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ADDRESS IN MEDICINE.

SOME POINTS IN BACTERIOLOGY.¹

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"Vere scire est per causas scire."
—BACON.

There are three planes in the history of medicine. The first is the study of the symptoms or appearance of disease. It is the period of the infancy of medicine. It is naturally the most crude period, and all irregular medicine still rests upon this plane. It gave us a pharmacopœia, and the highest expression of it made of the practice of medicine an art. The second plane begins with the observation of the effects or lesions of disease. It made us familiar with the natural history of disease, and thereby nearly destroyed the pharmacopœia. The third is the present plane, upon which are being prosecuted investigations into the cause of disease. Investigators have just set foot upon its threshold. When it shall have been fully attained medicine will be entitled to a place among the sciences which are called exact.

The progress made in this direction during the past year so completely overshadows all other work in range and promise of practical value as to justify in this report, to the exclusion of everything else, a brief review of the conclusions reached.

The etiology of acute infections is comprised under the single term, *bacteriology*, the bacterium having come in the course of time to include all pathogenic as well as many innocent micro-organisms.

The year just passed has not been as eventful in the definite discovery of new causes of disease as several that have preceded it in the first half of the present decade. What has especially characterized the past year is the fixation of facts previously acquired, whereby the so-called germ theory of infectious disease has been brought from the realms of the ideal to the region of the real. Coemans said several years ago, "the following up of a single bacterium through all its phases of development is far more valuable than the discovery of new germs," and this pursuit has now been made with such success in the case of many forms as to justify in our day the claim of Magni in the Roman Annals of Public Med-

icine, fifteen years ago, that the study of medicine should undergo a reform, making obligatory at least a three months' course with micro-organisms.

For it is now demonstrated beyond dispute that pathogenic micro-organisms do exist in distinct and definite entity. The views advanced by Beale, that bacteria are portions of diseased protoplasm from living tissues, and by Wigand, that they may spring up *de novo* in organic matter by transformation of organic molecules, are no longer held worthy of serious consideration. The view of Beale was never anything more than an ingenious hypothesis, and it fell to the ground with the first studies of the life history of bacteria, while Wigand's theory had no better support than any other *spontaneous generation*. The fate which so quickly overtook the illustration of this theory may well serve to show the danger of advocating spontaneous generation in our day.

Wigand remarked that for the purpose of dissipating all doubts concerning the spontaneous development of bacteria in the protoplasm of cells, he would call attention to the fact that moving bacteria could be seen at any time in the healthy living cells of the trianea bogotensis, and in the hairs of the labiata. This statement was brought to the notice of the eminent botanist of Strasburg, de Bary, who thus describes his investigations: The trianea is a South American floating water plant. A piece of its living tissue removed from a fresh, healthy plant, examined under the microscope, reveals in fact the most exquisite picture of bacteria. Slender bacilli, alone or adherent in short rows, follow about the movements of the protoplasm and other contents of the cell in the liveliest way. Such a picture is a model—as a picture. But the addition of a drop of dilute nitric acid quickly dispels the illusion. Instead of maintaining itself like a true micro-organism, the bacteria of the trianea are dissolved away at once. The same is true of the rods in the hairs of the lip-flowering plants. The "bacteria" are nothing else than small crystals of oxalate of lime frequent in this form in the cells of plants. This story is instructive, the author says, in showing how far astray preconceptions may lead otherwise excellent observers.

Wigand saw micro-organisms develop in fluids after exposure to boiling heat for half an hour, a temperature and time sufficient, he thought, to destroy all germs. But the experiments at Koch's laboratory at Berlin prove that individual spores resist a boiling heat for several hours. Wigand's erroneous conclusions were based upon an imperfect sterilization.

¹The Address of the Chairman of the Section of Practice of Medicine, Materia Medica and Physiology, at the Thirty-Seventh Annual Meeting of the American Medical Association, St. Louis, May 5, 1886.

What a contrast to these obscure conceptions is offered in the clear statements of Leeuwenhoek, the first individual to turn the lens, crude and imperfect as it then was, upon, and to discover, micro-organisms. It would almost seem as if great minds knew intuitively what is true and what is false, else how may we understand the observation made by Leeuwenhoek as early as 1685 of the minute organisms found in water: "they do not arise in the water," he says, "they develop from germs."

The germ theory of disease was never really in so much danger from its enemies as its friends. For many years it suffered ridicule and discredit because of the false conceptions of "undismayed pioneers" and over-zealous advocates. The Germans still speak of the "überreifer Eifer" of this class. Thus the cholera-phyton proclaimed in England, and later again in Germany, turned out to be nothing else than eggs of intestinal worms; the animalculæ of variola eventuated in the common bacteria of putrefaction, and the palmellæ of malaria disclosed by one of our countrymen were unmasked as foreign bodies, impurities, not even germs.

Claims of Convertibility of all Germs.—An original conception of this over-ripe zeal was the view of Hallier, that all kinds of germs, big and little, moulds, ferments, bacteria, are mutually convertible. Micrococci, said Zürn, are only stages of development of moulds. This view needed only the most accurate observations of Brefeld and de Bary to be entirely refuted. More serious was the claim of Grawitz that innocent mould fungi, aspergillus, mucor, etc., could be converted into dangerous forms. Grawitz saw that the injection of aspergillus into the blood of rabbits remained without effect, whereupon it occurred to him to change its natural, cool, acid soil to a warm alkaline soil with a view of changing its form and action. Such general permeation of various internal organs, especially the kidneys, followed these experiments, as to seem to have demonstrated the conversion of the innocent into a dangerous parasite.

But when Koch and Gafsky came to repeat these experiments, with the precautions implied in control observations, it was soon discovered that the species of aspergillus, mucor, etc., included a whole series of pathogenic germs, some of which had entered with the injection of innocent forms. Grawitz's erroneous conclusions were based upon the use of impure cultures.

The field had now become limited to the bacteria proper. It may be said at once that all practical interest hinges upon the question of the constancy or inconstancy, *mutability or immutability*, of the forms of pathogenic micro-organisms. If they are not specifically different, as Nägeli claimed, but are forms of one or a few species, so that the same species, by assuming different forms, may, in the course of years or decades, effect at one time the souring of milk, the ageing of wine, putrefaction, the decomposition of urea, the red coloration of starchy food, and at other times produce typhus, malarial or relapsing fevers, diphtheria and cholera—if such mutability of form and action exists as this; if the myriad micro-organisms of the earth and air may at any time as-

sume deadly properties—all effort at investigation is futile, if not foolish, and every effort at destruction is not only powerless but paralyzed.

This idea of the unity of species, first advocated in our day by Ray Lancaster, met with warm advocacy at the hands of Billroth, who derived the different forms from variations in the soil or substratum, and later of Warming, who considered the different forms as so many different stages of development of the same species, like, to use a coarse comparison, the different stages of development of tapeworms in different hosts. Klebs was also inclined to accept this view, though with the reservation that certain forms occur preferably in the form of bacilli, others of micrococci.

Hay and Milzbrand Bacillus.—Perhaps no single statement seemed to lend such support to the negation of species as the claim of Buchner to be able to transform the innocent bacillus of hay infusion into the deadly organism of milzbrand. Buchner observed under continued cultivation the gradual change of the hay bacillus into the milzbrand bacillus, and with the reversal of this change, which he was likewise able to produce, maintained that the loss of virulence of the milzbrand bacillus was not an attenuation, as Pasteur had claimed, but a veritable transformation. Buchner was sufficiently well acquainted with the gross differences of the two bacilli, but he regarded them as accommodations of the same form to different soils. Hueppe credits Buchner also with a knowledge of the spore formation of the two bacilli—the most distinctive characteristic of different forms—which Buchner considered identical, a consideration which misled Brefeld to adopt Buchner's conclusions, but de Bary insists that with the gross differences in the spore formation of the two bacilli, it is doubtful if Buchner ever really studied the hay bacillus in this essential particular.

At any rate, it was easy for Koch, by pointing out these differences, as well as the difference in the resistance of the spores, the difference in the optimum and minimum temperatures in the process of reproduction, etc., to prove that Buchner was experimenting with two distinct species or forms, and that the apparent transformation was really a case of substitution or displacement of one form by the other. Inasmuch as no one has since succeeded in effecting such a transformation, this question may be regarded as definitely settled. Final disproof of Buchner's claim was made by Prazmowski in 1884, with the exhibition of such distinct differences in the two forms as to demonstrate their independence, so that whatever dispute remained concerned simply the possibility of attenuating the bacilli of milzbrand, a subject to be noticed again.

Bacteria of Milk.—A much more simple and easily refuted illustration of the inconstancy of action of micro-organisms was the observation of Nägeli, that fresh milk on standing becomes sour but boiled milk bitter. Fresh milk becomes sour, Nägeli says, under the action of a certain bacterium. Boiling the milk changes the character of the soil and the action of the same germ. Here, then, is an everyday observation of the transformation of the same micro-organism.

That this illustration may not seem too trivial, it may be said that it was, up to the time of Buchner's experiments, just mentioned, the sole apparently indisputable proof of the change of one definite ferment into another.

The fallacy of it became obvious when it was discovered that milk is made sour by many causes, among others, by many varieties of bacteria, of which Nägeli assumed the existence of but one. It did not occur to him to inquire if one variety might not get the upper hand before, another after boiling. The truth turned out even more simple than this, for Huppé showed that of the many forms of micro-organisms present in milk, one, the micrococcus lacticus, exuberates in a low temperature, and renders milk sour by the formation of lactic acid. Boiling kills this micro-organism with many others, but the spores of the butyric acid germ, the bacillus amylobacter, also present, survive boiling heat to develop later into the mature form. This bacillus effects in boiled milk a decomposition of the albuminates, attended with a bitter taste. Neither form nor action has been changed in a single germ.

Deviations that do Occur.—But the strongest advocates of constancy of form and function, Cohn and Koch, do not maintain that certain deviations may not occur. They claim only that these deviations occur within certain limits, such limits as are to be observed in structures higher in the vegetable scale. Gardeners, florists, farmers, succeed in effecting, under varying surroundings, marked variations from the primitive plant, but they may never change an apple to a pear tree, wheat into rye, or a sunflower to a rose. Koch himself admits the possibility of changing one form of micro-organism to a nearly allied form. He goes so far as to say that it is not without the bounds of possibility to convert a pathogenic into an innocent form. What he asks is simply that the specificness of one form shall not be surrendered until the proof is furnished. There are monomorphous and pleomorphous bacteria. No one claims that every micro-organism shows itself under all circumstances in but one form, as Koch admits the occurrence of Finkler's vibrio in three forms, the curved rod, the lemon shape and the spirilla, but he still insists that the individual preserves the reproductive form of its cells, that is, that it appears as a micrococcus, a bacillus or a spirilla, and that it does not change these forms. For, as Mittenzweig maintains, it has never yet been shown that a bacterium appears at one time as a genuine micrococcus, at another as a genuine bacillus, and again as a genuine spirilla, and even if we admit the form changes which Buchner and Gruber have observed in the organism of Finkler, and Babes has observed in the cholera germ, we must also admit, as Buchner has himself observed, that in the cultivation of the different forms the typical curved rod invariably appears, so that all these secondary changes are to be looked upon simply as so many variations upon the typical form. With the experience of the botanist and florist cited, it is not a matter of surprise that micro-organisms have been seen to undergo changes of form which are not observed in nature. Attenuations of virulence, for in-

stance, in virulent germs never occurs spontaneously.

The Germ, not the Form, Essential.—The conclusion reached by the mycologists of the present day is that under natural circumstances micro-organisms show themselves in the rule, not with variations but in permanent forms, but that disease is not produced so much by a distinct and definite form as by a distinct and definite germ. Most of the diseases of plants, de Bary says, are produced by parasites, and as investigations develop more and more distinct species it is seen that definite diseases are produced by definite parasites, whose specific properties are no more to be doubted than those of higher organisms or worms. This claim, the author concludes, is not simply convenient, as Nägeli observes, it is the only view which is consistent with acquired facts.

Ubiquitous and Indigenous Germs.—The world of micro-organic life falls naturally into two great divisions. One is found everywhere, at all times and in all places, and, as has been shown, in abundance enough to realize the panspermism of the ancients. Such germs are known as omnipresent, or, from the fact of their ability to obtain sustenance everywhere, as omnivorous germs. Hallier proposed to call them cosmopolitan, but Cohn devised the best appellation when he spoke of them as ubiquitous. Myriads of these germs are entirely innocent to man. Others are injurious only under certain circumstances. Thus the ubiquitous germs of common putrefaction may penetrate the body from a slough or a gangrenous part, to produce by their presence, or the chemical changes they induce, the condition known as septicæmia. Thus the pus-producing micro-organisms, probably of many kinds, belong to the class of ubiquitous germs.

On the other hand, most pathogenic micro-organisms are indigenous to certain definite places. These are the epidemic germs. Thus the mouths of the Ganges and Brahmaputra are the centres of cholera, Lower Egypt of the plague, the Antilles of yellow fever, Ireland of typhus. But just as plants of higher organization may be transplanted to other soils, may original endemics assume epidemic and finally pandemic proportions or extent. Thus small-pox first showed itself in Germany in 1493, an importation from the Netherlands, but it was not until 1527 that it was transported to our continent, making its appearance with wholesale slaughter in Mexico, and gradually extending thence over the whole of North America. Scarlet fever, which was first heard of in Arabia, was not seen in our country until 1735. It reached Iceland in 1827, South America in 1829, Greenland in 1847, and Australia in 1848. Measles had not been carried to Australia up to the beginning of our own decade. Cerebro-spinal meningitis, in all respects the most irregular of all epidemic diseases, first sprang up in Geneva, and first fell upon our country in 1806. Cholera was unknown with us until the memorable year of 1832. Even tuberculosis, which has long since assumed pandemic extent, was, as Liebermeister has shown, not originally ubiquitous, as it remained unknown to our own Indians, to the aborigines of Australia and the negroes of Central Africa until carried to them by more civilized races. There is therefore no longer question of the

spontaneous, or so-called autochthonous, origin of infection. Typhoid and typhus fevers, dysentery and diphtheria, pyæmia, erysipelas and puerperal fever, appear only at times when lurking germs and spores from previous cases find favorable conditions for development, or after fresh importations of the disease. All this disease, all infectious disease, is of exclusively parental birth, and can no more originate spontaneously than can serpents and crocodiles originate from heat and mud, as Lepidus maintained, bees be produced from the putrefying entrails of steers, as Virgil described, or mice be generated from sawdust and old shirts, as Van Helmont claimed. In keeping with these theories were the views since maintained that the plague arose from the putrefaction of corpses, yellow fever from the crowding of slave ships, cholera from decaying vegetable food, typhoid fever from the emanations of human excrement, consumption from bad ventilation, or oftener from a bad cold, and diphtheria from sewer gas. These are factors which do undoubtedly favor the spread of the infectious maladies, but never originate the birth of one. A fright may cause a premature birth, Jürgensen remarks facetiously, but it would never conceive a fœtus. So, rabies and hydrophobia can no more arise spontaneously than can dogs and men.

Thus is explained the specificness of acute infectious disease. Each one of these diseases produces itself alone. Measles begets measles, small-pox begets small-pox, cholera begets cholera. Figs would be born of thistles, or grapes of thorns, as soon as cholera of small-pox or diphtheria of typhoid fever. The introduction into the blood of a specific germ begets the specific disease, and the fact that each one of the acute infections has always presented the same characteristics, proves most conclusively that *no change has occurred* in the properties or peculiarities of the specific cause. For so long as observations have been recorded, measles, for instance, has always been the same disease, with the same period of incubation, the same prodromata, and the same eruption, the same complications and the same termination. New interpretations of the phenomena of the acute infectious diseases have been made from time to time, more searching means of study have developed new signs, but the characteristic features of each of the acute infections have always remained the same. The accurate observations rendered possible by the adoption of the solid culture soil are in thorough accord with these conclusions. The essential nature of pathogenic bacteria is not changed by alterations in the soil or other surroundings. Bacteria may be shriveled or dwarfed or reproduction checked by lack of oxygen, unsuitable nutrition, improper temperature, but they may not be changed in nature. Up to the present time it has been found impossible to convert innocent into pathogenic forms, and the observations recorded which seem to lend support to the transmutation theory, as by Buchner, Bastian, Nägeli, and others, have been shown to rest upon inaccuracies or impurities.

Attenuation not Change of Nature.—But the case is very different with the converse of this view, which opens up one of the most interesting studies in mycology. Is it possible to deprive the pathogenic forms of

their pathogenic properties? The belief is still maintained, by some clinicians at least, that vaccinia is smallpox which has lost its virulence by passing through the body of a cow, and the question of attenuation of the so-called virus of virulent disease with the view of inoculating it in milder form, occupies the attention of prominent mycologists at the present time. Within the present decade this question has been answered in the affirmative with reference to the virulent bacteria of charbon. For it has been discovered by Pasteur and by Koch that under the influence of high temperature and various chemical agents, the bacteria of charbon may be made to suffer loss of their pathogenic properties, while they still retain all other characteristics, including the capacity of reproduction. Pasteur claims to have effected the same attenuation in the case of hydrophobia. But these observations do not support the view that any change of nature has been experienced in this way. Bacteria thus treated are not changed into innocent forms. They have simply lost the physiological property of infection. Baumgartner puts it pertinently when he says it is not a question of changing poisonous into innocent snakes, but of extracting the poison fangs from animals which otherwise remain the same.

The Morphology of Bacteria is not simply a question of size and shape. The term is extended to include also motion, color and affinity for color, as well as the manner of growth or disposition of the colonies. In many cases such distinctive peculiarities are already demonstrated as to render it possible to absolutely diagnose disease in life by one or more of these points. As Hueppe says, this is the most interesting question for the clinician. May we make a differential diagnosis from morphology alone?

Bacteria vary greatly in both length and breadth, but are for the most part so small as to be on the confines of the visible with the microscope. In fact, it is chiefly by reason of the recent improvements in the illumination and magnification of the microscope, the oil immersion lens and Abbé illuminating apparatus, that they have been rendered visible at all. Some of them are to be seen only with a power of 700 diameters, which is the magnification generally used in the study of all micro-organisms. Mycologists speak of micro-, meso- and mega-coccus, or bacteria, of the micrococ-coccus prodigiosus, and of the bacillus subtilis, but these are all, of course, relative terms. Pathogenic micro-organisms vary in length from 1 to 40 mikro-millimetres, and in breadth from 0.5 to 7mm. Many micrococci are too minute to admit of any accurate measurement. The largest micro-organism is the spirilla, which may reach the length of .2 of a millimetre. Perhaps a better idea of size can be conveyed by comparison with a familiar object. The bacillus tuberculosis, which occupies in respect to size a median place, varies in length from 1-2000 to 1-3500 of an inch, the smaller measure being the average diameter of a corpuscle of human blood.

Although some distinction may be made between pathogenic and innocent organisms by their size and shape, the most skilful mycologist would hesitate to express an opinion on this fact alone. But micro-

organisms may look alike and yet be very different. Spermatozooids of different animals may present the same general appearance, but they are endowed with very different properties. We remain as yet at too great distance to make out the distinguishing features even of innocent and dangerous micro-organisms. As Birch-Hirschfeld remarked, it would be impossible to declare of a man standing on the spire of the Strasburg cathedral, whether he was black or white, and even the same configuration in every particular would furnish no more definite criterion than in the case of full grown serpents of the same appearance, some of which only are poisonous. We await now with intense interest the revelations which are to follow the experiments with the new theory worked out by Professor Abbé, which it is claimed already exhibits differences in the structure of bacteria.

The general construction of bacteria, so far as it can be studied, is simple enough. Bacteria are cells because they are constituted, grow and divide like cells, and although nuclei have not yet been discovered in them, they are in this regard not unlike other low forms of vegetable cells. The protoplasm of the cell seems homogeneous in the minutest, but more or less granular in the larger and more distinctly visible forms. It shows the same reactions and takes up the same colors as other protoplasmic bodies, differing as they do in different forms. The cell is invested with a membrane which may be separated from the protoplasm by agents like the alcoholic solution of iodine, which shrink the protoplasm. The membrane assumes prominence also at the period of spore formation. It is in most cases firm and closely apposed to all contents, while in the spirochetes it is extensile and elastic. Dark, transverse lines forming across the protoplasm indicate the division of a bacterium into daughter cells, which separate in the process of reproduction. Hence the name schizomycetes. A billiard ball, a lead pencil and corkscrew, indicate in the homely comparisons of de Bary the chief varieties of bacteria as micrococci, bacilli and spirillæ.

Distinction of Bacteria.—A glance would reveal the difference between a bacillus and a spirilla, and there could be no question of mistaking a micrococcus for either. In many cases even gross morphological resemblances could create no embarrassment in the mind of the practitioner. What possible doubt could exist, for instance as between the comma bacillus of the stools and intestinal contents of cholera and the innocent comma bacillus found in the mouths of healthy people? The condition of the patient decides it at once, or if there could still be a doubt, it would be dissipated with a knowledge of the fact that the cholera bacillus is not found in the mouth. But in many cases differences in form alone are too slight, and variations in size too great to be recognized by the clinician. In some cases these differences can be seen. Thus the slight deviations between the forms of the bacilli of milzbrand and malignant œdema enable mycologists to separate diseases which are often confounded. But these distinctions may be made out only in the laboratories of experts. Hence for practical use appeal must be made to other fac-

tors in morphology. Thus the bacillus of tuberculosis, syphilis and leprosy closely resemble each other, that is closely to the clinician, though coarsely to the mycologist. But the tubercle bacillus distinguishes itself from all other bacilli save one, by two peculiarities: first, lack of affinity for all dyes, that is, the resistance it shows to colors, and, secondly, when it is colored with alkaline dyes, by the persistence with which it retains its color in the presence of mineral acids. This persistence is shown only by the bacillus of leprosy, but the bacillus of leprosy may be differentiated by the fact that it may be colored with Weigert's nucleus color, (hæmatoxylin, alcohol, alum, aa 2, distilled water, glycerine, aa 100), which has no effect upon the bacillus tuberculosis. The colored bacilli of syphilis are decolorized by mineral acids. By the method mentioned Gaffky discovered characteristic bacilli in the sputum of tuberculosis in 938 of 982 cases.

Considering the fallacies of the observations, and the stage of prephysical signs, it is safe to say that the time is close at hand when we shall no longer think of using the pleximeter and the stethoscope in the diagnosis of tuberculosis.

A skilled mycologist would alone detect the fine differences in morphology of the bacilli of cholera and cholera morbus, but any one would notice at a glance the difference in the funnel and cone or stocking shaped colonies of the two varieties. As, however, the length of time that must necessarily lapse to make this observation precludes its practical value to clinicians, quicker conclusions can be reached by the physiological test, that is the introduction of the germs, or matter containing them, into the stomachs of guinea pigs. These animals are very susceptible to cholera morbus, but insusceptible to true cholera, without special preparations or precautions. Perhaps this test would be resorted to only in cases where doubt existed as to the commencement of an epidemic of Asiatic cholera.

The method in which the bacteria aggregate themselves in the process of growth in the culture soil, the process of colonization it would be called in the tissues of the body, or *the formation of zooglea*, furnishes some, but uncertain information regarding the nature of the germ. Cohn thought at one time that the whole class of bacteria might be divided into two distinct species, one of which formed a mucus-like mass, the other fibrils or threads. These classes he proposed to designate as gleogenous or mucus-forming, and nematogenous or thread-forming families, but he was compelled subsequently to abandon the idea on observing the changes in the mode of growth in different soils and at different temperatures. Thereupon Koch observed that the formation of zooglea in the form of membranes or fibrils, squamous, dendritic, fenestrated, nodular, globular, circular, etc., immediately preceded the development of spores. Both Cohn and Koch soon reached the conclusion that while the form of the colony might serve to separate families and groups, estimates based upon such observations must be accepted with much reserve. But while it is admitted that the form of the zooglea varies in different soils, it is nevertheless true that a typical

form is shown under the same conditions, a fact which Hueppe remarks, essentially lightens a differential diagnosis. To give but one example, the bacillus anthracis may be macroscopically distinguished from the non parasitic bacillus subtilis by the fact that the anthrax bacillus forms in its soil a flocculent deposit, while the bacillus subtilis develops a dry membrane upon its surface.

The development of bacteria does not differ from the higher vegetations in requiring the necessities of life; food, heat, oxygen, water, etc.

Pure Culture Soils.—The question of food is connected with the subject of cultivation in the so-called pure culture soils, which consists in selecting the food best adapted for the rapid multiplication of micro-organisms. The fact that bacteria remain sterile in certain soils and luxuriate in others does not surprise us when we reflect upon the predilections of higher forms of vegetation.

While, then, many bacteria may be cultivated in almost any kind of culture soil, they differ in the degree of development according to the nature of the soil. Thus Wilkommen has observed that the germs which thrive upon the South American potato can not be made to grow upon the European potato. The micro-organisms which give the peculiar piquancy to Stilton and Roquefort cheese grow better in certain cellars than in others. The first experiments in cultivating bacteria were in fluids, solutions of meat, beef tea, chicken soup, malt extracts, infusions of hay, etc., but fluids are open to the objection that they admit other germs, to coalesce with and rendered impure the special variety to be studied. Pure cultivation became possible only with the use of the pure culture soil, first employed by Koch. Germs falling upon a solid surface remain fixed in the same place. The solid culture soil made practicable the absolute isolation of germs, without which accurate investigation is impossible. Koch made his first studies with the common potato. The potato was the key to the whole subject of solid cultures. We might say that what the apple was to Newton the potato was to Koch. Subsequently gelatine was employed, then aqueous humor, then gelatinized meat preparations, peptonized gelatine, etc., and as a climax for the epicures, gelatinized blood. Thus has been determined the peculiar soil in which the varieties of pathogenic bacteria thrive the best. Thus while the bacillus of both forms of cholera develop upon both animal and vegetable soils (both being really exanthropic germs), the bacilli of tuberculosis will not grow in a vegetable soil as upon the surface of a potato, but will thrive in infusions of meat and luxuriate in the serum of the blood. The micrococcus of chicken cholera grows to swarms in neutralized chicken-soup, and the comma bacillus, which is really not a bacillus, but a form of vibrio or spirilla, develops in such luxuriance in alkaline meat soups as to have enabled Schottelius to detect it in minimum amount. In such cases, where but very few or doubtful specimens were present in the intestinal contents, Schottelius added to the contents two and a half times as much slightly alkalisied infusions of meat, or ten times as much gelatinized meat peptones. In this mixture preserved

uncovered in a warm place at a temperature not above 40° C. cholera germs developed in myriads within twelve hours.

Effect of Bacteria on Food.—In this connection a remark may be made upon the effect of bacteria upon the food selected, foreshadowing the local effects of micro-organisms upon the tissues of the body in the so-called local symptoms of disease. It is observed and distinctly tabulated if the gelatine or other food be fluidified, granulated, colored, decomposed, with or without the development of odors and gases, and the time required to induce these changes. Thus have the mycologists made us familiar with characteristic features of the vibrios of both forms of cholera, which fluidify gelatine, while the micrococci of pneumonia have no such effect; have pointed out the nail cultures of pneumonia, the air vesicles of Asiatic cholera, the flat scales of tuberculosis, the fern leaves of the micrococcus of erysipelas, the acacia leaves of one form of the micrococci of pus. So also of the effect of puncture or stick cultures show peculiarities different from plate cultures, and different effects are observed again with the same bacteria in different kinds of soil or food. Eisenberg has recently (Hamburg and Leipsic, 1886) published a *Bacteriologische Diagnostik*, which consists of a series of tables wherein are noted, in a form of inestimable value to the student of bacteriology, all these peculiarities of all known germs.

Concerning Temperature.—Three cardinal points are recognized of the temperature: the maximum, the minimum and the optimum. The optimum is the temperature most conducive to fructification, to spore formation. Excesses in either direction arrest certain processes, extremes destroy life. As might have been premised, non-parasitic enjoy much wider latitude than parasitic germs. Thus, according to Cohn, the bacterium termo grows between 5° and 40° C., with its optimum at 30° to 35° C., while the border temperatures of the bacillus tuberculosis, according to Koch, are 28° and 42°, with an optimum at 37°, the temperature of the human body. The conjoined influence of soil and temperature is shown in the conduct of certain bacilli (tyrothrix) found in cheese. The optimum temperature of this germ is 25° to 35° C. In a neutral fluid they are killed by a temperature of 90° to 95° C., while in a weak alkaline fluid they live at 100°. The mature spores of this species remain productive in a weak alkaline fluid after being boiled at a temperature of 115° C. Tyrothrix filiformis survives in milk a temperature up to 100° C., a degree fatal in one minute in an acid fluid. The spores of this species survive in milk a temperature of 120° C., while in gelatine they are destroyed at 110° C. This knowledge of the range of temperature gives a differentiation at once of parasitic from non-parasitic bacteria, as germs whose range is limited to 28° to 42° C., may not constantly find anywhere upon earth, outside of animal bodies, the necessary means of existence.

Need of Oxygen.—Such differences prevail regarding the need of oxygen that Pasteur separated all micro-organisms into two classes, ærobes and anærobes. As, however, all known pathogenic micro-

organisms must have oxygen more or less, the division is of more value to the mycologist than the clinician. One point in this connection regarding the ammoniacal degeneration of urine is of interest to the practitioner.

Bacteria of Urine.—This degeneration, as is well known, results from the conversion of urea by the absorption of water, into the carbonate of ammonia, during which process the originally clear fluid becomes cloudy and opaque. A drop of this urine under the microscope discloses myriads of germs of all descriptions. Cohn has shown that one of them, the micrococcus ureæ, is the prime cause of the ammoniacal change. Pasteur had already discovered that this micrococcus cultivated pure in a fluid containing urea induced in it the same change as in urine, and Musculus has since disclosed the fact that the change is induced by a chemical product, an enzyme separable by alcohol, excreted from this particular germ.

The presence of oxygen is a necessary condition of the life of the micrococcus ureæ, which cannot, therefore, be the cause of the ammoniacal degeneration that in bad cases of catarrhal inflammation takes place within the bladder, a sac shut in from the outside air. It was then assumed that this degeneration must be affected by other anerobic bacteria, and in fact, minute forms are found in freshly voided urine.

It is interesting to know that Miquel discovered in dust a very delicate bacterium which vegetates in the absence of oxygen. This bacillus he named the bacillus ureæ, because it has the power of converting urea into the carbonate of ammonia. Hence the force of Teuffel's warning, "Put no soiled catheter into the bladder."

The Fecundity of Micro-Organisms has been so often demonstrated in explanation of the suddenness of appearance of them in multitudes, and of the virulence of infectious disease, as to require mention here only for the purpose of checking the riots of the imagination. It is known that a particle from a milzbrand bacillus, so small as to be invisible under an ordinary lens, introduced beneath the skin of a guinea pig, multiplies sufficiently to kill the animal in forty-eight hours, and a drop of the blood of the animal thus affected, properly inoculated, destroys the largest ox in a few days. It is useless to dwell upon this point of propagation. It was the recognition of it that more than another compelled the return to the germ theory of infectious disease when it seemed to have been routed even with contumely. No purely chemical substance possesses this property. The power of reproduction or self multiplication is limited to living things. Chemical substance admit of great subdivision, as best exemplified, perhaps, in the dissemination of odors, but such subdivision is attended always with gradual loss of substance.

Reproduction takes place in bacteria, whether by fission or spore formation, a rapidity bordering on the marvelous. Cohn indulged himself in the pursuit of a calculation, reaching the conclusion that the progeny of a single bacterium, unchecked in growth, would in the course of three days reach the appalling weight of fifteen million pounds Troy, and in five days fill up a space of 928,000,000 cubic miles, the estimated capac-

ity of the entire ocean. But while some such calculations may be justifiable to convey some adequate idea of the degree to which the earth and the air may be filled in a few days during the prevalence of an epidemic, it must be remembered that it was flights of fancy like these that first brought the germ theory into discredit and derision. Check is put upon the development and reproduction of all bacteria by the lack of nutrition, which sooner or later must ensue, as well as by the inimical action of different varieties upon each other. Thus the bacteria of decomposition cease to multiply and perish by the myriad so soon as the material of their food is converted into inorganic matter; the bacteria of fermentation are destroyed, or their reproduction checked by the alcohol which they form; the bacteria of cholera with dessication, etc. The bacteria of most diseases perish with the death of their host, as well as from various other causes in life, as by the fever they evoke, or are themselves destroyed by the bacteria of putrefaction.

Thus it has been proposed to cure trachoma with the gonococci of gonorrhœa, lupus and epithelioma with the micrococci of erysipelas, and tuberculosis by the inhalation of the bacteria of putrefaction.

Spore Formation.—The conditions affecting the process of fructification are of extreme importance to the proper understanding of the cause and prevention of acute infectious disease. A single bacterium is made up of several cells of parts, of which each cell forms one spore. Pasteur first recognized these "brilliant corpuscles," but it remained for Koch to determine their significance, and for Prazmowski and Hueppe to establish their supreme value from the point of view of differential diagnosis. The difference in the method of spore formation is also a chapter of itself which could find no discussion in the limits of this report. It is enough to say here that characteristics of specific bacteria are as definitely determined in the observation of these phenomena as in the effects of inoculation. Spores constitute the permanent forms.

Endospores and Anthrospores.—There is now quite general acceptance of de Bary's division of all bacteria into classes, one multiplying by endospores and one by arthrospores. Endospores are spores evolved from protoplasm in the body of bacteria in such a way that the spore forms its own membrane, while an arthrospore is a transformation of an entire part or cell of a bacterium, the membrane of the bacterium forming the membrane of the spore. True bacteria develop by endospores. Such are the pathogenic bacteria, whether in the form of micrococci, as of erysipelas, pneumonia, gonorrhœa, suppuration; bacilli, as of tuberculosis, syphilis, leprosy, diphtheria, milzbrand, glanders and typhoid fever.

Spores are distinguished from micrococci by their bluish, opalescent cast, their high refractive power, and their obstinacy to color, because of the impermeability of their membranes. Strong acids and extreme heat, which kill the protoplasm of the bacteria, injure the vitality of the spore membrane, to make it permeable and admit color. Under such conditions spores may be colored intensely while the body of the

bacterium is only feebly or not at all affected by color. Spores of all kinds are characterized by extreme tenacity of life. Most endogenous spores remain productive after exposure to 100° C., many even to 130° C. Anthrax spores survive a dry heat of 123° C. Endospores survive dessication on an average about one year; those of the *Bacillus subtilis*, according to Brefeld, three years. Pasteur claimed to have kept spores in hermetically sealed tubes, capable of reproduction after twenty-two years. Such long sustentation of life is capable, of course, only under favoring conditions. Botanists generally admit persistence of vitality in seeds from ten to twelve years. Statements of persistence for centuries, as from mummies' tombs, are considered mythical. As a rule, as stated, spores perish in a few years, so that limit is to be put upon the assertion of an enthusiast in antiseptics that "time does not destroy septic dirt."

Bacteria of the Alimentary Canal.—The surface of the earth is the bottom of an ocean of air teeming with micro-organisms of every description. The origin, character and distribution of these germs is a subject of itself. Myriads of them, among others, pathogenic germs are ingested and inhaled every day. The alimentary canal throughout its length is described as a rich garden of vegetating bacteria. Most mature forms are destroyed in the stomach under the action of the gastric juice, but many spores, and some mature forms—*sarcinæ*, for instance—escape to reach the intestine with all the favoring conditions of a hot-house. The mycologists speak of the flora of the feces; in fact, masses of feces are almost wholly masses of bacteria.

Bienstock, who has made a special study of these bacteria, succeeded in isolating one *Bacillus* endowed with the specific property of decomposing albumen and fibrin. Cultivated to obtain sufficient quantity it separates albumen and fibrin through all the successive stages of decomposition with its gases down to its final products, carbonic acid gas, water and ammonia. No other bacteria have this property. Artificial albumen is not attacked, and casein is not touched by it. Hence it is that the stools of sucklings emit no fecal odor.

These bacteria of the intestinal canal belong to the class of *saprophytes*. They have to do with the resolution of organic into inorganic matter, and they are hence the greatest friends of man. They have no power of penetration to the blood. It is now almost universally conceded that no germs exist in the physiological interior of the healthy body. No germs exist in healthy blood. An apparent exception proves the rule. In a number of observations with negative results, Klebs once found bacteria in the blood of an apparently healthy dog. It was subsequently learned that bacteria of decomposition had been previously introduced into this dog in an experiment on wound sepsis. The animal had long since perfectly recovered. The germs found by Klebs had still survived, and were remaining at the time of the observation quiescent. It was an observation useful also in illustration of the latent stage of disease. But even useful saprophytic germs become dangerous when they do enter the blood

through breaks, sloughs or ulcers formed by pathogenic germs. Such secondary saprophytic immigration occurs in diphtheria, typhoid fever and small pox as to have until recently occasioned much confusion in the recognition of the true pathogenic germs. Invasions of this kind, independently of these diseases, are probably responsible for many non-infectious septicæmias of surgery and obstetrics, as well as for many vague "rheumatisms," "malarias," "colds," "teethings," and "gastric fevers" of internal medicine.

Pathogenic micro-organisms enter the blood through solutions of continuity in the surface of the skin and mucous membrane, including the lungs. The germs of tuberculosis, pneumonia and all the acute exanthemata probably enter the blood by way of the lungs, which permit the passage of larger and grosser matters in the dust of coal, iron, etc. Each micro-organism has its own history in its preference of site, *mode of invasion, dissemination* and effect upon the tissues of the body. A notice of one or two of the best studied will serve in illustration.

The micrococci of erysipelas are deposited upon the epidermis at some break of the surface, which break may have entirely healed by the time the disease is recognized, to distribute themselves chiefly in the lymph vessels of the skin and subcutaneous fat. Hence the superficial character of the disease. They multiply, according to Fehleisen, in a direction opposite to that of the lymph currents. They are never found in the blood or in distant organs.

The bacteria of decomposition take quite a different course. One set, the staphylococci, multiply in the connective tissue without entering the lymph vessels; another set, the streptococci, enter the lymph vessels and follow their course to constitute the lymph—angiectatic processes. Suppurative phlegmonous tracts indicate their presence.

The micrococci of gonorrhœa are endowed with the property, according to Bumm, of penetrating to and multiplying in the protoplasm of the urethral cells to effect their dissolution. Hence they are distributed by the lymph vessels or are carried directly, to be found in the bladder, kidneys, Bartholine glands, periurethral abscesses, rectum, neck and body of the uterus, sacs of the conjunctivæ, and joints of the knee.

The *Bacillus tuberculosis*, which is at the present time perhaps the most universally distributed of all pathogenic germs, finds less ready victims than that of cholera and milzbrand, because of its immobility, its slower growth and less poisonous products. On account of these factors the extension of the disease in the body remains, as a rule, circumscribed. Wandering cells sometimes carry it, but its transfer to distant organs, bones, joints, testes, meninges of the brain, etc., is chiefly effected by a quite accidental irruption into blood and lymph vessels. Thus, Weigert has demonstrated at local depots the erosion of and penetration into the walls of veins, Koch a direct irruption into small arteries, and Ponfick the perforation of the thoracic duct with the sudden inundation of the whole body to constitute the clinical picture of miliary tuberculosis. Thus, also, is easily explained the sudden aggravation of tuberculosis in

latent, quiescent and convalescent cases of the disease.

Eberth and Gafky likewise describe the penetration by typhoid bacilli of the intestinal mucous membrane, with subsequent infiltration of the submucous tissue, muscular coat, mesenteric glands, and escape thence into the blood to accumulate in the spleen. Hein claims to have discovered them in the spleen during life, but Fränkel and Simmonds (*Die etiologische Bedeutung des Typhus Bacillus*, Hamburg and Leipzig, 1866), with good reason discredit this claim, though they were able to make pure flat cultures from the spleen post-mortem in twenty-five of twenty-nine cases. The bacilli of typhoid fever increase in the spleen so rapidly soon after death as to render their detection easy.

The Effect upon the Tissues of the body presents the same differences as the effect upon culture soils outside of the body, and here again each micro-organism shows its own peculiarities. The superficial catarrhal and diphtheritic processes, parenchymatous infiltrations, coagulation necroses, neoplasms, etc., coarsely correspond to the alterations observed in the artificial culture soils.

Erysipelas, again, a surface disease, open to inspection, offers in the studies of Fehleisen perhaps the most accurately recorded observations in this regard. Fehleisen found that he could distinguish four layers or zones of inflammation. The first, the peripheric, extended about one centimetre beyond the reddened and elevated border wall. It showed no visible lesion, either in color or thickness, though its lymph vessels were stuffed with micrococci. The wall mentioned is itself the second zone, the zone of inflammatory reaction. It consists of the rapidly multiplying micrococci with wandering cells which have partly taken up, included or ingested the bacteria, to finally displace and substitute them altogether. A small celled infiltration with a total absence of bacteria marks the third zone, while the fourth shows only pallor or anæmia of the skin in process of restitution *ad integrum*. The accompanying fever and gastric catarrh—out of all proportion at times to the extent of the disease—are the results of chemical changes induced by the micrococci.

The fact that the same local phenomena are present in erysipelas migrans without constitutional signs, would indicate that this disease is due to a different, though allied germ. Rosenbach found this disease often in individuals whose avocation deals with animal matter. Slight wounds of the hands in butchers, tanners, cooks, are frequently points of origin for a brownish-red infiltration which takes the precise course of erysipelas. From this infiltration he was able to cultivate a special micrococcus inoculable by puncture, to produce the same condition.

True erysipelas is entirely unattended with suppuration or other destructive change than fatty degeneration of the epithelial cells and restitution by new formation. Suppurative or phlegmonous processes indicate a mixed infection with the staphylococcus or streptococcus which produce this condition. The supervention of a still graver complication, gangrenous emphysema, is due to another micro-organism,

this time a bacillus, of entirely different nature, whose effect is to produce hæmorrhagic infiltration of the deeper muscular structure, with the development of the gases of decomposition.

Action of Micro-Organisms on an Internal Surface.

—A good illustration of the action of micro-organisms on an internal surface soil is offered by Löffler in the growth of the dumb-bell bacillus of diphtheria, which produces deep and extensive layers of false membrane in the fauces, pharynx, and trachea. The glutinous and pultaceous mass thus formed is a quicksand to catch and entangle the myriads of micro-organisms ingested and inhaled, in such inextricable confusion as to have made it for a long time impossible to pick out the specific cause of the disease. Beneath this superficial layer Klebs and Löffler at last succeeded in finding a special layer containing numerous cells among which, aggregated in small colonies, were special bacilli which admitted intense coloration with methylene blue. The layer beneath this again, directly superimposed upon the dilated vessels, is a fibrinous mass composing the bulk of the false membrane. It contains but few cells and no bacteria, and represents the product of reaction of the mucous membrane to the virus of the bacteria. This deepest layer is produced by the coagulation of a fibrogenous exudation which escapes from the blood-vessels and opposes a barrier to the further advance of the bacilli. Breaks in this barrier permit the absorption of the virus emanating from the bacteria or their products, to produce the constitutional symptoms of the disease.

Production of Neoplasms by Bacilli.—The bacilli of tubercle, leprosy, syphilis and glanders affect the soil of their selection in the body quite differently, in that they produce granulation tumors, neoplasms characterized by a tendency to rapid dissolution by fatty or calcareous degeneration. The cellular element of these tumors resembles that of the lymph glands. Taking tubercle as a sample, they are round cells, of various size, the medium size resembling a white blood corpuscle, with small, round, shining nuclei, provided with nucleoli. The large cells contain two, even up to twelve nuclei. Accumulation of these cells constitutes the nodule which the old anatomists named tubercles.

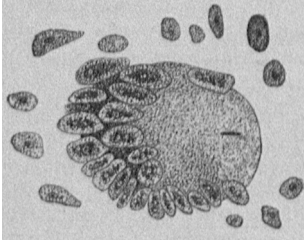
A tuberculous mass, on schematic section, shows an outside ring of round cells provided with a single nucleus about a narrow ring of epithelioid cells, which finally enclose one or more giant cells. The bacilli of tuberculosis are found in all parts of the tuberculous mass, free—that is, between the cells—as well as in the interior of the cells.

Behavior of Bacilli in Giant Cells.—But the most characteristic as well as curious phenomena are presented in the behavior of the bacillus in giant cells, a question which brings the subject to its most intimate ultimate relations.

The giant cell, as is well known, is distinguished by the number of its nuclei, as well as by its size. When now but a single bacillus penetrates to the interior of a giant cell, whose nuclei are disposed about the circumference of the cell, it is commonly found in the free space at or near the middle of the cell. But it

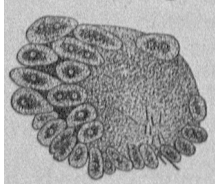
is more common to find all the nuclei grouped together at one end, with the bacillus at the opposite, often at the extreme opposite, end of the cell. The poles of the cell are thus occupied, one by the nuclei, the other by the bacillus. Thus they stand facing each other like foes, and it is impossible to resist the conclusion that there exists between them an antagonism which keeps them as far as possible apart.

When two bacilli are present it is not unusual to find one at each end or pole of the cell, while the



The Bacillus in the Giant Cell.

nuclei are all grouped about the centre or equator, or the relations being changed, the bacilli are disposed at the equator while the nuclei are grouped at the poles. It looks, Mittenzweig says, as if each group of nuclei was holding a bacillus in check. When the number of bacilli is greater, they do not

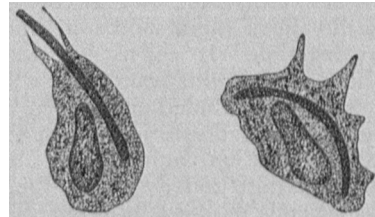


long remain in this passive state. For they are soon to be seen at different places in the cell, close to and between the nuclei, with their long axes perpendicular to the surface of the cell. The wall of the nucleus is thus broken down and the giant cell succumbs. Groups of bacilli are thus found arranged in stellate form, but no longer surrounded with nuclei.

Koch concludes, hence, that the penetration of an epithelioid cell by one or more bacilli is the first step or stage in the origin of a tubercle. The virus or poison emanating from the bacillus irritates the cell to such degree as to lead to increase in its size and multiplication of its nuclei; in other words, directly to produce the giant cell. The irritation extends to neighboring cells, to induce hyperplasia, and to vessels, to lead to emigration of the white blood corpuscles. Meantime, the struggle continues in the giant cell, to end occasionally in the destruction of the bacillus, but far more frequently in the triumph of the germ. They then break through the circle of nuclei, escape from the wall of the cell to attack new cells with similar fate. The ruptured cell suffers necrosis, the plasma current ceases, plasma and nuclei coagulate, nuclei are broken up into debris, and the whole cell is converted into a homogeneous, inert, dead mass. The condition may be arrested at this stage, as in the spleen, or may, as is usual elsewhere, suffer a later conversion into caseous matter. Bacilli which have not escaped to other cells perish with the

death of the cells, their hosts. Syphilitic neoplasms show the same phenomena, except that they are more prone to undergo fatty degeneration, resorption and cicatrization (Mittenzweig).

Bacteria in the Blood-current.—The conduct of bacteria in the blood-current itself or their effect or action upon the elements of the blood is but little known. In most cases the stay is too short for any permanent effect. But one curious observation has been made by Metschnikoff concerning the bacilli of milzbrand and the white blood corpuscles, which throws light upon the question of susceptibility and immunity of disease. With suspicion based upon the familiar fact of the absorption of food and foreign bodies into the interior of amœboid bodies, by protoplasmic protrusions and inclusions, and more especially upon the observation of a disease in small crustacea caused by the entrance or ingestion of a peculiar spore into the coloring blood corpuscles of the animal, Metschnikoff concluded to study the relations of the milzbrand bacillus to the white blood corpuscles of vertebrate animals. He soon discovered that the blood corpuscles of susceptible animals (rodents) only exceptionally incorporated virulent bacilli, whereas the blood corpuscles of insusceptible animals (frogs, lizards) took them up abundantly. Being thus ingested or included, they soon perish in the interior of the cell, to finally entirely disappear. The same fate awaits milzbrand bacilli in the bodies of susceptible animals, when the virulence has been attenuated or abstracted in any way, as by artificial heat.



Leucocytes as Phagocytes.

Immunity.—These observations, should they meet with wider confirmation, must throw light upon the obscure subject of immunity conferred by an attack of disease against its repetition, as well as upon protective vaccination. For we lack as yet a sufficient or satisfactory explanation of the immunity thus conferred, though three plausible hypotheses have been proposed. The first is the theory of exhaustion, which assumes that the germs of the disease exhaust the elements in the blood necessary to their nutrition. Something analogous to this is seen in vegetation of higher structure, which cannot be made to grow indefinitely in the same soil. The second is the antidote theory, or the theory of antagonism, which supposes that certain products evolved from the soil in the multiplication or growth of germs react upon them fatally. The analogy here is found in the process of fermentation, whereby the torulæ cease to produce themselves, become quiescent and sink to the bottom of the vessel as soon as the proportion of alcohol reaches twenty per cent. There is reason to think that the fever evoked by micro-organisms is

in some cases fatal to their growth and life. The third is the theory of accommodation, which maintains that the tissues in their first struggle with the micro-organisms acquire a higher degree of energy or vitality, whereby they are enabled to endure or resist future attacks. Perhaps a simile may be found for this hypothesis in the process known as acclimatization.

Incorporation and Absorption of Germs.—The observations regarding the incorporation and absorption of non-virulent or less virulent germs tend to support the theory of accommodation. For it would follow from them that protective vaccination, or more properly inoculation of weak bacteria, must confer upon the blood corpuscles the power to incorporate and destroy virulent bacteria. When protection is not sufficiently secured at once by a certain grade of attenuation, it might be accomplished by successive attempts with gradually increasing potencies. Thus successive inoculations of gradually increasing virulence would finally permit the introduction into the body of the most intensely virulent bacteria with impunity. It is upon this theory that Pasteur bases his claim to secure prophylaxis in hydrophobia, a disease in which sufficient time lapses, as a rule, between the wound and the symptoms to make experiments even after the wound, in the hope of anticipating the attack of the disease. The fact that virulent bacteria are not absorbed would indicate, in the absence of any morphological difference, the presence in these bacteria of some chemical substance which antagonizes the cell. Moreover, the character of the constitutional symptoms; sopor, stupor, coma, delirium, which supervene in cases of grave acute infections, speak in favor of this view, and against the belief that bacteria act mechanically or by the abstraction of oxygen. In fact, neither the local nor the general signs of infectious disease are ever produced or can be produced in this way.

How do Micro-organisms Produce Disease?—The question now arises, how do pathogenic micro-organisms produce the phenomena of disease? From the rapidity of their multiplication, it might be inferred that the symptoms and lesions of the infectious maladies were caused by the mere presence of these organisms as foreign bodies. But it has been observed that the bacilli of milzbrand alone multiply in the body in such number as to produce extensive occlusions of vessels. Further, it has been shown that no mere mechanical presence, no mere foreign bodies, aniline particles, or granules of cinnabar, ever induce the signs of fever or toxemia. The micro-organisms of disease live in the body, and must therefore be nourished at its expense, whereby they withdraw from the blood or tissues elements essential for their nutrition. Pathogenic micro-organisms require oxygen. In processes of fermentation, outside air is excluded, that the germs of fermentation may be compelled to withdraw oxygen from its soil. Pathogenic micro-organisms multiplying in great abundance seize upon the oxygen of the blood with such avidity as to develop in fulminant forms the symptoms simulated by prussic acid poisoning. But the other symptoms mentioned do not correspond

either to deficient oxygenation or carbonic acid poisoning.

These symptoms indicate toxicæmia, and since the injections of fluids from which bacteria have been separated by porcelain filters remains innocuous, it follows that the toxic agent inheres with the bacteria. Then, inasmuch as blood corpuscles show their reaction against bacteria on simple contact, it follows that the poison must lie upon or issue from their surface.

Ptomaines.—The only hitherto known poisons which may in such minute quantities induce such grave toxic signs are the poisons resulting from the action of the bacteria of decomposition upon organic matter. As these intensely virulent poisons were first observed only in dead organic matter, they were called ptomaines (from *πτῶμα*, the fallen, a corpse, hence more grammatically ptomatins). These matters, the ptomaines, though so newly known, have received so much attention in the past year as to form a subject in themselves. It may be said here that some cadavers develop no ptomaines, that ptomaines are developed as putrefaction advances in the course of weeks, next that they are also found sometimes in animal products, as in cheese, urine, feces, etc., and lastly, that many ptomaines are perfectly innocent. Then it might be added that many phenomena attributed to their action have been found due to simpler causes. Thus the claim of Passet that any one of the eight forms of bacteria which he cultivated from pus would coagulate sterilized milk were found to rest upon simple lactic acid fermentation.

Briege, who has made the most exact observations, operated with the Koch-Eberth bacillus of typhoid fever, which he cultivated from the spleens of fatal cases, and found to be identical with the pure cultures in the laboratory of Koch. These bacilli thrive in solutions of sterilized grape sugar, to which have been added the proper nutritious salts. This clear fluid, kept in sealed tubes at a temperature of 30° C., becomes opaque in twenty-four hours after introducing the bacilli, and emits, on opening the tubes, a distinct odor of ethyl-alcohol, which increases from day to day. Besides the ethyl-alcohol, there develop small quantities of volatile fatty acids, together with acetic acid in large quantity. The typhoid bacillus has also the property of inducing in solutions of grape sugar the lactic acid fermentation. Sterilized bouillon or minced meat used as soils, soon become alkaline, but develop, even after the lapse of eight weeks, none of the products or gases of decomposition. From these as from all albuminous cultures, Breiger was frequently but not always able to obtain a basic product which gave the chemical and physiological reactions of a ptomaine. In guinea pigs it produced a slight ptalism and an increased rapidity of respiration, to be followed later by a loss of power in the muscles of the extremities and trunk, without a distinct paralysis. There is diarrhœa throughout; death takes place in twenty-four to forty-eight hours. The same observer is now experimenting with the septic diseases whose abnormal temperature elevations, interruption of functions, benumb-

ing of the intellect, perverse action of the digestive apparatus indicate abnormal chemical changes in high degree.

Nicati and Reitsch, Villiers, Pouchet, have all made similar investigations with the bacteria of cholera. According to Pouchet, chloroform extracts of cholera dejections furnish an easily oxydisable and intensely poisonous oily substance which is certainly a ptomaine. Mere traces of it introduced into the bodies of frogs induce retardation of the pulse, with speedy death attended by muscular rigidity.

Villiers also succeeded by the method of Stas in isolating a ptomaine from the intestines, kidneys, liver and blood in two cases which had succumbed to cholera. It was abundant in the intestines, but very scant in the blood. It had a sharp taste and an odor like the flowers of the white thorn. It had no effect upon frogs, but caused in guinea pigs retardation of the pulse, tremor and death.

According to the same author cultures of the cholera bacteria have a peculiar ethereal odor which is not unpleasant. Solutions of this culture not over eight days old in bouillon or gelatine filtered free of bacteria, injected into the blood of dogs induces diarrhoea and great depression, with dyspnoea, disturbances of motion and sometimes death.

These experiments are cited merely as samples to show the direction of research at the hands of the most advanced observers in the past year. They indicate the lines of study by means of which we shall be able to combat the cause of infectious disease in a direct way. They show us that the time is at hand when, as Brieger observes, we may as practitioners of medicine no longer be compelled to rely upon a raw empiricism, when we may find a specific therapy, if not remedy for a specific cause, since we have already learned that the accumulation of certain products of bacteria kill them. They show us that inflammation is not the cause but the effect of disease which is caused by infection. They show us the direct road to cure through comprehension of the nature of infection.

ORIGINAL ARTICLES. *

SUGGESTIONS ON THE PURITY OF CHICAGO DRINKING WATER.¹

BY H. GRADLE, M.D.

EYE AND EAR SURGEON TO MICHAEL REESE HOSPITAL.

No question of local sanitation has been more often and less intelligently discussed in Chicago, than the purity of our drinking water. While alarmists have filled the newspapers with sensational exaggerations, our authorities have denied all danger on grounds insufficient to prove the point.

The starting-point of any discussion must, of course, be the fact, that the sewerage of this enormous city is carried into the lake—the source of our drinking water, whenever the current of the river runs towards the lake, which occurs a large part of

the time. Now, as there is no direct evidence that any one disease or class of diseases are due solely to the drinking water thus contaminated, how can we decide whether any danger to health lurks in this water? Chemical examination can only tell us whether organic material exists to a larger extent in our drinking water than it does in other parts of the lake remote from our shore, or than it did in the same waters many years ago.

But a positive result of such analysis would not necessarily condemn the water unless there were an excess of albuminoid ammonia larger than the limit shown by experience to be safe in drinking water.

On the other hand, when the analysis shows no marked change in the quantity of organic constituents in the water, it does not decide the question as to the safety of the water. For there is no reason to think that in our present case, where the sewerage is diluted by the enormous body of water in the lake, there can be enough of any chemical substance present to produce any poisonous effects. A chronic poisoning or a cumulative effect produced by the continued ingestion of an *organic* poison in such small quantities as not to produce any immediate sensible action is not known, and such a possibility is a gratuitous assumption not based on clinical evidence. We are forced, therefore, to look for living micro-organisms in any suspicious water—for at the present no other *direct* causes of diseases are known.

The algæ and diatoms, and occasional infusoria, figured by amateur scientists in the newspapers as existing in our drinking water, are about as harmless as any other vegetable or animal tissues we might eat as food. It has never been shown that they are really poisonous or parasitic to the body. The micro-organisms which demand our attention as suspicious, are the bacteria. Since they are not numerous in any but stagnant water, the direct examination of the water with the microscope teaches very little. Besides, hardly any variety likely to exist in the water could be identified on finding a specimen or two with the microscope.

In order to tell what there is in the water, we must do exactly as if we had a few seeds mixed with a lot of sand, and were unable to recognize them. We would sow them over a large surface of ground free from other plants and wait for the result,—identifying the plants as they grew up.

I have made a few such analyses of our lake water, according to the methods devised by Koch. The sample bottles with flat sides which I show you here, are thoroughly cleansed and boiled, and then partly filled with a small quantity of nutrient gelatine and their mouths plugged with cotton. The bottles and their contents are then sterilized by heating them in a steam bath for a few minutes on several successive days. This being properly done, they will keep forever without the occurrence of any bacterial growth in them. If now one or more drops of water flowing from the faucet or received in a sterilized beaker are dropped into these culture bottles while momentarily lifting the cotton plug, any bacteria or their spores thus introduced with the water will grow in the gelatine. If the drops of water are thoroughly mixed by shak-

¹ Read before the Chicago Medical Society, May 3, 1886.