, the proportion of A grades varies from 16.6 per cent. to 62.4; the proportion of A and B grades combined, from 48.9 per cent. to 93.6 per cent.; and the proportion of grades below C +, from 0 to 17.9 per cent. Since it is unusual for a man with an intelligence rating below C + to make a satisfactory record in an officers' training school, it is clear that the pedagogic treatment of these several student groups should differ more or less radically and that elimination must vary through a wide range if the several schools are to graduate equally satisfactory groups of officers.

Far more important than the contrast in student officers training groups noted above are the differences in the intelligence status of officers in different arms of the service as revealed by psychological examining. Figure 11 exhibits the data obtained for several groups. The variations are extreme and seemingly unrelated to the requirements of the service. Medical officers, for example, show a relatively large percentage of men rating C + or below, whereas engineering officers head the list with relatively few men whose intelligence is rated below B. There is no obvious reason for assuming that the military duties of the engineer demand higher intelligence or more mental alertness than do those of the medical officer. Since it is improbable that any arm of the service possesses more intelligence than can be used to advantage, the necessary inference is that certain arms would benefit by the elimination of low grade men and the substitution of officers with better intellectual ability.

*Relation of Intelligence to Occupation.*—The occupa-

tional classification of soldiers in the army afforded opportunity for a study of the relation of intelligence to occupation. Various features of this relation are exhibited for a few military occupations by Fig. 12, in which are represented the proportions of the several grades of intelligence for the several occupations.

In order of diminishing intelligence exhibited these groups may be classified as follows: professions, clerical occupations, trades, partially skilled labor and unskilled labor. The greatest differences in intelligence required or exhibited appear at the upper end of the scale, whereas the differences within the trade group are relatively small. The differences in range of intelligence occurring in the several occupations are considerable and in all probability significant. In general the range diminishes from unskilled labor to intellectually difficult professions.

The data of this occupational study, which are merely sampled by Fig. 12, suggest both the possibility and desirability of preparing intelligence specifications for use in connection with civilian occupations. Such specifications, if satisfactorily prepared, should be useful alike as partial basis for educational advice and procedure and subsequently for vocational guidance. It must be emphasized in this connection that the data of Fig. 12 are not strictly comparable with such information as may be gathered concerning civilian groups because various selectional factors operate in the army.

*The Applicability of Mental Measurements.*—The utilization of methods of mental testing by the army has at once increased military efficiency by the improved utilization of brain power and demonstrated the applicability of the group method of measuring intelligence to educational and industrial needs. The army methods, although not adapted to the usual educational or industrial requirements, can readily be modified or used as a basis for the development of similar procedures.

There are abundant indications that the future will wit-

ness the rapid development of varied methods for improving scientific placement and vocational guidance. It is highly probable that grading in the public schools, in colleges and professional schools will shortly be based in part upon measurement of mental ability instead of exclusively on measurements of acquisition. The war has worked a miracle for what may properly be called mental engineering by precipitating expectations, surmises and desires which have long sought expression. Yesterday a few men believed in the probability of the early appearance and practical usefulness of this new branch of engineering; to-day scores of business men, educators and men of other scientific professions are convinced that it has arrived and demand its rapid and effective development.

The complete scientific report on the psychological data which the army has supplied and of which mere glimpses have been given in this article should constitute the basis for further important advances in methods of mental measurement and should greatly add to the knowledge of the distribution of intelligence and its varied and significant relations. These reports are in preparation and it is hoped that they may be published without undue delay.

# XII. CONCEPTIONS AND MISCONCEPTIONS IN PSYCHOANALYSIS

(Read before the Harvey Society of Johns Hopkins University)

BY

TRIGANT BURROW, M.D.

NOT infrequently a discussion purporting to relate to a given subject expresses nothing more than the unsophisticated views of the speaker concerning some notion or other which he mistakenly conceives the subject to be. Perhaps no theme has suffered more from the disfigurements of these naïve tendencies than psychoanalysis, so that one does well to distinguish between psychoanalysis and rumors of psychoanalysis.

The truth is, psychoanalysis labors under the grave difficulties surrounding any subject which offers us an entirely novel point of interpretation; and far more formidable than the barriers of novelty and strangeness is the fact that psychoanalysis is a method which is essentially revolting to our conventional social consciousness, entailing harsh incriminations from which we would prefer to turn away. It is a therapeutic procedure which our moral conventions hold in natural repugnance; it is an unpleasant discipline that thrusts before us those things which we dislike to look on. But if the theory on which the method rests is correct, such an inbred antagonism to the precepts of psychoanalysis is of the very essence of its thesis, for

psychoanalysis, rightly understood, is a method of treatment based on the recognition of a psychic conflict in the life of the patient arising precisely from his inherent revulsion against the artificial inhibitions which are imposed on him under the constitution of society. The conflict is therefore a social one.

It would seem, then, that we all have within us the elements of the neurotic diathesis; that the difference between the normal and the neurotic is more a matter of circumstances than of constitution; that the interval between the two is proportional rather than generic.

If, therefore, psychoanalysis, unlike the gently conciliatory procedures characteristic of other forms of psychotherapy, is a method whose specific task it is to lay bare the pious devices through which we seek to evade life's sterner verities, we shall very naturally incline to resent it as an impertinent intrusion. Indeed, it requires no small measure of courage to view with equanimity the unwelcome factors which psychoanalysis thrusts before our eyes.

It is, then, because of the essential significance of psychoanalysis, with its open hostility to the wide social repression of those insatiate biologic demands which belong, broadly speaking, to the sexual sphere, and the consequent affront it offers to our habitual sense of outward reserve, that I am led to utter a warning lest in estimating the value of this inimical method we allow traditional prejudice to distort our judgment.

The psychoanalytic method, introduced by Sigmund Freud, is, of course, concerned solely with the treatment of nervous disorders. In reality the term "nervousness" or "neurosis," as commonly applied, is etymologically misleading, for the morbid condition involved in such psychic disturbances is not neural; it is moral. There is question not of a disease of the tissues but of a disharmony of the personality; not of a lesion of organs but of a schism of consciousness. We are dealing not with the pathology of

the neural elements but with the psychology of the social element as presented in the individual unit, for the disturbances with which psychoanalysis has to cope entail in every instance a psychic disharmony based on the individual's relation to the social environment. It is an interesting fact that in every psychoanalysis there is discovered the influence of some hidden presence who stands in such instance in the closest personal relation to the patient and constitutes the important factor in the production of the neurosis.

Before considering, however, the theory, the instruments and the aims of psychoanalysis, it may be well to mention certain misconceptions in regard to the method. Perhaps we shall gain ground if, before attempting to say something of what psychoanalysis *is,* I say a word as to what psychoanalysis is *not.*

Already I have made intimation of the element of sexuality as an etiologic factor in the manifestations we call neurotic. Many will doubtless have heard of the inevitable implication in the psychoanalytic method of treatment of the sexual sphere of the patient's life. Some probably will either have explicitly heard, or have tacitly gathered, that psychoanalytic presupposes the existence in the life of the patient of some secret perversion of the sexual instinct, and that it is the task of the psychoanalyst to extort a confession of some such hidden misdemeanor. Therefore it is but natural if, from the prevailing trend of current hearsay, it will have been inferred that this new method of psychotherapy proceeds on the assumption that nervous disorders—hysteria, obsessional and imperative states, so-called neurasthenia and psychasthenia—are invariably to be explained by the hidden presence of some abnormal mode of sexual indulgence, and, therefore, the origin of a neurosis, according to Freud's interpretation, is linked with the idea of some species of sexual delinquency.

As widespread as this conception has become, nothing

could be further from the truth. In point of fact, the proposition it maintains is precisely the contrary of that posited by psychoanalysis. In his "Drei-Abhandlungen zur Sexualtheorie," Freud [1] clearly defines the neurosis as the negation of abnormal sexuality. He distinctly says that the neurotic and the sexual delinquent stand at exactly opposite poles to one another. It cannot be too strongly emphasized, therefore that the manner in which the patient's sexuality is related, according to Freud's interpretation, to the etiology of neurotic disorders is one which, far from incriminating him, wholly absolves him from the stigma of abnormal sexuality.

Still another very prevalent misapprehension is the view that psychoanalysis is synonymous with the obtaining of a general confession from the patient.

Far be it from me to deny the time-honored psychotherapeutic axiom that an honest confession is good for the soul. No one, I think, realizes better than the psychopathologist the undoubtedly remedial effect which follows on the unbosoming of some secret conflict in the mental life. But the whole point in the psychoanalytic interpretation of the neuroses is that these disorders arise precisely from conditions which render voluntary confession impossible, it being the nature of the disturbing element that it remains of necessity wholly unknown to the patient himself.

The typical clinical picture confronting the psychoanalyst is that of an individual who, on examination, either reveals no evidence of disease whatever, or else presents a condition which cannot be accounted for by any demonstrable physical lesion. Indeed, it is not infrequent that in the opinion of the ablest clinical experts he is pronounced absolutely free from organic disorder. Often the patient himself declares that he feels in excellent physical condition, that he eats wholesomely, sleeps soundly, and

[1] Freud, Sigmund: *Drei Abhandlungen zur Sexualtheorie*, Vienna, Deuticke, 1910.

realizes that he has everything that ought to make a man well and happy, and yet whose every moment is one of unmitigated wretchedness. He is perhaps a prey to phobias, obsessions, apprehensions, depressions, sudden and unremitting imperatives, the appalling loss of the sense of reality, to mention the most characteristic symptoms of neurotic states, or he may suffer from digestional disturbance, respiratory inhibition (stammering), muscular contractions, etc., and yet is utterly perplexed to account for the plight in which he finds himself, and completely powerless to furnish data that might throw light on these abnormal manifestations.

In other words, we are in the presence of factors which operate *unconsciously*. That is, we have to do with organic effects and reactions which fail to attain the level of conscious perception and which are therefore from the conscious standpoint equally impalpable to patient and physician. Let us bear in mind, then, that *the sphere of psychoanalysis lies exclusively in the field of unconscious mentation.*

With these distinctions before us, I shall try to explain briefly the basic principles of psychoanalysis, and to show something of what the method seeks to attain.

In many fundamental respects, Freud's teaching, as has been said, marks a wide departure from the hitherto prevailing view as to the interpretation of neurotic states.[2]

In the first place, Freud ascribes all neurotic disorders to the existence in the patient of wishes which are unrecognized, that is, not directly envisaged by him. Wishes of this unpremeditated character he subsumes under the term "unconscious," and gives to the realm of psychic activity constituting, as it were, the abode of such unconscious trends, the name of "the unconscious" (*das Unbewusstsein*).

Secondly, he regards the neurosis as a spontaneous ex-

[2] Forchheimer, Frederick: *Therapeusis of Internal Diseases*, New York, D. Appleton & Co., 1913, 4, 569.

pression of the tendency toward the fulfilment of such unconscious wishes. Thus he ascribes to the neurosis a purposive significance—a moral import. The neurosis contains a motive. It embodies an underlying intention: tends to supply a void not clearly cognized and defined, because existing outside the precincts of consciousness.

Thirdly, the ideas or wishes which thus occupy the sphere of unconsciousness possess the generic character of being invariably such as are ethically inadmissible in the sight of consciousness, so that the psychologic account of the creation of this limbo of the unconscious is to be found in the psychic conflict arising out of the opposition of consciousness to these ethically unwelcome desires and their consequent enforced banishment from consciousness —a process which Freud calls the mechanism of repression (*Verdrängung*).[3] Hence, in accordance with the hypothesis, a psychic conflict, with the attendant repression of the unseemly element, is the basic factor in the production of the neuroses.

Fourthly, it is Freud's thesis that all such conflicts as issue in such unconscious repression have their ultimate basis in the sphere of the sexual instinct. In other words, psychoanalysis posits a sexual *repression* as the essential condition in the etiology of a neurosis.[4]

And lastly, the theory assumes that such symptoms as are the expression of a tendency toward the fulfilment of these forbidden trends are but an indirect, cunningly veiled representation of them; that they are substitutions employed by reason of their associative affiliation with the original underlying idea. Each symptom is the dramatic

[3] Brewer and Freud: *Studien über Hysterie,* Vienna, Deuticke, 1910.

[4] It should be explained, however, that the word "sexual," as Freud uses it, has a far more general and inclusive meaning than is conveyed by the term as commonly employed. Contrary to the specific connotation of conventional usage, the term denotes, with Freud, the entire sphere of the primary, biologic pleasure-affects.

portrayal of the repressed wish subjected to a process of modification through the effort of consciousness to evade its real significance. The symptoms thus expressive of a neurosis are in each instance the resultant of contrary and opposed psychic trends, and represent in their outcome a compromise between the two.

Such remodeled, distorted expressions of the brute, primitive instincts as appear in the symptoms of neurotic disorders, Freud has called the phenomena of unconscious symbolization. This unconscious symbolization of instinctive trends whereby is effected the necessary palliation required by the censor of consciousness is the crux of Freud's interpretation of the neuroses.

According to Freud, the instinct of reproduction is paramount in the life of the individual. Yet the sexual trend is not the simple, unitary, static phenomenon it is generally assumed to be, but, like other factors of evolution, is a dynamic process having its integrative components derived from simpler elements. Freud points out that the sensations contributory to this impulse are originally composed of dispersed and inarticulate components, having their seats in various erogenic zones located over the body surface and situated chiefly in the regions composing the body orifices. The sensations arising from such erogenic zones are present, he tells us, in earliest infancy, and it is of these scattered, incoherent elements that the characteristic sexual feelings pertaining specifically to the organs of reproduction are later constituted. The ultimate attainment of the instinct directly conducive to reproduction consists, then, of a process of integration representing the product of individual evolution. Accordingly, there are three possible courses in the development of the ultimate sexual life of the individual:

First, the sexual life may take a normal course leading to the gradual absorption, so to speak, of these scattered auto-erotic trends into the resultant allo-erotic instinct comprised in the ultimate reproductive quest, and having

its physiologic center in the organs of generation. In such case we have the integration which results in the individual of a normal sexual life.

Secondly, there may be a persistence of the original auto-erotic interests and of the sexual satisfaction attaching to these primary erogenic zones, with failure of the aforesaid integration into the sexual impulse which tends toward the goal of reproduction. In this case there are presented the variations of the normal sexual impulse which constitute the *perversions*.

Finally, the sexual interest or *libido* pertaining to the different erogenic zones through repression may be deflected into vicarious avenues of sexuality corresponding symbolically to such frustrated interests. Such an outcome epitomizes the mechanism of the neuroses as envisaged by Freud. Of course no rigid line of demarcation separates these three possible developmental issues, but there is among them more or less of interlacement of the characters distinctive of each.

The neuroses, then, represent in a negative way a miscarriage of the sexual instinct analogous to that represented in a positive way in the sexual perversions. Freud's thesis, therefore, is that the neuroses betray an inadequacy in the development of the psycho-sexual life. This inadequacy marks a regression toward a sexual mode appropriate to an earlier, infantile period and postulates a latent, unconscious fixation of the *libido* on its original, infantile object. Hence the sexuality of the neurotic is hindered, repressed and, as it were, preoccupied elsewhere than with the immediate and contemporary object of sexual interest, and the psychologic situation presented by the patient is summed up by Freud in what he terms the patient's "sexual resistances" (*die sexuelle Widerstände*).

Such is the fundamental idea of psychoanalysis in regard to the origin and development of the neuroses. The primary factor in the production of the disorders is the

repression of the individual's sexuality due to the ban set on the manifestations of this elemental instinct by the strictures of social and religious conventions. It is the conflict between the forces of artificial culture and those of an inherent instinct of sex, the former imposing the repudiation of sexuality, the latter insisting as resolutely on a due recognition of the basal significance of this elemental factor in the biologic economy. The sexual instinct stoutly insists that it be granted recognition in consciousness, and consciousness, in its narrow intolerance, is as fiercely resolved to debar so unseemly an intruder. The final upshot of the situation is a compromise. It is agreed that the unruly element be admitted to consciousness on condition that it soften its tone and, as it were, adopt conventional apparel conformable to the requirements of adult, social consciousness. It is to this end that the psychic organism assumes the social defense it finds in the elaborate metaphorical usages presented in the patient's "symptoms." For it is only through dissembling that the repressed complex can succeed in evading the anathema of the conscious censor. But, though disguised in consciousness, this discordant, outlawed element still lurks in the unconscious, where, acting surreptitiously, it incites dissension amid the constituents of the personality, impairing its unity and destroying the mental synthesis requisite to the purposes of concerted function.

It is Freud's thesis, then, that the neurosis entails a psychic conflict due to an attempt to exclude from a fit acknowledgment, in consciousness, the biologic factors whose prerogatives are fundamental and inalienable. As has been said, such an exclusion of normal interests from participation in current consciousness Freud calls a *repression*. A psychic repression being the essential mechanism of a neurosis, the question for psychotherapeutics is, How may disorders arising from a psychic conflict, issuing out of the arbitrary and extraneous repression from consciousness of such contraband associations, be

remedied? Freud, seeking to give the direct logical answer, contends that disorders embodying psychic conflicts due to repression of elements which have a right to tenancy in consciousness are to be effectually cured only by removing the repression and freely admitting such contingents to their hereditary rights in consciousness.

So much by way of outline of the principles contained in Freud's system of psychotherapy. Now as to the method.

### METHOD OF PSYCHOANALYSIS

It will be clear from the foregoing that the task of the psychoanalyst is to bring into the high light of consciousness the ideas or associations which have been relegated to the recesses of the unconscious. The sole clue, however, to such repressed fancies lies in the symbolic equivalents into which these unconscious ideas have been converted through the process of repression. And the source of such surrogate symbolizations is to be sought in the symptoms themselves, in every spontaneous, unguarded reaction of the patient, and, most critically of all, in the patient's dreams. For it is in the drama of dream imagery, which the mind enacts during sleep, when the sentinels standing guard at the outposts of consciousness grow lax in their vigil, that these harpies of the unconscious most easily escape durance and venture to disport themselves with least danger of surprise.

Here, then, is our opportunity to take the demon of the unconscious unawares. Not that this unconscious ogre, be it remembered, is wont, even in dreams, openly to expose itself, but there are revealed in the creations of dream phantasy traces of its presence whereby it may be tracked to its hiding. This tracing of the repressed interests contained in the ideas lying behind the dream images constitutes the method of dream analysis, as developed by Freud, and it is the analysis of the patient's

dreams which is by far the most important resource of the psychoanalyst.

In Freud's conception, the actual dream, as revealed to consciousness, that is, the *manifest content* of the dream, is but an enigmatic congeries of psychic images—a charade that condenses in scenic productions a whole mass of related, interconnected meanings or dream thoughts, and it is the latter which constitute the real or *latent content* of the dream. Dream analysis or dream interpretation consists precisely in reaching these concealed fancies and so correlating them in accordance with precepts empirically determined as to render them coherent and significant. To do this it is required that the patient retrace the mental threads out of which he has woven together the elements of his dream tapestry. Such threads are composed of links in interconnected chains of associations, and it is the task of psychoanalysis to follow these threads of associations to their source, in order to reach the material out of which the dream images were originally spun.

Such a proceeding is fraught with difficulties, for obviously as the dream creation is precisely the outcome of the effort of consciousness to disguise, and so evade, the real meaning underlying the manifest dream elements, analysis involves a task no less formidable than that of pitting the patient against his own inherent will. It really means setting the patient at cross purposes with himself by forcing him to face frankly the thoughts and wishes which he has perhaps for a lifetime sought to repudiate; that is to say, the ideas which have been ruthlessly debarred entrance into consciousness and which in consequence pursue their career beyond the pale of apperception, manifesting themselves subtly in the symptoms and obsessions characteristic of neurotic states. These ideas are one by one readmitted into consciousness and are through this procedure deprived *de facto* of the essential motive of their existence.

As the analysis constitutes per se the entire system of psychotherapy introduced by Freud, an adequate account of the psychoanalytic method would entail a full description of its technic. The technic of psychoanalysis, however, is too varied to be susceptible of definite formulation. Indeed, the technic of psychoanalysis is too intimately bound up with the delicate psychologic *rapport* existing between physician and patient to be separate from it, for each detail of the patient's behavior conveys its own nuance of meaning that is of the utmost import to the psychoanalyst.

The practical procedure which is followed in the analysis of dreams, however, may be broadly indicated. The patient, having repeated his dreams, is asked to relate quite freely whatever occurs to his mind in connection with the different elements of which the dream is composed. This method Freud calls that of "free-association." From the ultimate ideas at which the patient arrives at the end of each of the chains of associations leading from the several elements of the *manifest dream content,* the physician is enabled to reconstruct the underlying trend contained in the latent content of the dream and so discover the patient's dream thoughts.

The links in the chains of associations do not succeed each other at regular intervals, but frequently the patient halts, showing signs of discomfort and unwillingness to continue. It is apparent that in such instances the patient's flow of thought is blocked by resistances, that is, he has come on a trend which he has long put away from him as distasteful, as unfit to hold a share in his contemporary consciousness. At such crises, the patient must be encouraged to continue without fear or reserve. He is reminded that the self-criticism which interposes itself in the current of his spontaneous associations tends to thwart the course of the analysis and to frustrate the whole purpose of the procedure. So when he resumes again the thread of associations, concentrating his atten-

tion anew on the reminiscences occurring at the point of interruption, it is usual that he will be brought to reveal some incident or trend of marked significance in his affective life. In other words, one comes in such intervals on psychic material which has been submitted to the process of repression and which, with its clusters of associations, constitutes a deterring "complex" in the patient's psychic life.

In fairness it must be said that the psychoanalytic method of procedure is far simpler to set down in writing than to carry out in actual practice. From the very nature of the neurosis, with its repression or rendering unconscious of the most vital trends in the psychic life of the individual, there are, of course, enormous habitual resistances to be overcome. To lead the patient to break through this habitual reserve is a task requiring the utmost expenditure of time, patience and ingenuity on the part of the physician, so that not infrequently hours are consumed in arriving at the determination of an objective statement which it would require but a few minutes to set down in writing.

Of course the central interest in dream analysis lies in Freud's dynamic theory of dreams. Freud teaches that the basic factor in every dream is an unconscious wish fulfilment: that whatever the manifest content may be, however foreign apparently to the idea of a coveted purpose, every dream will, on adequate analysis, reveal the presence of a repressed wish. How totally dissimilar in their content are the repressed wishes of the unconscious from what we commonly accept as the interests of our conative life, how utterly abhorrent to our ethical sensibilities such latent "wishes" invariably are, what, in short, is the real nature of an unconscious wish, in the sense of Freud, may be gathered only from a thorough study of Freud's dynamic psychology of the unconscious as contained in his major work "Die Traumdeutung." [5] It is

[5] Freud: *Die Traumdeutung,* Vienna, Deuticke, 1910, translation of A. A. Brill.

here alone that one is enabled to comprehend the very original and revolutionary conceptions on which Freud bases his theory of the unconscious and in which he elaborates the principles underlying his searching study of the biology of mind.

Next in importance to dream analysis is the association experiment which Jung of Zurich has adapted to practical psychoanalytic application.[6] The association experiment is useful chiefly as an instrument of diagnosis and for the purpose of a long-continued study of some specific problem, as the differences of reaction types. But it is also most valuable to the student in beginning psychoanalysis as a means of obtaining a preliminary survey of the general reaction of the patient and of opening the way toward gaining insight into his unconscious mental processes.

The association experiment has three chief advantages: First, it affords a *direct* avenue to the patient's repressed interests; second, it offers access to such repressed spheres of affectivity in spite of the patient's own unyielding resistances, and, third, it affords us a means of investigation which includes in it the conditions of an objective control so essential to an exact experimental study of the data required in comparative psychologic tests.

In arrangement and actuation the association experiment is very simple. The idea of the test is this: Every word represents for each person a psychologic situation. This may have, according to individual circumstances, an accent of greater or less emotional value. To say that a word possesses an emotional value is the equivalent of saying that it makes a deep impression on the psychic organism, that is, that it stirs a strong wave of response in the consciousness into which it falls.

Manifestly, if the length of such emotional wave may be estimated, we have obtained a measure of the relative

[6] Jung, C. J.: *Diagnostische Associationsstudien.*

strength of the emotional tone represented by it. This is precisely the result which is affected by the conditions of the association experiment.

A series of words called test words, usually 100, are repeated to the patient, who is required to respond at once with the first word associating itself in his mind with the test word given. By measuring with a stop watch, recording fifths of a second, the interval occurring between the stimulus (the calling of test word) and the reaction (the patient's response), a mathematical estimate is given of the relative emotional value of the situation recalled by the test word in question; for the more profoundly the consciousness of the patient is stirred, the longer will be the interval required in order to return to the mechanical routine of response required by the concrete conditions of the experiment.

Hence, having obtained the length of the patient's probable average of reaction time, any marked excess of this interval indicates the presence of a significant reminiscence, that is, of an underlying complex. A marked variation in the length of reaction time is, then, the most important of the complex indicators.

A further aid in unearthing the hidden complexes is that of obtaining the patient's "reproductions," that is, having obtained his responses to the series of stimulus words, to test his memory of each of his responses by again repeating the test words. In this procedure a wrong reproduction or failure to recall at all the original reaction word is indicative of a complex having been stirred. Here again the excess of the affect carries the mind of the patient from the immediate verbal image to some intimately associated impression, and the significance of the reaction word as such is lost in the greater emphasis of the remembrance awakened by it.

Still a further complex indicator consists in the successive decrease of the heightened interval of reaction time effecting the three or four immediately subsequent reac-

tions. To this species of complex indicator Jung has given the name "perseveration."

The frequent recurrence of the same reaction word throughout the experiment, the assimilation of the test word in an unusual sense, repeating the stimulus word before reacting, replying with more than a single word, offering explanations, etc., are among the many additional indications that a complex has been excited.

Such are the chief means affording a clue to the lines along which the analysis may most judiciously direct its inquiry and so contribute to effect the release and thorough ventilation of the repressed affects which are responsible for the inner psychic disharmony.

It is thus that the physician succeeds in establishing a synthesis amid the discordant, mutually exclusive elements of the personality. It is thus that the psychic tension due to the mental conflict is eliminated and the dissociated elements of the ego are brought together in a simple unitary stream of consciousness.

Such is the treatment of psychic disorders by the method of psychoanalysis. The statement given here affords but the merest hint of the full import of the method. This is long and laborious, often entailing in actual practice many months for the adequate analysis of a single case. To gain anything like a commensurate idea of the full significance of the psychoanalytic method, one must put himself in touch with Freud's conceptions of the unconscious as presented in his writings. In his various contributions to the literature of psychopathology, Freud has presented an account of the system of psychology on which he bases his explanation of the essential processes underlying neurotic disorders and in which he defines the rationale of the psychoanalytic method of treatment.

### USES OF PSYCHOANALYSIS

While, in my opinion, the discoveries made by Freud through his long and laborious investigations are as sound

scientifically and as important economically as any in the history of modern medicine, I do not by any means regard psychoanalysis as a universal panacea for nervous disorders, but on the contrary consider it as the particular method of psychotherapy that is most restricted in its possibilities of application,[7] a reflection, however, which is rather comforting than otherwise when we consider the length of time required—frequently, as I have said, as much as an hour daily for weeks and even months—for the adequate analysis of a single case. This being true, it seems a fortunate circumstance that psychoanalysis is not the suitable method in all cases—that other and simpler methods of psychotherapy are applicable in many types and degrees of nervous manifestations, and even if sometimes unscientific, they are at least effective for the ignorant masses to whom they are applicable.

The fact is that psychoanalysis is practically adapted to only a few persons, but those few belong, generally speaking, to the most educated classes and are precisely those personalities who, from the nature of the conditions of the onset of a neurosis, are the most sensitive, highly developed and worth while among us, and whose re-education through self-analysis will be most far-reaching in its influence on the body social.

Psychoanalysis can never hope to become popular for the reason that it is honest. It does not flatter or cajole the patient or seek to appease him with subtle blandishments; on the contrary, it mercilessly thwarts and assails him. The mawkish and artificial will find in it little unction of their boredom. Psychoanalysis offers nothing brilliant or spectacular, but, being a robust, uncompromising method of scientific investigation, it proceeds in the laborious, unobtrusive manner of all earnest research, and is adapted to the needs of only earnest and intelligent men and women.

[7] Freud has himself been most explicit in the practical limitations he has recognized in the use of the psychoanalytic method.

Though lacking in frills, the method is not without its practical compensations. One need not be irresistible to be a psychoanalyst. In psychoanalysis "personality" is no asset. The method places no premium on the personal charms of the physician.

The misconception concerning psychoanalysis which seems to me of all the most unfortunate is the view that there exists an inherent opposition between the principles of psychoanalysis and those of experimental psychology. On the contrary, the psychoanalyst of far perspectives can hardly fail to recognize the possibilities of mutual gain in the complementary positions which these two departments of research occupy in relation to one another, nor can he fail to see the opportunity he has in the objective controls of the experimental method for the substantiation of his results. Nothing, it seems, to me, can more certainly cripple the researches of the psychoanalyst than this very fundamental misapprehension.

I believe William James once said that when any discovery is newly given to science the cry at first is that it is not true, but that later, as the truth of the new theory becomes manifest, this attitude is replaced by the admission, "Yes, it is true, but *I* discovered it." Now that psychoanalysis is entering this latter phase of its career, there begin to appear various bogus psychoanalytic procedures which are in truth mere travesties on the original method by Freud, and we need be on our guard against the cunning decoys of such spurious artifices.

We shall do well, therefore, to discriminate between psychoanalysis as represented in the systematic, laborious, time-consuming method of psychotherapeutic research introduced by Sigmund Freud—a method imbued throughout with the spirit and ideals of the laboratory—and the pseudopsychoanalytic substitutes which pervert Freud's method to sensational uses. Psychoanalysis proper is wholly incompatible with the business of medicine. The hurrying practitioners who say that they use psychoanaly-

sis as occasion arises, as though they kept it on a shelf in bottles, simply fail to understand the first principles of the method; for psychoanalysis is not a tablet but a system. It is not to be summoned by caprice or expedience but must be acquired by careful study and training, and above all by the exacting discipline of a thoroughgoing self-analysis.

# EINSTEIN'S LAW OF GRAVITATION

(Address of the President of the American Psysical Society, St. Louis, 1919)

BY

J. S. AMES

*Professor of Physics Johns Hopkins University*

IN the treatment of Maxwell's equations of the electromagnetic field, several investigators realized the importance of deducing the form of the equations when applied to a system moving with a uniform velocity. One object of such an investigation would be to determine such a set of transformation formulæ as would leave the mathematical form of the equations unaltered. The necessary relations between the new space-coördinates, those applying to the moving system, and the original set were, of course, obvious; and elementary methods led to the deduction of a new variable which should replace the time coördinate. This step was taken by Lorentz and also, I believe, by Larmor and by Voigt.

Lorentz' paper on this subject appeared in the Proceedings of the Amsterdam Academy in 1904. In the following year there was published in the *Annalen der Physik* a paper by Einstein, written without any knowledge of the work of Lorentz, in which he arrived at the same transformation equations as did the latter, but with an entirely different and fundamentally new interpretation. Einstein called attention in his paper to the lack of definiteness in the concepts of time and space, as ordi-

narily stated and used. He analyzed clearly the definitions and postulates which were necessary before one could speak with exactness of a length or of an interval of time. He disposed forever of the propriety of speaking of the "true" length of a rod or of the "true" duration of time, showing, in fact, that the numerical values which we attach to lengths or intervals of time depend upon the definitions and postulates which we adopt. The words "absolute" space or time intervals are devoid of meaning. As an illustration of what is meant Einstein discussed two possible ways of measuring the length of a rod when it is moving in the direction of its own length with a uniform velocity, that is, after having adopted a scale of length, two ways of assigning a number to the length of the rod concerned. One method is to imagine the observer moving with the rod, applying along its length the measuring scale, and reading off the positions of the ends of the rod. Another method would be to have two observers at rest on the body with reference to which the rod has the uniform velocity, so stationed along the line of motion of the rod that as the rod moves past them they can note simultaneously on a stationary measuring scale the positions of the two ends of the rod. Einstein showed that, accepting two postulates which need no defense at this time, the two methods of measurements would lead to different numerical values, and, further, that the divergence of the two results would increase as the velocity of the rod was increased.

In assigning a number, therefore, to the length of a moving rod, one must make a choice of the method to be used in measuring it. Obviously the preferable method is to agree that the observer shall move with the rod, carrying his measuring instrument with him. This disposes of the problem of measuring space relations. The observed fact that, if we measure the length of the rod on different days, or when the rod is lying in different positions, we always obtain the same value offers no informa-

tion concerning the "real" length of the rod. It may have changed, or it may not. It must always be remembered that measurement of the length of a rod is simply a process of comparison between it and an arbitrary standard, *e.g.*, a meter-rod or yard-stick. In regard to the problem of assigning numbers to intervals of time, it must be borne in mind that, strictly speaking, we do not "measure" such intervals, *i.e.*, that we do not select a unit interval of time and find how many times it is contained in the interval in question. (Similarly, we do not "measure" the pitch of a sound or the temperature of a room.)

Our practical instruments for assigning numbers to time-intervals depend in the main upon our agreeing to believe that a pendulum swings in a perfectly uniform manner, each vibration taking the same time as the next one. Of course we cannot *prove* that this is true, it is, strictly speaking, a definition of what we mean by equal intervals of time; and it is not a particularly good definition at that. Its limitations are sufficiently obvious. The best way to proceed is to consider the concept of uniform velocity, and then, using the idea of some entity having such a uniform velocity, to define equal intervals of time as such intervals as are required for the entity to traverse equal lengths. These last we have already defined. What is required in addition is to adopt some moving entity as giving our definition of uniform velocity. Considering our known universe it is self-evident that we should choose in our definition of uniform velocity the velocity of light, since this selection could be made by an observer anywhere in our universe. Having agreed then to illustrate by the words "uniform velocity" that of light, our definition of equal intervals of time is complete. This implies, of course, that there is no uncertainty on our part as to the fact that the velocity of light always has the same value at any one point in the universe to any observer, quite regardless of the source of light. In other words, the postulate that this is true underlies our definition.

Following this method Einstein developed a system of measuring both space and time intervals. As a matter of fact his system is identically that which we use in daily life with reference to events here on the earth. He further showed that if a man were to measure the length of a rod, for instance, on the earth and then were able to carry the rod and his measuring apparatus to Mars, the sun, or to Arcturus he would obtain the same numerical value for the length in all places and at all times. This doesn't mean that any statement is implied as to whether the length of the rod has remained unchanged or not; such words do not have any meaning—remember that we cannot speak of true length. It is thus clear that an observer living on the earth would have a definite system of units in terms of which to express space and time intervals, *i.e.*, he would have a definite system of space coördinates $(x, y, z)$ and a definite time coördinate $(t)$; and similarly an observer living on Mars would have his system of coördinates $(x', y', z', t')$. Provided that one observer has a definite uniform velocity with reference to the other, it is a comparatively simple matter to deduce the mathematical relations between the two sets of coördinates. When Einstein did this, he arrived at the same transformation formulæ as those used by Lorentz in his development of Maxwell's equations. The latter had shown that, using this formulæ, the form of the laws for all electromagnetic phenomena maintained the same form; so Einstein's method proves that using his system of measurement an observer, anywhere in the universe, would as the result of his own investigation of electromagnetic phenomena arrive at the same mathematical statement of them as any other observer, provided only that the relative velocity of the two observers was uniform.

Einstein discussed many other most important questions at this time; but it is not necessary to refer to them in connection with the present subject. So far as this is concerned, the next important step to note is that taken in

the famous address of Minkowski, in 1908, on the subject of "Space and Time." It would be difficult to overstate the importance of the concepts advanced by Minkowski. They marked the beginning of a new period in the philosophy of physics. I shall not attempt to explain his ideas in detail, but shall confine myself to a few general statements. His point of view and his line of development of the theme are absolutely different from those of Lorentz or of Einstein; but in the end he makes use of the same transformation formulæ. His great contribution consists in giving us a new geometrical picture of their meaning. It is scarcely fair to call Minkowski's development a picture; for to us a picture can never have more than three dimensions, our senses limit us; while his picture calls for perception of four dimensions. It is this fact that renders any even semi-popular discussion of Minkowski's work so impossible. We can all see that for us to describe any event a knowledge of four coordinates is necessary, three for the space specification and one for the time. A complete picture could be given then by a point in four dimensions. All four coördinates are necessary: we never observe an event except at a certain time, and we never observe an instant of time except with reference to space. Discussing the laws of electromagnetic phenomena, Minkowski showed how in a space of four dimensions, by a suitable definition of axes, the mathematical transformation of Lorentz and Einstein could be described by a rotation of the set of axes. We are all accustomed to a rotation of our ordinary cartesian set of axes describing the position of a point. We ordinarily choose our axes at any location on the earth as follows: one vertical, one east and west, one north and south. So if we move from any one laboratory to another, we change our axes; they are always orthogonal, but in moving from place to place there is a rotation. Similarly, Minkowski showed that if we choose four orthogonal axes at any point on the earth, according to his method, to represent

a space-time point using the method of measuring space and time intervals as outlined by Einstein; and, if an observer on Arcturus used a similar set of axes and the method of measurement which he naturally would, the set of axes of the latter could be obtained from those of the observer on the earth by a pure rotation (and naturally a transfer of the origin). This is a beautiful geometrical result. To complete my statement of the method, I must add that instead of using as his fourth axis one along which numerical values of time are laid off, Minkowski defined his fourth coördinate as the product of time and the imaginary constant, the square root of minus one. This introduction of imaginary quantities might be expected, possibly, to introduce difficulties; but, in reality, it is the very essence of the simplicity of the geometrical description just given of the rotation of the sets of axes. It thus appears that different observers situated at different points in the universe would each have their own set of axes, all different, yet all connected by the fact that any one can be rotated so as to coincide with any other. This means that there is no one direction in the four dimensional space that corresponds to time for all observers. Just as with reference to the earth there is no direction which can be called vertical for all observers living on the earth. In the sense of an *absolute* meaning the words "up and down," "before and after," "sooner or later," are entirely meaningless.

This concept of Minkowski's may be made clearer, perhaps, by the following process of thought. If we take a section through our three dimensional space, we have a plane, *i.e.*, a two-dimensional space. Similarly, if a section is made through a four-dimensional space, one of three dimensions is obtained. Thus, for an observer on the earth a definite section of Minkowski's four dimensional space will give us our ordinary three-dimensional one; so that this section will, as it were, break up Minkowski's space into our space and give us our ordinary

time. Similarly, a different section would have to be used for the observer on Arcturus; but by a suitable selection he would get his own familiar three-dimensional space and his own time. Thus the space defined by Minkowski is completely isotrophic in reference to measured lengths and times, there is absolutely no difference between any two directions in an absolute sense; for any particular observer, of course, a particular section will cause the space to fall apart so as to suit his habits of measurement; any section, however, taken at random will do the same thing for some observer somewhere. From another point of view, that of Lorentz and Einstein, it is obvious that, since this four dimensional space is isotropic, the expression of the laws of electromagnetic phenomena take identical mathematical forms when expressed by any observer.

The question, of course, must be raised as to what can be said in regard to phenomena which so far as we know do not have an electromagnetic origin. In particular what can be done with respect to gravitational phenomena? Before, however, showing how this problem was attacked by Einstein; and the fact that the subject of my address is Einstein's work on gravitation shows that ultimately I shall explain this, I must emphasize another feature of Minkowski's geometry. To describe the space-time characteristics of any event a point, defined by its four coordinates, is sufficient; so, if one observes the life-history of any entity, *e.g.*, a particle of matter, a light-wave, etc., he observes a sequence of points in the space-time continuum; that is, the life-history of any entity is described fully by a line in this space. Such a line was called by Minkowski a "world-line." Further, from a different point of view, all of our observations of nature are in reality observations of coincidences, *e.g.*, if one reads a thermometer, what he does is to note the coincidence of the end of the column of mercury with a certain scale division on the thermometer tube. In other words, thinking of the world-line of the end of the mercury column

and the world-line of the scale division, what we have observed was the intersection or crossing of these lines. In a similar manner any observation may be analyzed; and remembering that light rays, a point on the retina of the eye, etc., all have their world lines, it will be recognized that it is a perfectly accurate statement to say that every observation is the perception of the intersection of world-lines. Further, since all we know of a world-line is the result of observations, it is evident that we do not know a world-line as a continuous series of points, but simply as a series of discontinuous points, each point being where the particular world-line in question is crossed by another world-line.

It is clear, moreover, that for the description of a world-line we are not limited to the particular set of four orthogonal axes adopted by Minkowski. We can choose any set of four-dimensional axes we wish. It is further evident that the mathematical expression for the coincidence of two points is absolutely independent of our selection of reference axes. If we change our axes, we will change the coördinates of both points simultaneously, so that the question of axes ceases to be of interest. But our so-called laws of nature are nothing but descriptions in mathematical language of our observations; we observe only coincidences; a sequence of coincidences when put in mathematical terms takes a form which is independent of the selection of reference axes; therefore the mathematical expression of our laws of nature, of every character, must be such that their form does not change if we make a transformation of axes. This is a simple but far-reaching deduction.

There is a geometrical method of picturing the effect of a change of axes of reference, *i.e.*, of a mathematical transformation. To a man in a railway coach the path of a drop of water does not appear vertical, *i.e.*, it is not parallel to the edge of the window; still less so does it appear vertical to a man performing maneuvers in an

airplane. This means that whereas with reference to axes fixed to the earth the path of the drop is vertical; with reference to other axes, the path is not. Or, stating the conclusion in general language, changing the axes of reference (or effecting a mathematical transformation) in general changes the shape of any line. If one imagines the line forming a part of the space, it is evident that if the space is deformed by compression or expansion the shape of the line is changed, and if sufficient care is taken it is clearly possible, by deforming the space, to make the line take any shape desired, or better stated, any shape specified by the previous change of axes. It is thus possible to picture a mathematical transformation as a deformation of space. Thus I can draw a line on a sheet of paper or of rubber and by bending and stretching the sheet, I can make the line assume a great variety of shapes; each of these new shapes is a picture of a suitable transformation.

Now, consider world-lines in our four dimensional space. The complete record of all our knowledge is a series of sequences of intersections of such lines. By analogy I can draw in ordinary space a great number of intersecting lines on a sheet of rubber; I can then bend and deform the sheet to please myself; by so doing I do not introduce any new intersections nor do I alter in the least the sequence of intersections. So in the space of our world-lines, the space may be deformed in any imaginable manner without introducing any new intersections or changing the sequence of the existing intersections. It is this sequence which gives us the mathematical expression of our so-called experimental laws; a deformation of our space is equivalent mathematically to a transformation of axes, consequently we see why it is that the form of our laws must be the same when referred to any and all sets of axes, that is, must remain unaltered by any mathematical transformation.

Now, at last we come to gravitation. We can not imag-

ine any world-line simpler than that of a particle of matter left to itself; we shall therefore call it a "straight" line. Our experience is that two particles of matter attract one another. Expressed in terms of world-lines, this means that, if the world-lines of two isolated particles come near each other, the lines, instead of being straight, will be deflected or bent in towards each other. The world-line of any one particle is therefore deformed; and we have just seen that a deformation is the equivalent of a mathematical transformation. In other words, for any one particle it is possible to replace the effect of a gravitational field at any instant by a mathematical transformation of axes. The statement that this is always possible for any particle at any instant is Einstein's famous "Principle of Equivalence."

Let us rest for a moment, while I call attention to a most interesting coincidence, not to be thought of as an intersection of world-lines. It is said that Newton's thoughts were directed to the observation of gravitational phenomena by an apple falling on his head; from this striking event he passed by natural steps to a consideration of the universality of gravitation. Einstein in describing his mental process in the evolution of his law of gravitation says that his attention was called to a new point of view by discussing his experiences with a man whose fall from a high building he had just witnessed. The man fortunately suffered no serious injuries and assured Einstein that in the course of his fall he had not been conscious in the least of any pull downward on his body. In mathematical language, with reference to axes moving with the man the force of gravity had disappeared. This is a case where by the transfer of the axes from the earth itself to the man, the force of the gravitational field is annulled. The converse change of axes from the falling man to a point on the earth could be considered as introducing the force of gravity into the equations of motion. Another illustration of the introduction into our equations of a

force by means of a change of axes is furnished by the ordinary treatment of a body in uniform rotation about an axis. For instance, in the case of a so-called conical pendulum, that is, the motion of a bob suspended from a fixed point by a string, which is so set in motion that the bob describes a horizontal circle and the string therefore describes a circular cone, if we transfer our axes from the earth and have them rotate around the vertical line through the fixed point with the same angular velocity as the bob, it is necessary to introduce into our equations of motion a fictitious "force" called the centrifugal force. No one ever thinks of this force other than as a mathematical quantity introduced into the equations for the sake of simplicity of treatment; no physical meaning is attached to it. Why should there be to any other so-called "force," which, like centrifugal force, is independent of the nature of the matter? Again, here on the earth our sensation of weight is interpreted mathematically by combining expressions for centrifugal force and gravity; we have no distinct sensation for either separately. Why then is there any difference in the essence of the two? Why not consider them both as brought into our equations by the agency of mathematical transformations? This is Einstein's point of view.

Granting, then, the principle of equivalence, we can so choose axes at any point at any instant that the gravitational field will disappear; these axes are therefore of what are called the "Galilean" type, the simplest possible. Consider, that is, an observer in a box, or compartment, which is falling with the acceleration of the gravitational field at that point. He would not be conscious of the field. If there were a projectile fired off in this compartment, the observer would describe its path as being straight. In this space the infinitesimal interval between two space-time points would then be given by the formula

$$ds^2 = dx^2_1 + dx^2_3 + dx^2_4,$$

where $ds$ is the interval and $x_1$, $x_2$, $x_3$, $x_4$, are coördinates. If we make a mathematical transformation, *i.e.*, use another set of axes, this interval would obviously take the form

$$ds^2 = g_{11}dx^2{}_1 + g_{22}dx^2{}_2 + g_{33}dx^2{}_3 + g_{44}dx^2{}_4 + 2g_{12}dx_1dx_2 + \text{etc.},$$

where $x_1$, $x_2$, $x_3$ and $x_4$ are now coördinates referring to the new axes. This relation involves ten coefficients, the coefficients defining the transformation.

But of course a certain dynamical value is also attached to the $g$'s, because by the transfer of our axes from the Galilean type we have made a change which is equivalent to the introduction of a gravitational field; and the $g$'s must specify the field. That is, these $g$'s are the expressions of our experiences, and hence their values cannot depend upon the use of any special axes; the values must be the same for all selections. In other words, the expression of the facts of gravitation is really a statement involving a relation between the $g$'s; and this expression must be the same for all sets of coördinates. There are ten $g$'s defined by differential equations; so we have ten covariant equations. Einstein showed how these $g$'s could be regarded as generalized potentials of the field. Our own experiments and observations upon gravitation have given us a certain knowledge concerning its potential; that is, we know a value for it which must be so near the truth that we can properly call it at least a first approximation. Or, stated differently, if Einstein succeeds in deducing the rigid value for the gravitational potential in any field, it must degenerate to the Newtonian value for the great majority of cases with which we have actual experience. Einstein's method, then, was to investigate the functions (or equations) which would satisfy the mathematical conditions just described. A transformation from the axes used by the observer in the falling box

may be made so as to introduce into the equations the gravitational field recognized by an observer on the earth near the box; but this, obviously, would not be the general gravitational field, because the field changes as one moves over the surface of the earth. A solution found, therefore, as just indicated, would not be the one sought for the general field; and another must be found which is less stringent than the former but reduces to it as a special case. He found himself at liberty to make a selection from among several possibilities, and for several reasons chose the simplest solution. He then tested this decision by seeing if his formulæ would degenerate to Newton's law for the limiting case of velocities small when compared with that of light, because this condition is satisfied in those cases to which Newton's law applies. His formulæ satisfied this test, and he therefore was able to announce a "law of gravitation," of which Newton's was a special form for a simple case.

To the ordinary scholar the difficulties surmounted by Einstein in his investigations appear stupendous. It is not improbable that the statement which he is alleged to have made to his editor, that only ten men in the world could understand his treatment of the subject, is true. I am fully prepared to believe it, and wish to add that I certainly am not one of the ten. But I can also say that, after a careful and serious study of his papers, I feel confident that there is nothing in them which I cannot understand, given the time to become familiar with the special mathematical processes used. The more I work over Einstein's papers, the more impressed I am, not simply by his genius in viewing the problem, but also by his great technical skill.

Following the path outlined, Einstein, as just said, arrived at certain mathematical laws for a gravitational field, laws which reduced to Newton's form in most cases where observations are possible, but which led to different conclusions in a few cases, knowledge concerning which

we might obtain by careful observations. I shall mention a few deductions from Einstein's formulæ.

1. If a heavy particle is put at the center of a circle, and, if the length of the circumference and the length of the diameter are measured, it will be found that their ratio is not $\pi$ (3.14159). In other words the geometrical properties of space in such a gravitational field are not those discussed by Euclid; the space is, then, non-Euclidean. There is no way by which this deduction can be verified, the difference between the predicted ratio and $\pi$ is too minute for us to hope to make our measurements with sufficient exactness to determine the difference.

2. All the lines in the solar spectrum should with reference to lines obtained by terrestrial sources be displaced slightly towards longer wave-lengths. The amount of displacement predicted for lines in the blue end of the spectrum is about one-hundredth of an Angstrom unit, a quantity well within experimental limits. Unfortunately, as far as the testing of this prediction is concerned, there are several physical causes which are also operating to cause displacement of the spectrum-lines; and so at present a decision cannot be rendered as to the verification. St. John and other workers at the Mount Wilson Observatory have the question under investigation.

3. According to Newton's law an isolated planet in its motion around a central sun would describe, period after period, the same elliptical orbit; whereas Einstein's laws lead to the prediction that the successive orbits traversed would not be identically the same. Each revolution would start the planet off on an orbit very approximately elliptical, but with the major axis of the ellipse rotated slightly in the plane of the orbit. When calculations were made for the various planets in our solar system, it was found that the only one which was of interest from the standpoint of verification of Einstein's formulæ was Mercury. It has been known for a long time that there was actually such a change as just described in the orbit of Mercury,

amounting to 574″ of arc per century; and it has been shown that of this a rotation of 532″ was due to the direct action of other planets, thus leaving an unexplained rotation of 42″ per century. Einstein's formulæ predicted a rotation of 43″, a striking agreement.

4. In accordance with Einstein's formulæ a ray of light passing close to a heavy piece of matter, the sun, for instance, should experience a sensible deflection in towards the sun. This might be expected from "general" considerations. A light ray is, of course, an illustration of energy in motion; energy and mass are generally considered to be identical in the sense that an amount of energy $E$ has the mass $E/c^2$ where $c$ is the velocity of light; and consequently a ray of light might fall within the province of gravitation and the amount of deflection to be expected could be calculated by the ordinary formula for gravitation. Another point of view is to consider again the observer inside the compartment falling with the acceleration of the gravitational field. To him the path of a projectile and a ray of light would both appear straight; so that, if the projectile had a velocity equal to that of light, it and the light wave would travel side by side. To an observer outside the compartment, *e.g.*, to one on the earth, both would then appear to have the same deflection owing to the sun. But how much would the path of the projectile be bent? What would be the shape of its parabola? One might apply Newton's law; but, according to Einstein's formulæ, Newton's law should be used only for small velocities. In the case of a ray passing close to the sun it was decided that according to Einstein's formula there should be a deflection of 1″.75 whereas Newton's law of gravitation predicted half this amount. Careful plans were made by various astronomers to investigate this question at the solar eclipse last May, and the result announced by Dyson, Eddington and Crommelin, the leaders of astronomy in England, was that there was a deflection of 1″.9. Of course the detec-

tion of such a minute deflection was an extraordinarily difficult matter, so many corrections had to be applied to the original observations; but the names of the men who record the conclusions are such as to inspire confidence. Certainly any effect of refraction seems to be excluded.

It is thus seen that the formulæ deduced by Einstein have been confirmed in a variety of ways and in a most brilliant manner. In connection with these formulæ one question must arise in the minds of everyone: by what process, where in the course of the mathematical development, does the idea of mass reveal itself? It was not in the equations at the beginning and yet here it is at the end. How does it appear? As a matter of fact it is first seen as a constant of integration in the discussion of the problem of the gravitational field due to a single particle; and the identity of this constant with mass is proved when one compares Einstein's formulæ with Newton's law which is simply its degenerated form. This mass, though, is the mass of which we become aware through our experiences with weight; and Einstein proceeded to prove that this quantity which entered as a constant of integration in his ideally simple problem also obeyed the laws of conservation of mass and conservation of momentum when he investigated the problems of two and more particles. Therefore Einstein deduced from his study of gravitational fields the well-known properties of matter which form the basis of theoretical mechanics; *i.e.*, he established the identity of gravitational and inertial mass. A further logical consequence of Einstein's development is to show that energy has mass, a concept with which everyone nowadays is familiar.

The description of Einstein's method which I have given so far is simply the story of one success after another; and it is certainly fair to ask if we have at last reached finality in our investigation of nature, if we have attained to truth. Are there no outstanding difficulties? Is there no possibility of error? Certainly, not until all the pre-

dictions made from Einstein's formulæ have been investigated can much be said; and further, it must be seen whether any other lines of argument will lead to the same conclusions. But without waiting for all this there is at least one difficulty which is apparent at this time. We have discussed the laws of nature as independent in their form of reference axes, a concept which appeals strongly to our philosophy; yet it is not at all clear, at first sight, that we can be justified in our belief. We cannot imagine any way by which we can become conscious of the translation of the earth in space; but by means of gyroscopes we can learn a great deal about its rotation on its axis. We could locate the positions of its two poles, and by watching a Foucault pendulum or a gyroscope we can obtain a number which we interpret as the angular velocity of rotation of axes fixed in the earth; angular velocity with reference to what? Where is the fundamental set of axes? This is a real difficulty. It can be surmounted in several ways. Einstein himself has outlined a method which in the end amounts to assuming the existence on the confines of space of vast quantities of matter, a proposition which is not attractive. deSitter has suggested a peculiar quality of the space to which we refer our space-time coördinates. The consequences of this are most interesting, but no decision can as yet be made as to the justification of the hypothesis. In any case we can say that the difficulty raised is not one that destroys the real value of Einstein's work.

In conclusion I wish to emphasize the fact, which should be obvious, that Einstein has not attempted any explanation of gravitation; he has been occupied with the deduction of its laws. These laws, together with those of electromagnetic phenomena, comprise our store of knowledge. There is not the slightest indication of a mechanism, meaning by that a picture in terms of our senses. In fact what we have learned has been to realize that our desire to use such mechanisms is futile.

# INDEX


*Abruzzi, Duke of,* 103
Acapnia, 107
Acclimatization, 105
*Adams, F. D.,* 56
Acidosis, 105, 106, 107
Aircraft, 48
"Air-staleness," aviators', 96
*Allen,* 92
Altitudes, effect on system of high, 97, 112
*Ames,* 12, 230
Amphibians, length of life of, 94
Anaphylaxis, 130-135
  compared to immunity, 132
Anesthesia, 154
Anthrax, 116, 118, 119
Antiseptics, 154
Antitoxin, 122
*Armstrong,* 82, 83
*Arrhenius,* 124
Asepsis, 185
Association experiment, 224
Atom, divisibility of, 14
  its nucleus, 18, 23
  structure of, 23
Atomic number, 23
Atoms, 9
*Auer,* 134
*Auld,* 11, 61
Aviator, physiology of, 95-114
  tests for, 109, 110, 112

*Bacon,* 58
Bacteriology, 11, 115-151
*Barkla,* 19
*Bayard,* 177
*Behrens,* 110
*Behring,* 119, 120, 122, 123, 12
*Bell, C.,* 158
*Bell, J.,* 158, 159, 160, 163, 18
Benzyl bromide, 69
*Bert,* 97
*Bertrand,* 82, 83
Beryllium, 25
*Bigelow,* 129, 182
*Blowes*
*Boer* War, 168
*Bogdanow,* 87
*Bohr,* 22, 23, 24, 25, 27, 31
*Bolin,* 83
*Bordet,* 124, 125, 142, 144
Bore hole, 56
*Born,* 26
*Boulton,* 36
*Bowlby,* 185
*Bragg,* 20, 28, 45, 47
Brain power, measurement an utilization of in the army 192-210
*Brewer,* 216
*Briggs,* 173, 174
*Bristowe,* 163
*Bryant,* 177
*Buchner,* 77, 80
*Burrell,* 114
*Burrow,* 12, 211

*Caisson* disease, 98
*Cameron,* 160

*Campbell*, 174, 175
Cancer research, 140, 141
*Canniff*, 173
Carbolic acid, 167, 174
Carbon, 23
  See charcoal
*Carnot*, 35
*Carpenter*, 173
*Carrel*, 91, 186
*Carrel-Dakin* method of disinfection, 191
*Carroll*, 144
Catalyst, 76
Cerium, 23
*Championnière*, 172
Charcoal, 68
Chemical reactions, effect of temperature on, 88
Chemotherapy, 145-148
*Chenu*, 164, 165
*Cheyne*, 186
Chicken-pox, 137
Chlorine, 23
  in gas warfare, 63
Cholera, 119, 126
Cinchona bark, 146
*Civil* War, 152, 164
  casualties, 166
*Clerk*, 41
Coal, 53
Colloids, 79, 80
Complex salts, structure of, 30
*Cooper*, 183
*Crewe*, 58
*Crimean* War, 164
  casualties, 165
*Crocé-Spinelli*, 103
*Crommelin*, 244
Crystal structure, 19
Crystalloids, 79
Cultivation of bacterial growths, 119
*Curie, Madame*, 9

*Dalton*, 9
*Davaine*, 116, 119
*Dawson*, 175
Death, cause of, 86
  meaning of, 88
  natural, and the duration of life, 85-94
*Delorme*, 188
*Democritus*, 13
*Dennis*, 179
*Dernby*, 86
Diphtheria, 115, 119, 120, 121, 123
Disintegration, body, 85, 86
*Dodge*, 193
*Douglas*, 103
Dreams, significance of, 220
  analysis of, 221
*Duane*, 22
*Duncan*, 164, 165
*Dunlap*, 110
Dysentary, 119
*Dyson*, 244

*Eddington*, 244
*Ehrlich*, 122, 124, 125, 147, 186
*Einstein*, 230, 231, 233, 234, 235, 236, 239, 240, 241, 242, 243, 244, 245, 246
*Einstein's* theory, 12
  law of gravitation, 230-246
  deductions, 243
Electricity, 14, 50
Electron, 10, 17, 21
Elements, relations between, 20
Enzymes, 11, 76-84
  as catalysts, 76
  isolation of, 78, 80-84
  "specificity" of, 78
  characteristic properties, 79
*Erichsen*, 154
Erosion of propellers, 57
*Estes*, 163
*Euclid*, 243
*Euler*, 83

*Falk*, 84
*Fehling's* solution, 78

Ferments, 77
See enzymes
*Filippi*, 103
Filterables, 135-141
Fischer, 78, 83
*Fitzgerald*, 105
*Flexner*, 11, 115, 130, 138
Flies, aseptic, 87, 88
duration of life of, 89
influence of temperature on, 94
Fluorine, 27, 32
Fluosilicate ion, 29
*Forchheimer*, 215
Fourth dimension, 234
Fowl cholera, 117, 118
*Fraenkel*, 80
*Franco-Prussian* War, 167
*Freud*, 212, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 226, 227, 228
Frog, metamorphosis of, 92
*Frosch*, 136
Fruit fly, metamorphosis of, 93

*Galen*, 157
Gas masks, 11
Gas shells, 67, 69, 70
advantages, 70
their future, 73
Gas warfare, 11, 61-75
compounds used, 74
early methods, 62
protection against, 64, 68
Gaseous explosions, 41
*Gates*, 138
*Geiger*, 18
Germ theory, 172-191
*Gibbs*, 111
*Girard*, 173
*Gorgas*, 165
*Graham*, 79, 80
Gravitation, 238
*Einstein's* law of, 242
*Great Eastern* (ship), 38
*Gudernatsch*, 92, 93
*Guérin*, 159
Guinea-pig, 132
*Guyénot*, 87

*Hadfield*, 40
*Haggard*, 106, 107
*Haldane*, 103, 104, 105
*Hamilton*, F., 173
*Harrow*, 9, 76
*Hartmann*, 188
Hay fever, 123, 134
*Heath*, 58
Helium, 23, 25
*Henderson, L. J.*, 104
*Henderson, Y.*, 11, 95, 103, 106, 107
*Hewitt*, 177
*Hewson*, 173
Hexamethylenetetramine, 67, 74
*Hodgen*, 173
*Holmes, O. W.*, 161
*Holmes, T.*, 163, 176
*Hopkinson*, 41
Hospital gangrene, 160, 167, 180, 181
Hospitals, at present, 163, 169,
state of, several decades ago, 159, 162, 163
*Hull*, 20, 29
*Hunt*, 22
Hydrogen, 23, 32

Immunity, 115-130
Infantile paralysis, 137, 138
Infection, 148-151, 174
Influenza, 150
Intelligence, methods of measuring, 196-198
relation to occupation, 208
Ion, 28
Isosteric substances, 33

*Jackson*, 165
*James, W.*, 228

Jaundice, 144
*Jenner*, 117, 118
*Johnson*, 156
*Joule*, 35
*Jung*, 224, 226

*Keen*, 11, 152, 153, 166, 182
*Keith*, 46
*Kelvin*, 35, 53
*Kinloch*, 173, 175
*Kitasato*, 120
*Kitchener*, 64
*Koch*, 119, 179
*Kossel*, 30
*Kühne*, 77

Laccase, 82
Lachrymators, 68, 69, 71, 73
*Lacomblé*, 30
*Landé*, 24, 26
*Lang*, 111
*Langevin*, 47
*Langmuir*, 10, 23
*Larmor*, 230
*Larrey*, 182
*Laue*, 19
*Lavoisier*, 9, 108
*Lebailly*, 138
*Lemaire*, 170
*Lentner*, 81
*Lewis*, 24, 31
Life, definition, 85
  duration of, 91
  prolonging, 85
Ligature, 156
*Lindpainter*, 181
Lipases, 84
*Lister*, 11, 154, 160, 161, 170, 171-173, 175, 191
  applies antiseptic methods, 178
  before and after, 152-191
Lithium, 23, 25
*Loeb, J.*, 11, 85, 87, 89
*Loeb, L.*, 91
*Loeffler*, 136
*Lorentz*, 230, 233, 234, 236
Luetin, 135
*Lynch*, 168

*McGraw*, 175
*McGrigor*, 164
*Magendi*, 130
Magnesium, 28, 30
*Mahan*, 95
*Malgaigne*, 156, 163
Manganese, 83
Manganese dioxide, 76
*Markoe*, 173
*Marsden*, 18
*Martin*, 183
Matter, kinetic theory of, 13
  electrical origin of, 16
*Maunder*, 176
*Maxim*, 47
*Maxwell*, 53, 230, 233
*Mayos*, 183
Measles, 137
Meningitis, 119, 126, 127
Mental examination, purpose of, 194
  reliability of methods, 198
  summary of results, 200
Mercury, 146
*Metchnikoff*, 88, 122, 124, 125, 142, 144
*Millikan*, 10, 13, 15, 22
*Minkowski*, 234, 235, 237
*Moore*, 174
*Mosely*, 20, 21
*Motley*, 164
*Mott*, 182
Mountain sickness, 98
*Mumford*, 184
*Murphy*, 140
*Muschet*, 40
Mustard gas, 72

*Nancrede*, 175
Neon, 23, 28, 29
Neurosis, 215, 218, 219
*Newcomen*, 35

*Newton*, 239, 242, 243, 244
Nickel, 23
*Nicolaier*, 120
*Nicolle*, 138
*Nightingale*, 164
Nitrogen, in *Caisson's* disease, 98
*Noguchi*, 138, 142, 143, 144
*Northrop*, 87, 89
Nucleus of the atom. See atom, its nucleus
*Nussbaum*, 172, 180

Octet group of electrons, 26
Old age, cause of, 88
*Olitzky*, 138
Operations, types of, 182-184
*Osborne*, 80, 81
*Ostwald*, 13
Oxidases, 83
Oxygen, 28, 76
  at high altitudes, 97, 111
  lack of, 101

*Paget*, 46, 177
*Pancoast*, 182
*Panzer*, 83
*Paré*, 155, 156, 157, 170, 189
*Parson*, 24
*Parsons*, 10, 34
Passive immunization, 122
*Pasteur*, 11, 77, 116, 117, 118, 119, 120, 131, 161, 170
*Paton*, 110
*Paul the Apostle*, 154
*Peckelharing*, 80
*Peninsula* campaign, 164
*Pfeiffer*, 138
Phenylcarbylamine chloride, 73
Phosgene, 64, 67
  protection against, 65, 67
Phosphorus, 29
Phosphorus pentafluoride, 29
*Pierce*, 110
Plague, 119, 126
*Planck*, 27
Pneumonia, 126, 127
Potassium chlorate, 76
*Pouchet*, 170
*Preece*, 41
Pressure, changes of, 99, 100
*Prince*, 175
"Principle of Equivalence," 239
Prussic acid, 68
Psychanalytic method, 212
  basic principles, 215-220
Psychoanalysis, conceptions and misconceptions, 211-229
  technic, 222
  uses of, 226
  what is is not, 213, 214
Psychologists, in the army, 193
Ptomaines, 121
Pyemia, 166, 180
Quantum relations, 22
  theory, 27
*Queen Elizabeth* (battleship), 43

Rabies, 117, 118
Radio-activity, 14
Radium, 23
*Reed*, 144
Research, value of, 58
Respiration, 108
Respirator, 67, 73, 74
*Richardson*, 46
*Richet*, 131
*Rivière*, 156
*Roentgen*, 9
*Rohan*, 157
*Rous*, 141
*Roux*, 120
*Rowland*, 16, 188
*Russell*, 39
*Russo-Japanese* War, 168
*Rutherford*, 10, 18, 23, 53
*Ryan*, 45

Salamanders, metamorphosis of, 93, 94
Salvarsan, 147

*Satterthwaite*, 173
*Savory*, 177
*Saxtorph*, 172
Scarlet fever, 137
*Schaudinn*, 142, 144
*Schick* test, 123, 135
*Schneider*, 103, 110
*Semmelweiss*, 161
"Serum sickness," 134
Serum therapy, 122
Sexual life, possible courses in the development of, 217
*Sherman*, 80, 81
Silver, 23
*Simpson*, 161, 162, 165, 189
Sleeping sickness, 147
Smallpox, 117
"Sneezing gas," 73
Sodium, 28
Sodium fluoride, structure of, 28
Sodium phenate, 65, 67
Sound ranging and listening devices, 44
*Souttar*, 187
*Spanish-American* War, 168
*Spence*, 177
Spirochetes, 141-145
Splenic fever, 116
Steam, laws of, 34
Sulfur, 30
Sulphur hexafluoride, 29
*Stark*, 24, 31
Steam engine, 34, 35
*Stewart*, 176
*Stimson*, 144
*Strong*, 165
Sucrase, 78
*Swingle*, 93
*Syme*, 172, 179, 182
Syphilis, 135, 142, 146

*Tait*, 177
*Taylor*, 40
"Tear" shells, 69
Tetanus, 119, 120, 121, 167, 187
*Teudt*, 30
*Thiersch*, 172
*Thomson, J. J.*, 9, 16, 31
Thyroid gland, 92, 93
*Tissandier*, 101, 103
*Titanic* (ship), 46
Toxalbumins, 121
*Trélat*, 163
Trench fever, 137
Trichloromethylchloroformate in gas shells, 70
*Trillat*, 83
Tuberculin, 135
Tuberculosis, 119, 126, 135
Tungsten, 23
Tungsten steel, 40
Turbines, 36-38
*Tyndall*, 143
Typhoid fever, 119, 123, 126, 188

*Uhlenhuth*, 94
Ultra-microscope, 142
Uranium, 23
Urotropine, 67

Vaccination, against smallpox, 117
Valence, chemical, 27, 32
maximum, positive and negative, 30
*Van Buren*, 173
*Van Slyke*, 106
*Voigt*, 230
*Volkmann*, 172, 180

War casualties, 164
*Wassermann* reaction, 123
Water power, 53
*Watt*, 34, 35, 36, 37
*Werner*, 30
*White, M.*, 40
*White, Sir W.*, 38, 39, 45
*Whitney*, 110
*Widal* test, 123
*Wilmer*
*Woker*, 84

*Wolf*, 83
"World-line," *Minkowski's*, 236
*Wrench*, 154, 176
*Wright*, 186

X-rays, 14, 19, 21
Xenon, 26
Xylyl bromide, 69

Yellow fever, 137, 142, 144
*Yerkes*, 12, 192
*Yersin*, 120