Billings (J.S.) & Abbott (A.C.)

A SYLLABUS

OF THE

LECTURES ON HYGIENE, VITAL STATISTICS, ETC.

BY

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AT THE

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PREFACE.

In issuing the following Syllabus, the editor desires to acknowledge his indebtedness to Prof. Billings and Dr. Abbott for the many courtesies extended and much assistance rendered; to impress upon the students that this effort is designed to supplement and not to substitute more extended reading on the subjects discussed, and to distinctly state that he alone is responsible for any errors or misstatements that may appear in the work.

A SYLLABUS.

PART I.

LECTURES BY DR. BILLINGS—VITAL STATISTICS, ETC.

LECTURES I. TO III.

WHY should physicians and medical students study hygiene? 1. Because many States, the army and navy, and all branches of the government service require it of those practising in them. 2. The laity are becoming educated in sanitary matters, and will judge of a physician's acquirements and ability by his knowledge of hygiene. 3. A knowledge of hygiene is now essential to the treatment as well as to the prevention of disease. 4. The highest reason. It is a physician's duty to prevent disease and to educate the people as to how they may best care for themselves.

The physician can often prevent unnecessary alarms. We are getting through with our half-knowledge about hygiene now, though there was much "sanitary shrieking" in the past.

Health is a means, not an end. It is sometimes necessary to sacrifice health for some other object, since there are things more valuable than life. There are also times when we must put aside thoughts of the *healthfulness* of an occupation. Again, the value of health in money-values may be over-urged. Sanitation is considerably a matter of insurance.

We must take care of the *whole* people in order to protect the better part. But one class must not be oppressed to benefit another. There is plenty of ancient hygiene, but it did not respect individual rights; *e. g.*, Hebrews, Spartans,

Romans. The modern problem is to secure the public health while maintaining individual rights.

Modern hygiene is about fifty years old. It dates from the beginning of English registration of deaths. Dr. Parr was the prime mover. The cholera epidemics of 1832 and 1849 first attracted attention to and caused an investigation of sanitary conditions. Army and navy hygiene began with the Crimean war. Note difference in mortality between English and French troops during the first winter; also among English in first and second years. The improvement in the second year due to organization and sanitation. Soldiers have a definite money-value to their government.

Hygiene deals with the preservation of life and the improvement of health. There are two kinds of hygiene: 1. To destroy or avoid disease. 2. To strengthen the organism and its powers of resistance.

Living matter has a time-relation—*chronometry*. Magendie's law (?): The potential life of an organism is equivalent to five times the time required for its full development. The average human life is not nearly so great, for many causes shorten the period.

Causes of disease: 1. Those arising from within—hereditary, cognate, and subsequently acquired. 2. Those from without—physical, chemical, mechanical, and vital. Some diseases are preventable, others are not. We must know the effects of the latter to estimate the effects of the former ones; *e. g.*, the weather often a non-preventable cause of disease.

There are many millions of cells in the human body. All are probably never in perfect harmony or health; hence there is not the same exactitude in physiology as in chemistry. Sanitarians and physicians have to deal with *probabilities; e. g.*, chances of scarlet fever contagion, typhoid infection, etc. Like causes under like conditions produce like effects, but the conditions are not always alike. We have immediate or exciting causes of disease, and predisposing or modifying causes or conditions. The physician that best knows the probabilities of disease is the best equipped. One must know *all* the con-

ditions before he can estimate results accurately. Can predict very closely if we only know enough.

We study diseases by *observation* or by *experiment*. Our knowledge in the past has been mainly gained by observation at the bedside and at the post-mortem table. But we may now experiment with diseases by trying to reproduce them in susceptible animals: can only experiment with diseases common to both men and animals.

Observation may be of two kinds: 1. By noting and comparing individual cases, or by following the track of a particular outbreak. 2. By observing large classes and bodies of men. This latter constitutes *vital statistics*. Vital statistics, in the broadest sense, is the data of the life of peoples or communities—*Demography*. Includes a record of births, marriages, diseases, and deaths.

Mortality.—The *ratio* of deaths to the population—the *death-rate*. It is *not* the number of deaths, but the deaths per thousand. May be expressed in terms of "years of life." Nor is a mortality report a *mortuary* (or undertaker's) report.

To get the mortality: $m = \frac{d}{p} \times 1000$, where m = mortality, d = number of deaths, and p = population. But a record of deaths alone does not give complete information. We need also a record of births, diseases, etc.

Note: In determining ratios we must eliminate irrelevant factors; *e. g.*, to determine birth-rate,

$$n = \frac{\text{No. births}}{\text{No. women between 15 and 50 } \textit{only}} \times 1000.$$

A count or *census* is necessary as a basis for vital statistics, as well as for many other reasons. The most important feature of a census for vital statistics is the age-record, since the death-rate, etc., varies with the age.

To find the population at any time between two censuses, we must find the rate of increase of the population. Rule: log. of last census — log. of previous census ÷ No. of periods between censuses = log. of ratio of increase. This multiplied by No. of periods since last census and added to log. of last

census gives log. of present population. Result is not exactly accurate.

May estimate the population also by the number of houses. Number of persons in each house averages about the same for *each* city, but differs for different cities. The tendency of local authorities is to overestimate the population, and police censuses are invariably too high. Censuses in different countries give different data.

The number of *deaths* in a community is given by the registration records. The registration law should require burial permit for each case to identify the person, give cause of death, and guard against criminal acts or neglect. Danger of premature burial only 1 in 10,000,000.

In certifying to death certificates, the physician becomes part of the governmental machinery, and has a right to certain privileges in return. The community decides as to his qualifications for its own sake and benefit, not his.

The average physician cannot determine cause of death in 25 per cent. of cases without a post-mortem. In two post-mortems out of ten will still need a careful microscopical examination to determine cause of death.

The census now gives population and data for "sanitary districts" even smaller than wards; can thus compare rates of different parts of a city, and with those of different years. There is great difficulty in getting the population of these districts; also in getting a proper registration of deaths. Any system for collecting the deaths only at the end of the year will lose from 25 to 40 per cent. of the number. The gross death-rate varies with the size of the community.

Newly-settled communities have a lower death-rate than those not so, because the proportion of adults is larger and of children smaller in the former.

The physician is especially liable to be called upon to interpret the death-rate of a community. How is this to be done?

We must know the *number* of deaths and the *population* as well as the death-rate, in order to form an intelligent opinion. With *large* communities and *short* periods the probabilities of

error are very great. The longer the period the less likelihood of variation from the normal rate. The simplest formula for the *possible* variation from the normal death-rate is about the square root of the normal rate. The *probable* variation will be less than this. Example: normal rate = 16. Possible variation $= \sqrt{16} = 4$. Possible rate $= 16 + \sqrt{16} =$ from 16 to 20.

Poisson's formula for variation $= \frac{\sqrt{2\ m\ n}}{q^3} \pm \frac{m}{q}$, where $m + n = q$. Is of use wherever we wish to estimate the variation between m and n.

In estimating a death-rate we must consider the ages of those who die, since the liability to death varies at different ages, being highest in infancy and old age. We may get the death-rates of each *group* of ages from *life-tables*, which have been calculated by certain formulæ.

Each community should have its own life-table.

Expectation of life—the time any person, at a given age, of average good health may be expected to live, as shown by the life-table of that locality.

Besides age, sex, race, and occupation affect the expectation of life; *e. g.*, colored men are more liable to lung affections than whites; females to cancerous diseases than males; metal miners to phthisis, etc. Germans more liable to cancer than Irish, the latter more liable than native Americans. Jews not very liable to tuberculosis, but are especially so to diabetes, nervous diseases, etc.

Note that young insured persons are above the average as to expectation of life, since only the extra healthy are accepted; but that insured persons past middle age are below the average, since the very healthy have probably allowed their policies to lapse, the sickly keeping theirs up as business policy. This applies especially to plain life insurance.

We must eliminate the effect of such factors as age, sex, etc., before estimating the sanitary condition of a locality from its death-rate.

Circumstances leading to variations in mortality are very complicated. Expectation of life is not the *probable duration*

of life, which latter is the age when any number of children born will be reduced one-half:

$$= \frac{\text{total No. yrs. all the children live}}{\text{total No. children.}},$$

If we could get life-tables for each "sanitary district" we could accurately estimate the sanitary condition of those districts. We must have the *age*-distinction before we can get proper results as to occupation, etc. Certain diseases also have geographical limits; so we can make "disease maps;" *e. g.*, a high death-rate from cancer indicates that the community is old and healthy, and the people well along in years, for cancer attacks the aged especially.

Many of the above remarks apply also to *medical statistics*, which consider diseases and cases not fatal; but the same precautions must be used in medical as in vital statistics. We cannot get all the statistics of disease that we desire.

The best returns are to be had from army and navy medical officers, but in large communities physicians are now required to report contagious diseases. The age should be entered in all notifications and death reports by physicians.

Lecture IV.—EPIDEMICS.

Epidemics may be said to be, in general, the effects which certain bacteria produce on a great scale. We know the specific cause of certain contagious diseases, of others we do not. Prefers *microdemes* (little living things) to microbes to designate the cause of such diseases as are due to living organisms. Such diseases are *specific;* they have a definite cause, period of incubation, course, duration, etc. It is desirable also to retain the distinction between contagious and infectious diseases, though all are *portagious; i. e.*, their germs can be carried by either persons and their clothing (contagious), or by the air, drinking-water, etc. (infectious). All are in a sense *parasitic*. *Zymotic* is an improper term to use in connection with these diseases, since they are not really due to a ferment, as the word implies.

When one of these diseases occurs among a number of people in the same locality at the same time it is *epidemic*. When it is practically permanent in a locality it is *endemic*. When it extends over a large portion of the earth's surface it is *pandemic*. When a disease spreads from one country to another it is an *exotic* epidemic. An epidemic is *pestilential* when the disease is one whose mortality is very high; *e.g.*, cholera, yellow fever, and the true plague. Influenza is not usually considered pestilential, as its mortality is not as high as that of the above.

When is a disease epidemic? Dr. Buchanan's rule was—when it causes a death-rate of 1.2 per 1000, provided there are at least four deaths. But this neither takes nor gives any account of the number of cases. In New Orleans it was agreed that six cases of yellow fever occurring in native or acclimatized residents of the city should constitute an epidemic.

Great epidemics with great loss of life have occurred from the earliest times. 10 plagues in Old Testament; 23 in Rome B. C.

The true or oriental plague has caused the greatest epidemics. Two are historical. The *Justinian plague*, 543 A.D., spread from Egypt to Constantinople, and then over all Europe. It lasted almost 100 years, is said to have killed 100,000,000 people, and broke up all existing institutions. It broke out again in 1347. Was then known as the *black death* or *great mortality*. It then killed 25,000,000 in ten years. Since then this plague, which is sometimes called the *bubonic* plague, on account of the characteristic glandular swellings, has only occurred at long intervals with comparatively low mortality. The last epidemic was twelve years ago in Astrakhan, with not over 1000 deaths. It is endemic in Mesopotamia. Its advent to a locality is always marked in advance by the rats coming out of their holes and dying.

Like its predecessors, the black death broke up all existing institutions. It was also followed for some years by nervous

epidemics, characterized by chorea, dancing, etc.—"Dancing epidemics."

Another great epidemic was the sweating sickness in 1485. It was marked by an acute paroxysm of fever and profuse sweats, lasting from 24 to 36 hours. Killed many in six hours. It lasted for a few years and then disappeared absolutely till 1802, when a short epidemic occurred in Franconia.

The first great cholera epidemic in Europe and America was in 1832. It is endemic in the valley of the Ganges in India.

The first great epidemic of yellow fever in the United States (in New York and Philadelphia) was from 1798 to 1803; the last (in Memphis and New Orleans) in 1878 to 1879. There has been practically no yellow fever in New Orleans for ten years. It is endemic in the West Indies, especially Cuba. Animals suffer in epidemics not from the disease, but from neglect. An exception, is the death of rats during the plague.

In any epidemic the physician is looked up to as the principal man. He has to consider the interests of the whole community as well as to take care of individual cases. People become almost insane with terror and unscrupulous, and the only check to this is the deliberate opinions and actions of the physicians whom the community trust. Often, commercial interests are at stake, and the physician must use his judgment as to what shall be said about the severity or nature of the epidemic.

The methods of dealing with epidemics on a large scale are by *isolation* and *disinfection*. Diseases are spread in many ways, by water, air, food, clothing. The germs cling tenaciously to woven goods and clothing. Must get rid of or destroy these germs.

Isolation on a large scale = *quarantine* from *quarante* = 40 or 40 days, a period of time connected with the old magic medicine. It was first instituted with regard to leprosy, and then became a period of observation and inspection for other diseases. But quarantine for a set time might favor what it is intended to check, for the microdemes of many diseases may

multiply and increase *outside* of the human body; *e. g.*, yellow fever. So the idea of a definite period has been done away with, and quarantine now means only a detention long enough to determine that no one is sick with the diseases likely to come in, viz., yellow fever, cholera, smallpox, and occasionally typhus fever. In a voyage of from 7 to 10 days cholera will have developed in some one if it is on board; such patients are removed to the hospital, the other passengers detained a day or two for any further development of the disease, and the vessel and cargo thoroughly disinfected. In yellow fever the danger is not in the person, but in the clothing. So here we employ disinfection.

Quarantine is only as strong as the weakest point; if weak in one place disease may slip in. But our seaboard is extensive, and it costs a great deal to establish good quarantine stations. Should the United States do this work? The great trouble is that the States can superimpose their quarantine on that of the Government, since it reserves to them the "police power."

A periodic increase or variation in the severity of a disease indicates that it is caused by a germ that produces immunity, for a time at least,—smallpox, scarlet fever.

PART II.

Lectures by Dr. Abbott.—Bacteriology.[1]

The success of modern hygiene depends largely on our knowledge of bacteriology. Its relation to sanitation is illustrated by cases of tuberculosis, typhoid fever, etc.

Bacteria are unicellular, vegetable organisms, which multiply by the simple process of transverse division or *fission*. Being deprived of chlorophyl, they cannot get their food from CO_2 or NH_3. They are *saprophytic* or *parasitic*. If saprophytic, they live on *dead* organic matter, and break up these complex

[1] See Principles of Bacteriology, Abbott.

compounds into simpler ones, among which are CO_2, NH_3, and H_2O, which go to nourish the higher plants. Upon these higher plants the animal life of the globe is dependent, and as there is not enough CO_2 and NH_3 from other sources for their needs, it is evident that the saprophytes, which constitute the great majority of the bacteria, are important benefactors to all higher plants and animals.

The parasitic bacteria live at the expense of *living* matter and produce substances poisonous to the organisms on which they live, thus causing a local or general death. In this class belong the *disease-producers*. Some bacteria may be at one time saprophytic and at another parasitic—the *facultative* group.

The bacteria have tolerably definite shapes. Have three classes, named according to the *form*. *a*. Spheres, *micrococci*, whose diameters are the same in all directions. *b*. Rod-shaped, *bacilli*, one diameter being longer than another, no matter how much so. *c*. Spiral forms, *spirilli*. These latter may vary in the way the spiral is constructed, or have only segments of spirals, as in the "comma" forms.

Bacteria will not grow under unfavorable conditions or without proper nutriment. They may, however, when subject to adverse conditions, enter a state of great resistance—the *spore* stage. Bacilli only can form spores, and only certain bacilli do this. Each kind of bacteria has a definite life-cycle. As long as the conditions are favorable only the normal shapes will be formed. But when the culture-medium becomes too acid or alkaline, or when the nutriment is exhausted, or the conditions are otherwise adverse, reproduction and growth are checked and the non-spore-forming bacteria may die. But with the spore-forming bacilli, when normal conditions cease, they enter "a stage in which they resist deleterious influences to a much higher degree than is possible for them in the growing or vegetative condition." The protoplasm becomes granular with highly refractive spots. These spots coalesce to form a highly refractive body, the spore, sharply circumscribed and that stains with difficulty, it evidently being surrounded by an

envelope of great resistance. The rest of the cell eventually disappears. "A single cell produces but one spore." Spores do not reproduce spores, but under favorable conditions develop again into individual rods like those from which they were formed. The discovery of spore-formation by Cohn overthrew arguments against bacteriology 200 years old, and removed all belief in spontaneous generation.

Under unfavorable conditions, some organisms may undergo a change in form in another way, producing the "*involution* forms." These are distorted in outline, but revert under favorable conditions again to the original rod-shapes, provided death has not already occurred.

We cannot convert one form of bacteria into another, as micrococci into bacilli, bacilli into spirilli, etc.

We know but little about the spirilli; they are not often found in the human body. The germ of relapsing fever is probably a spirillum.

Different names are given to the micrococci, according to the manner of their growth. Where they grow in pairs they are called *diplococci;* in fours, *tetracocci;* in threads, *streptococci;* in irregular bunches, *staphylococci:* where the organisms divide in three directions of space, forming cubes, *sarcinæ.* Micrococci and bacilli held in masses in a pellicle by a gelatinous substance form *zoöglœa.*

The envelope of bacteria and spores is probably akin to cellulose; the interior is protoplasm.

We know that bacteria grow and require organic matter for growth, the latter usually in the form of *soluble albumen* in the presence of moisture. It must have a neutral or slightly alkaline reaction in most cases, though a few bacteria grow best in faintly acid media. It is hard to find soluble albumen plus water wanting anywhere, so the bacteria grow in many places and on many things. We rarely find any species by itself, so must separate them to study individual species. We do this by shaking the mixed kinds in a medium fluid at a temperature lower than that required to kill them, but which solidifies at lower temperatures. The solidifying fixes the individuals—

or groups of the same species clinging together as zoöglœa—and from these develop *colonies*, which have no particular tendency to encroach upon one another. We can thus differentiate the bacteria by the appearance of the different colonies, and from these can get pure cultures. Koch, the inventor of this method of separating bacteria, showed that the conditions necessary were a suitable nutrient medium, solid at one temperature, but fluid at another slightly higher, an extended surface, such as that furnished by glass plates, and means and methods for sterilizing the nutrient medium and the plates.

Owing to the omnipresence of contaminating organisms, we must grow our bacteria in or on sterilized media in sterilized vessels, and use sterilized inoculating apparatus only. *Sterilization* means the destruction of organisms by *heat*, as opposed to disinfection, the destruction of organisms by chemicals. We have two methods of sterilization: *a, dry heat; b, moist heat* or *steam*. The former does not have the penetrating power of the latter and must be used at *high* temperatures for a *long* time to be effectual. But this extreme temperature will ruin many substances, as the nutrient gelatine, so we sterilize these substances by steam. Expose them to steam for different lengths of time, but always for a less time than to dry heat. May use either a Koch's or an Arnold's steam sterilizer: both simple and good.

We may use continuous, or discontinuous or *fractional* sterilization by steam. Certain substances, like blood-serum, are spoiled by the use of heat continued long enough to destroy both bacteria and their *spores*, the latter needing a higher degree of heat. So we destroy the ordinary forms by more moderate temperature, or by exposure for a shorter time, then allow the spores present to develop into ordinary forms for say 24 hours, and use the moderate temperature or short exposure, repeating the third day if necessary to destroy spores that have taken longer than 24 hours to develop; *e. g.*, the growing stage of the anthrax bacillus is destroyed almost instantly by moist heat of 70° C., while the spores have resisted steam for twelve minutes.

The culture-media are prepared without any attention to antisepsis; they are then placed in test-tubes and other vessels and sterilized for five minutes on three successive days to destroy any organisms present. We prevent the access of outside bacteria, etc., to the media by means of sterilized cotton plugs, which *filter* the bacteria out of the air.

We use generally as culture-media, bouillon, nutrient gelatine, nutrient agar, potatoes and blood-serum. Blood-serum coagulates at a low temperature; so subject it to 65° C. or 68° C. for one hour for *six* successive days, thus killing the bacteria, and then solidify it by raising the temperature to 76° C. Sterilize glassware, etc., by dry heat.

Differentiation of Bacteria.—This may be done by noting the characteristic growths on the various culture-media. Bouillon is a fluid media, containing all the elements necessary for the nutrition of most bacteria. It often serves to show the characteristic growth of an organism. But we often need a solid medium, and to obtain this we add to the bouillon—beef-tea—gelatine or agar-agar, the latter a Japanese vegetable gelatine.

Nutrient gelatine, beef-tea, gelatine both liquefies and solidifies at lower temperatures than nutrient agar, so we use the former for bacteria, which will grow at comparatively low temperatures, the latter for those growing only at higher temperatures. The growth of an organism is usually more characteristic on nutrient gelatine than on agar, but as the gelatine is liquid at the temperature of the body we have to use the agar in growing those organisms which do best at the body temperature, since the agar is not liquid below 38° or 39° C.

Some bacteria liquefy gelatine; others do not, and agar is never liquefied by bacteria. Gelatine liquefied by moderate heat will solidify again, but gelatine liquefied by bacteria will not. This liquefaction by bacteria is probably a *peptonization*, and is probably due to the relation of the organisms to oxygen. It occurs in different ways and this aids in the differentiation; *e. g.*, the cholera germ.

On boiled potatoes the growth of certain bacteria is char-

acteristic, and there are some which we can only differentiate on the potato. The *typhoid* and *diphtheria* organisms grow on potato in an almost *invisible* way. Blood-serum offers a favorable field for the growth of certain organisms; *e. g.*, the diphtheria germ, though the growth upon it is not very characteristic.

As stated, most bacteria grow best in neutral or slightly alkaline media; a few in slightly acid ones. An organism that produces an acid or alkali in its growth may soon check that growth by the excess of the alkali or acid, the growth being renewed when the medium is brought back to neutrality. The cholera germ and other bacteria produce indol under certain conditions; others produce other complex substances.

The extremes of temperature between which bacteria will grow are from 5° C. to 43° C., but they grow *best* from 37.5° C. to 40° C.

Organisms that require O are *ærobic;* those that are harmed by it are *anærobic.* Most bacteria are of the *facultative* group, growing with or without O, though this plays an important part in the chemical part of the organism; *e. g.*, in the chromogenic group in the presence of O one color is produced; in its absence, another.

Relation of Bacteria to Disease.—To determine whether an organism is or is not pathogenic we must experiment on animals, must use pure cultures of the organism, and must make our inoculations and autopsy under strictly antiseptic conditions. We must examine the blood and tissues of the diseased animal microscopically; if bacteria be present in these, must make cultures from them; if more than one kind of bacteria be present, must make plate cultures and isolate the colonies, making tube or potato cultures from each kind of these. When a pure culture is obtained, its characteristics on different media and its morphology are to be noted, and inoculations of healthy but susceptible animals made from it, and then note whether the organism produces the symptoms of the disease we are studying. Infectious diseases generally

have a period of *incubation* before the appearance of the symptoms.

Koch's Postulates.—Before we can say that an organism is the *cause* or *germ* of a disease, (1) we must find the organism in the blood or tissues of an animal sick or dead of the disease; (2) we must be able to produce a *pure* culture of the organism; (3) this pure culture when inoculated into a susceptible animal must produce the disease in question; (4) we must find the organism in the blood or tissues of the animal inoculated and made sick with the disease.

A Study of the Anthrax Bacillus.—The bacteria were first discovered in 1683, by Leeuwenhoek, but until 1880 practically nothing was done in classifying them or developing culture methods, though some advance was made in sterilization. In 1855 Pollender discovered rod-shaped bodies in the blood of animals suffering from splenic fever or anthrax; these were later shown to be bacilli, with the power of reproduction; and as the study of this organism is closely associated with the modern history and study of bacteriology, we may use it as an example for the study of any organism.

About 1880 Koch disproved Pasteur's theory that earthworms carried the germs of the disease from bodies buried in the earth, as he likewise did Von Buchner's hypothesis that the bacillus was developed from the Lannless hay bacillus—b. subtilis; and in the further study of this organism he developed his methods of isolation, cultivation, etc., and his renowned postulates. He also showed that its action in various media was characteristic, that it was not motile, and that it only produced spores in the presence of O. In the animal body the bacillus is generally in the form of short rods with square ends. In cultures at the body temperature these rods develop into threads, each thread being made up of a number of rods end to end. When nutrition becomes limited spores develop in these threads, one spore for each rod in the thread. The spores never form in the animal body, and only at from 18° C. to 43° C., 37.5° C. being most favorable.

In the diseased animal the bacillus is found in the capillaries of all organs, though the spleen is the only organ macroscopically affected. It is now known that the bacilli produce a chemical substance, a direct poison to the vital centers.

Birds, dogs, and frogs are exempt from anthrax; man is less susceptible than the lower susceptible animals.

The disease spreads through the bacilli being discharged upon the ground as a result of the rupture of capillaries of the kidneys engorged with them to the point of bursting. Belonging to the facultative group, and now growing as saprophytes till the food supply becomes exhausted, when they form spores, they may be taken into the circulation of other animals through lesions of either the skin or mucous membrane. In certain regions the disease is or was almost endemic.

The anthrax bacillus retains its vitality under normal conditions; the spores retain their vitality almost indefinitely. But if the bacillus be cultivated between 42° and 43° C. for a number of days, and through a series of cultivations it loses much of its virulence, and has its morphological and chemical properties slightly altered. So also, it loses its power of spore production if grown in the presence of certain chemicals. Hence the possibility of *preventive inoculations.*

The *Study of Suppuration* also gave much bacteriological information. Numbers of micrococci are to be found in pus, generally *between* the pus cells; though very exceptionally in ordinary pus they may be found *in* the cells, and in gonorrhœal pus, Neisser's *diplococci* are found in the cells.

The micrococci of pus occur as staphylococci and streptococci, stain readily, and produce pyæmia and multiple abscesses when pure cultures are inoculated into animals, except in the brain, spleen, and liver. But suppuration does not always follow inoculation, for there must be some alteration of nutrition, or alteration or interference of circulation at the point of inoculation, which lessens the normal resistance of the part. Injuries to the tissues lessen this resistance, so that

suppuration may occur after an injury, even though the skin is apparently not broken. In such cases the micrococci gain access to the subcutaneous tissue through the rupture of the hair follicles and sweat glands of the skin in which they may be lying. The pus organisms being very common in nature, easily gain access to these glands and follicles, so that perfect disinfection of the skin is almost impossible. On the other hand, the natural resistance of the tissues in the lower animals is very great, and it has been hard to produce suppuration in them till the resistance was lowered by injuring the tissues more or less.

The most common organism in *circumscribed* suppurations is the *staphylococcus pyogenes aureus;* less common are the *citreus* and *albus*. The organism of *spreading* suppurations is the *streptococcus pyogenes;* it is probably identical with the streptococcus of erysipelas, Fehleisen's streptococcus. The organism of specific urethritis—gonorrhœa—is Neisser's diplococcus.

Injection of the staph. pyog. aureus into the circulation causes a fatal pyæmia. After death are found many yellow spots—minute abscesses—especially in the kidneys, heart, and voluntary muscles. The center of these spots is made up of necrosed and dying tissues and many pus organisms; around this is a wall of resisting cells—w. b. c., and pus cells and granulation tissue. The micrococci form a plug or embolus in a capillary, albumoses are formed by the micrococci, which kill the surrounding tissues, a resisting wall of w. b. c. or leucocytes is thrown around the spot, these latter are attacked again by the micrococci or their products, and the weaker of the two opposing forces is overcome.

We may produce suppurations artificially by introducing acids or destructive irritants subcutaneously; but such abscesses contain no germs, and, besides, never occur naturally in man.

In old abscesses we will find no micrococci in the pus, because after a time they are killed by an excess of their own products.

Tuberculosis.—Its bacteriology only known since 1880, when Koch proved it to be due to the *tubercle bacillus;* though tuberculosis in cattle was studied in 1855, and soon thereafter investigators paid attention to the analogous appearance in man, and showed that the disease could be produced in cattle by the inoculation of tuberculous matter from man.

Miliary Tuberculosis.—Apparently healthy tissue with small necrotic centers, surrounded by zones of infiltration or reactive cells. In the necrosed masses are rod-shaped bodies, which attack the surrounding walls of reactive cells. These being destroyed, a new reactive zone surrounds the increased mass of necrosed tissue, and these *miliary tubercles*, thus enlarging and coalescing, form larger masses, called *conglomerate* tubercles. These also grow and coalesce, and, if in the lung, break through the walls of some of the bronchioles, allowing the dead masses to be thrown off as sputum, a cavity being left behind. Histologically, the cavity is like a miliary tubercle, with its necrotic center wanting. In the sputum thrown off from such a cavity will always be found many rod-shaped bacilli, like those in the primary tubercles. These tubercle bacilli produce a poison that causes the death of surrounding tissues.

In the lung cavities are always other organisms besides the tubercle bacilli, which we wish to separate from the latter. The b. tuberculosis take the basic aniline dyes with difficulty, thus differing from most other bacteria; but when once stained, they are decolorized with equal difficulty, while the other bacteria readily give up their color; consequently, we stain all the tissues and organisms with a highly penetrating dye that will stain the b. tuberculosis, and afterwards decolorize all but the latter by means of a strong acid solution. Can then stain the other tissues and bacteria with a contrast-stain if we desire.

To stain tubercle bacilli.—Spread out sputum on a dark plate; pick out a small cheesy body—the center of a past miliary tubercle—smear this on a cover-glass, pass this rapidly through a gas flame three times to dry it, and stain. To

secure penetrating ability, add to an aniline dye an alkali, carbolic acid, or aniline oil. To use the latter, to 100 c.c. distilled water in a small flask, add aniline oil, drop by drop, shaking after each addition until the liquid is opaque. Filter this through moistened filter paper till perfectly clear. To 100 c.c. of the filtrate, add 10 c.c. absolute alcohol and 11 c.c. concentrated alcoholic solution of fuchsin, gentian-violet, or methylene-blue. Put a little of this in a watch-glass, and float the prepared cover-glass face down on the fluid for half an hour, warming to almost the boiling-point; or hold the cover-glass, with a few drops of the dye on it, face upwards over the flame, and bring the fluid to the boiling-point two or three times. Then decolorize in a 30 per cent. nitric acid solution, wash, and, if desired, stain with a contrasting color.

Modes of tubercular infection. a. From sputum. The sputum dries; is ground into powder beneath the feet, and the bacilli arise in the dust and are taken into the lungs, there to multiply and cause disease if the conditions are favorable. b. From tuberculous meat. It is very easy to infect the whole carcass of a slaughtered animal with the knife with which tuberculous glands and parts are cut away, even though in nature the bacilli do not infest the muscles. Such infection being on the surface, proper cooking should destroy it and protect those who eat the meat. It is doubtful whether the bacilli gain access to cow's milk in cases of bovine tuberculosis, unless the mammary glands be tuberculous. c. Through the skin. The infection of superficial glands is primarily in this way: *e. g.*, the enlarged glands in scrofulous children. The tuberculosis in such cases may be dormant for a long time, when it may suddenly light up either from injury to or the breaking down of these glands. The infection of bronchial glands is primarily through lesions of the lung tissue.

Tuberculin (Koch's).—A glycerine extract of the organisms themselves. The results from injections of this substance have

varied much during the past year; some accidents and bad reports.

If a susceptible animal be inoculated with tubercular *sputum* will it surely die of tuberculosis? It will, provided it does not first die of one of two other diseases. In the mouth cavity of 20 per cent. of even healthy persons is found what is thought to be the cause of fibrinous pneumonia, the *diplococcus lanceolatus*, d. of Fränkel, etc. This possesses the power of lighting up virulent septic processes in the lower animals. If this be not present, septic processes may be set up by the *micrococcus tetragenus*, which is often present in tubercular cavities and which was at one time thought to be the cause of tuberculosis. It produces a slow septicæmia. If the animal does not succumb to one of these two, it will in all probability die of tuberculosis. But we must remember that the tubercle bacillus grows very slowly, apparently not beginning to grow in culture tubes for 12 or 14 days. The tubercle bacillus has the property of forming spores within the animal body.

Typhoid Fever.—The study of this disease from a bacteriological standpoint is very unsatisfactory. In typhoid cases the bacilli are to be found present in the spleen and in the intestinal glands. They do *not* form spores, do not liquefy gelatine, grow on potatoes in an almost invisible film, are *motile*. They do not produce typhoid fever in animals as we see it in human beings, though the animals may die of the toxic inoculation. *Toxæmia* is the result from the inoculation of a poison. *Infection* results from the growth of an organism within the tissues. Sometimes with animals we do get intestinal ulcers and the enlarged and softened spleen after inoculation with the typhoid bacillus, *b. of Eberth*.

Why don't the typhoid organisms grow all the time, and why don't we have typhoid fever among us all the time? In the water and in the soil, etc., where the typhoid germs may be thrown, there are usually many saprophytic bacteria which use up the subsistence and produce substances that destroy the typhoid germ. But there are times when the saprophytes are

not present and the typhoid bacilli may get into the water-supply, the way in which the system is usually infected. Milk being a good culture-fluid, may also carry the infection; but it should be remembered that we usually require a continuous contamination, and not a solitary one.

In many cases the typhoid germs are undoubtedly spread by the water-supply; but the theory of Pettenkofer is in direct opposition to this, viz., "that diseases like typhoid fever are not the result of direct inoculation, but are due to fluctuations in the rise and fall of the ground water, which give rise to conditions which give rise to disease."

The typhoid bacillus is very susceptible to heat and some disinfecting agents, but withstands the action of carbolic acid to a considerable degree. It is destroyed in 5 or 10 minutes by boiling water, also by "milk of lime" or chlorinated lime. In disinfecting the discharges of typhoid patients, don't use solutions of corrosive sublimate, for the albumen in the discharges is coagulated by this agent and prevents its action on the bacilli.

Diphtheria is closely allied to true or membranous croup, which latter, as proved bacteriologically, is really in most cases diphtheria.

Löffler, in 1882, isolated an organism from diphtheritic membranes, but he was unable then to fulfil all of Koch's postulates in regard to it. These have since been fulfilled, and there is now no doubt that this organism is the cause of diphtheria. It is a bacillus, but is not constant in its morphology. Its normal form is probably a rod, but it is rarely found in its strictly normal condition, but usually in altered or *involution* forms, representing probably diseased conditions of the protoplasm of the organism. Its commonest forms, both in diphtheritic membranes and culture-media, are very irregular, curved wedges, spindles, clubs, etc.

Its growth in bouillon is very characteristic. In 36 or 48 hours are formed little clumps that subsequently fall to the bottom or adhere to the sides of the vessel. At times the

fluid will appear quite cloudy—"diffuse clouding"—due to many minute clumps, but each a separate one. The reaction of the bouillon is at first acid for 24 or 36 hours, but it then becomes alkaline. On potatoes the germ grows luxuriantly, but forms an invisible film. On gelatine and agar the growth begins as a little mass, closely granular; the colonies, dry and flat, look like scales, and are irregularly round, with periphery notched, and densest at the center.

The growth on blood-serum is characteristic, rapid, and luxuriant. For clinical diagnosis, use Löffler's blood-serum —1 part bouillon, containing 1 or 2 per cent. grape-sugar, to 3 parts beef blood-serum. On this one can usually establish cultures in 24 hours, the diphtheria germs growing luxuriantly, while other organisms have scarcely begun to grow.

To make cultures for diagnosis, have ready half a dozen blood-serum tubes. Gently scrape the false membrane in the patient's throat with a sterilized needle or loop; introduce this, without touching anything, into tube 1, and smear the surface of the serum; then, without sterilizing or recharging the needle, into tube 2, and so through the whole six. This is equivalent to the dilution process with melted gelatine or agar, each tube receiving fewer germs than the preceding one, and the results are entirely satisfactory. Keep the tubes at the body temperature in an incubator for 24 hours, when the characteristic growths will be seen and those of other bacteria scarcely started. If desired, pure cultures may be made from these characteristic patches.

If we inoculate a guinea-pig in the abdomen with a pure culture, the animal will die in from 1 to 5 days, but with no sore throat. However, if a kitten be inoculated with the germs through an opening in the trachea, both the characteristic sore throat and false membrane may be produced.

The above difference in the period required to kill is probably due to the varying virulence of the germ. Some of the germs may have lost their virulence altogether. At the autopsy of the guinea-pig we will find considerable œdema around the point of inoculation, points of hemorrhage, a few

fibro-purulent deposits, bacilli numerous around inoculation-wound, but disappearing as you go from it, rarely any beyond the first lymphatic gland, many degenerated bacilli, and many in the bodies of the leucocytes.

Internally we find the organs not much changed macroscopically, except the supra-renal capsules, which are enlarged and hemorrhagic; but microscopically we find the tissues undergoing fragmental disintegration of the cell nuclei, as if being killed by some virulent poison that acts especially on the nuclei. The liver nuclei are entirely broken up, cells roughly outlined, and the whole area studded with granular matter that takes the nuclear stains.

This bacillus of Löffler is always present in every case of diphtheria and can be carried through many cultures. But the pseudo-diphtheritic organism is strikingly like it, so much so that many believe it to be the true bacillus that has lost its virulence, though we do not know what conditions give rise to this. The pseudo-diphtheritic organism does not kill animals nor give rise to microscopical changes. We may find both kinds in the same throat, and we should treat all suspicious cases as diphtheria.

Some consider the angina of scarlet fever to be identical with that of diphtheria, but it has been proven that in the membranes of scarlet fever there is always a streptococcus, which seems identical with the streptococcus or that of erysipelas, but which does not produce the necrotic changes of diphtheria. May have diphtheria and scarlet fever simultaneously.

The importance of securing immunity from diphtheria is illustrated by the last census, which shows that in certain new towns in the West every child has been carried away by the disease. We can establish an immunity in susceptible animals by the inoculation of diphtheritic bacilli that have been growing on culture-media for some time and have then been heated between 60° and 70° C. for one hour. This kills the bacilli and in some way alters the poison. Without the aid of the bacilli the introduction of the normal poison produces exactly

the same histological changes as with the bacilli, possibly excepting the false membranes.

We only find the bacilli in the false membranes in the human body; they are not taken up by the circulation, and when inoculated into animals only go as far as the first lymphatic gland from the point of inoculation. But we find cell-death immediately ahead of the bacilli, showing absorption of the poison, and that the bacilli grow in dead tissue.

IMMUNITY[1] is a subject that cannot be taken up independently of infection, which must first be thoroughly understood. Nor can the study of immunity be made simple nor be taught dogmatically.

Infection.—If we inoculate a susceptible animal with the blood of an anthrax victim, the animal soon dies. After death we find the capillaries closely packed—often ruptured—with anthrax bacilli. Is the death due to the packing, or to a poison produced, or to the using up of something essential to life? It is evident that it is not a mechanical death, and from our present knowledge we know that death from anthrax is a result of a true septicæmia.

On the other hand, if we inoculate our susceptible animal with the bacillus of diphtheria, we find after death general œdema, ecchymoses, etc., about the point of inoculation and microscopically a condition of cell-death, but no organisms beyond the lymphatic glands nearest the point of inoculation. Here we have two different pictures; the diphtheria being evidently a *toxæmia*, where the "poisonous results are not necessarily accompanied by the growth of organisms in the tissues," as opposed to the *septicæmia* of anthrax, the latter being "that form of infection in which the blood is the chief field of activity of the organisms."[2] But if we study the subject further we shall find that we can produce death by toxic processes by introducing into the animal body the products of

[1] See article by Dr. Abbott on Immunity and Infection in Medical News for Nov. 7, 1891.

[2] The Principles of Bacteriology; Abbott. Pp. 194 and 228.

such bacteria as would, if they were themselves introduced into the body, produce death by septic processes. For instance, we can grow anthrax bacilli, rob the cultures of the living bacilli, but retain the poison produced by them, and with this poison bring about clinical and pathological results identical with those produced by the living bacilli; and so with other pathogenic bacteria. Consequently, infection is a *chemical* process, a destruction of the body, or of local parts of the body, by chemical action.

In the breaking up of complex organic bodies into simpler compounds, certain crystallizable bodies with toxic properties are produced called *ptomaines*, but these are probably not active infectious agents. But we do know that some of the bacteria produce non-crystallizable proteid bodies called *toxalbumins*, which are actively poisonous or *toxic* substances.

In certain infectious diseases a single attack generally protects the person against subsequent ones. Smallpox is a good example of this, though we have no bacterial knowledge of smallpox. Why does one attack protect?

Many theories have been proposed to explain this phenomenon, of which the following are the principal ones:—

1. *The Retention Hypothesis.*—That the bacteria produced in the primary attack something which was retained in the body and which prevented a growth of the same bacteria a second time. (Chaveau, 1880.) It was based on the fact that the organisms only grow for a certain time on a culture-medium and have to be changed to fresh tubes to keep up the growth. But here the interpretation of the facts was wrong, for in the test tubes the checking of the growth is due to a change in the reaction and an exhaustion of nutriment, and when the excessive alkalinity or acidity is corrected and additional nutriment supplied, the bacteria begin to grow again, provided they have not already died for lack of nutriment.

2. *The Exhaustion Hypothesis.*—That the bacteria during the first attack used up something essential to their growth which was not replaced. (Pasteur, 1880.) Disproved by the fact that the bacteria will still grow in the tissues of an animal

dead of the disease they produce, and that good culture-media —beef-tea, etc.—can be made from these tissues.

3. *Theory of Phagocytosis.*—"That immunity against infection was essentially a matter between the invading bacteria on the one hand and the leucocytes of the tissues on the other; that during the first attack of the disease the white blood-corpuscles gain a tolerance to the poisons of the bacteria, and so are able to resist the next incursion of the enemy." (Metschnikoff, 1884.) This was plausible, because it was known that certain mesodermic cells took up certain insoluble bodies that gained access to the body, and, if they were digestible, destroyed their protoplasm. The white blood-corpuscles—leucocytes, wandering cells—have this power, and, moreover, they have been seen apparently in the act of digesting bacteria. But the probability in this latter case was that the bacteria were already dead, and the leucocytes were merely acting as scavengers.

4. *Theory of Reactive Change.*—"That in the primary infection a 'reactive change' in the integral cells of the body occurs that enables them to protect themselves against subsequent inroads of the same organism." (Buchner, 1883.)

This, at present, receives the greatest support. In 1888 Nuttall showed that bacteria were killed by the *serum* of blood just as well, or even better, when the white blood-corpuscles were absent as when they were present. It was also shown that the introduction of the products of bacteria produced not only a simple tolerance to, but an immunity against the bateria, and it is very probable that the poisonous products of the bacteria bring about a *reactive* change in the tissues which renders the integral cells capable of producing a body in the blood-serum of an albuminous nature—probably *globulin*—which neutralizes *chemically* the poisonous albumens produced by the bacteria, and that this product remains in the blood for a greater or less period of time, giving immunity for that time. In fact, this albuminous body has really been isolated from blood-serum, and it has been shown experimentally that it antagonizes or neutralizes the poisonous proteids produced

by the pathogenic bacteria, isolated in a like manner. Moreover, the same reactive change can be produced by the products of one kind of bacteria, so that the animal will be protected against another kind.

To show how a practical immunity may be produced in man or animals the following example may suffice: If the bacilli of anthrax be grown under abnormal conditions, say at 42° or 43° C., we have a slight alteration in the morphology and cultural aspect, together with lessened powers of resistance to antagonistic forces and *lessened virulence*, the period of incubation being lengthened or destroyed. At 55° C. for one hour we can so reduce the virulence that the bacteria will not kill susceptible animals. Moreover, the bacilli have now the power of transmitting this attenuated virulence to their offspring.

After an animal has been inoculated with this weakened bacillus it becomes sick, but will recover; then if inoculated with a stronger (but not normal) bacillus, it again sickens, but not so much so as before, and finally is able to resist the most virulent forms of the bacillus. In such animals as are first inoculated with the attenuated bacilli we do not have a *general* septicæmia, but only around the point of inoculation. The blood carries the weakened products of weakened bacilli through the circulation, and these set up the reactive change in the cells and so protect the body subsequently against the disease.