PRESIDENT'S ADDRESS.

BACTERIOLOGY AND ITS PRACTICAL SIGNIFICANCE.

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Bacteriology has only recently been recognized as a cardinal science —probably less than fifty years—although the diseases of smallpox, rabies and plague were known hundreds of years before Christ and occurred with the same lesions and characteristc symptoms as they do today.

The first glimpse into its mysteries was simultaneous with the invention of the microscope. The origin of this instrument dates back to the period of the "renaissance"; about the time Harvey discovered the circulation of the blood. The real perfection of the microscope was not accomplished until well into the nineteenth century.

While bacteriology had its inception with the discovery of the microscope and its development for a time kept pace with the perfection of this instrument, the study of bacteria as such, while very important, was of interest only to the microscopist and botanist.

It required such geniuses as Louis Pasteur and Robert Koch to develop methods whereby one could correlate and associate the micro-organisms revealed by the microscope to the phenomena they produced. Thus the establishment of bacteriology as a modern practical science.

If one were to review the early historical development of this subject one would readily note that its forerunners were the ancient ideas of superstition relating to disease; followed by the germ theory; intermingled throughout with the theories of spontaneous generation of life; the development of the compound microscope and the marked stimulus it gave to investigational work in this field; the demonstration of the facts revealing the definite rôle micro-organisms played in fermentation and disease and finally the chemical and physiological developments.

A comprehensive consideration of this extended field is generally termed bacteriology and in practice it is the study of the smallest forms of living matter, e. g., bacteria, yeasts, molds, transitional forms, protozoa and ultra-microscopic organisms (viruses).

However, the subject in its broader scope would be more correctly called microbiology or better protistology. The word protist is about the equivalent of the colloquial term germ and signifies the lowest form of life whether plant or animal. The malaria germ, for instance, is an animal while the pneumonia germ is a plant.

All of these forms are important not only because they induce disease in man and animals but also because they are active in processes of putrefaction and fermentation in dead matter.

The nitrogen of the protein and the carbon of the carbohydrate molecules are by these processes rendered available for plant life which in turn are used by higher animals.

"Proc. Ind. Acad. Sci., vol. 33, 1923 (1924)."

The life of the higher beings is intimately associated with these smaller organisms; in fact the higher forms would be impossible without the lower ones.

When one recognizes that these micro-organisms are continually at work breaking down dead matter and preparing the way for new life one realizes that they are beneficial and indispensable.

A great practical industrial significance is attached to these one-celled organisms because many of the products, such as the alcohols, acetone, acetic, butyric and lactic acid and other organic compounds to which they give rise are directly utilized by man. In our own State of Indiana we have a mammoth plant which employs the industrious bacteria in the production of organic solvents used in commerce.

The vast deposits of sodium nitrate (soda saltpetre) in South America and the potassium nitrate (saltpetre) of India owe their origin to the action of bacteria on the guano, an excrement of birds.

Bacterial activity occurs to a large extent in the production of foods. Special flavors and characteristics in foods such as butter, cheese, sauerkraut, pickles, ensilage and koumiss are largely due to the desirable fermentative changes which occur.

The dairy industry has been revolutionized within the last few years due to the recognition of the rôle bacteria play in the manufacture of such products. With the knowledge that dairy products may give rise to certain diseases, the cows, as well as those employed in and about milk producing and handling establishments, are examined for certain bacterial diseases of which tuberculosis and latent typhoid fever are outstanding.

It is well known that bacteria develop non-poisonous chemical products, especially resembling certain of the poisonous vegetable alkaloids, when grown upon nitrogenous foods as meats and cheese, as well as in the cadaver. And because of their occurrence therein great importance was attached to them in legal medicine. Until the researches of Selmi revealed this fact undoubtedly convictions of otherwise innocent persons were committed.

It is now a recognized fact that there is practically no such thing as ptomaine poisoning. The ill effects, to an overwhelmingly large per cent, are due to acute infections primarily with *Bacillus enteritidis*, the para typhoid organisms and to the highly poisonous soluble products of bacterial growth (botulinus toxin). This knowledge has taught us how to more intelligently handle and prepare foods.

Micro-organisms also play an important part in the tannery as depilatories, in the bating and the tanning of leather. The flax and hemp industries are dependent upon bacterial activity; and the fermentation of such origin has proved of value in the handling of hay and the curing of tobacco.

Primative man thousands of years ago, although soil bacteriology, of course, was unknown, recognized the value of fertilizers; transfer of rich top soil to new or arid tracts; soil tillage; rotation of crops and green manuring. The members of the bean family were also considered as special soil enrichers.

While this was the practice in those remote times, it was only within very recent years that anything like the true significance of these basic agricultural principles have been discovered. Indeed soil microbiology is far from being understood even today.

We now know that there are (a) bacteria which are normal inhabitants of the soil which render the organic matter (humus) in such form that it is available to the growing plant. These "rotting bacteria" disintegrate the dead plants and animals forming ammonia and other compounds. It was commonly supposed that the nitrogen of the air was worthless unless changed to ammonia by electric storms or similar disturbances. There are (b) bacteria (azotobacter, clostridium) which grow in the soil as well as (c) those that live in symbiotic relationship (radicicola) and are found in the nodules (bacteroides) on the roots of certain plants (legumes) all of which have the property of changing atmospheric nitrogen into an assimilable form for the growing plant. Modern scientific agriculture which results in the increase of soil productiveness must necessarily embody and encourage the growth of these groups of helpful bacteria which elaborate chemical compounds required for proper development of the crop plant and discourage harmful forms of which there are also many.

Proper effective sanitary and public health methods become necessary in view of the fact that the soil harbors, in addition to those that are harmful to lower plants and animals, certain organisms that are pathogenic to higher animals including man, causing diseases such as lock-jaw, tuberculosis, typhoid fever, gangrene, anthrax, foot and mouth disease, lumpy jaw, hook worm and other intestinal parasitic infections. In certain parts of the country proper drainage and tillage of the soil have proven to be very beneficial by removing, as much as possible, the breeding places of mosquitoes which carry malaria and yellow fever.

The selection of a pure water supply and the proper disposal of sewage is of the greatest importance in the conservation of public health. A pure water supply is especially essential in the prevention of such diseases as typhoid fever, dysentery and cholera.

The extermination of pests such as chinch bug, rats, mice, rabbits and squirrels by means of microbes is at present apparently not entirely successful from a practical standpoint. It has, however, possibilities.

In the development of bacteriology the relation of bacteria to disease undoubtedly received the greatest prominence. Especially was this true because, with the discovery of the microscope, bold scientists often unhestitatingly declared that they had seen the germs causing such diseases as plague, syphilis and smallpox.

The germ theory of disease of Kircher of over two hundred years ago, coupled with van Leeuwenhock's observations and finally brought to a crowning climax through the works of Pasteur and Koch, is a thing of the past. Micro-organisms, as has been demonstrated thousands of times, are responsible for a great number of infectious diseases. This positively proven fact is unquestionably an important one and of even greater significance are the results which aid us to scientifically and successfully prevent and combat these diseases.

In the latter fifties, Ignatius Semmelweiss, a physician of Vienna, insisted upon using chlorinated lime for washing the hands and instruments previous to all examinations made in the maternity hospital. As a result deaths from puerperal infection fell from as high as 50 per cent to practically nothing. But he was ahead of his time, was persecuted and died insane. Twenty years later a monument was erected to him by the International Congress of Hygiene.

Years later, in 1867, Lord Joseph Lister, aided by Pasteur's work on fermentation, attempted to prevent infection by removing or actually destroying the causative organism by means of germicides. We are all familiar with the benefits accorded mankind through the practice of Listerism or antiseptic surgery.

METHODS OF INFECTION.

The prevention of infectious diseases as they may occur in sporadic, endemic, epidemic and even pandemic form may be greatly facilitated by taking into account how these organisms enter and later leave the infected animal. How they may be disseminated from individual to individual and how they are perpetuated in nature are also conditions well worth recognizing and of great practical significance.

I. It was formerly thought that germs could not penetrate into the interior of the body through the unbroken healthy skin or mucous membrane. But nowadays we can say with certainty that they can.

It was early found that pus organisms could be rubbed into the skin and cause boils.

Loos, 1902, in Egypt, showed that the hook worm is excreted in the feces, that the larvae are formed in the wet soil and that these larval forms could penetrate the whole skin and go to the intestine. If these relatively large organisms can do this, certainly the smaller, micro-organisms can do likewise.

With protozoal diseases we have a very clean-cut story. In Dourine (mal du coit; horse syphilis), a trypanosomal infection (*Trypanosoma equiperdum*) and also in syphilis in man (*Treponema pallidum*), the mucous surfaces are penetrated and probably it is not necessary to have a lesion.

Novy demonstrated that if the spirochaetes of the relapsing fevers come in contact with the mucous membrane of the eye 100 per cent infection ensues.

The application of the non-motile plague germ to the mucosa of the pharynx is more certain to infect than when injected into the body under the skin.

Fraenkel induced disease by causing the bacillus of tuberculosis to pass through the normal skin.

Probably all motile and non-motile micro-organisms can penetrate the uninjured mucous membrane and perhaps the skin.

II. Infection through the Alimentary Canal. This is closely associated with the previously mentioned avenue of infection. It may occur (a) through contaminated eating utensils; (b) through food contaminated in handling; by growth; by insects such as flies; and (c) by infections through water and milk.

III. Infection through the Respiratory Tract. Examples of this method of infection are: pneumonic plague, pulmonary tuberculosis, influenza, etc. These are infections mainly transmitted through "infective droplets" and "from hand to mouth". This fact was again clearly shown during the last influenza pandemic. An untold amount of suffering, incapacitation, loss of time and money can be avoided by simply guarding against these last two methods of infection ("infective droplets" and "from hand to mouth"). It is recognized that by far the greatest per cent of all infections gain entrance into the body in this way.

IV. Infection through Wounds. In this connection we must consider wounds as ranging all the way from slight abrasions to profound injuries. Slight cuts, accidents and minor operations many times necessitate no particular precautions, but there is always danger of an infection. Major accidents, such as bones crushed, are very productive of infection.

V. Infection through Insects. This source of infection was formerly altogether disregarded but it is now considered very important. The insect may play the part of a passive carrier (non-blood sucking), as the mechanical carrying of infective material by flies. The insect may also make its own wound (puncture) in which case it is blood sucking and is an active carrier of the disease. Malaria and yellow fever, as is well known, are examples of the latter method of infection.

VI. Congenital Transmission of Disease. Here the organism enters the body previous to birth, is present and active in the new born. In the latter eighties almost conclusive proof was given of anthrax passing from an infected cow to the calf and so spread. This was disregarded at the time because it was then held that uninjured tissue could not be penetrated by infective organisms. This view, of course, is no longer held. Especially in syphilis and tuberculosis scores of the still born show this infection.

Avenues of Exit.

Having thus briefly described the natural methods of infection one quite instinctively asks how do germs leave the infected body.

Micro-organisms make their exit in the secretions and through the excretions. The organisms usually tend to localize in certain organs, e. g., the typhoid bacillus in the kidneys, others in the liver, mammary gland, etc.

I. Saliva and Sputum. In hydrophobia (rabies) the salivary glands of the animal are infected and this is the chief manner of exit.

Tuberculosis is the most noted case of exit via the sputum. Pneumonic plague, pneumonia and influenza also are examples of the same.

II. Nasal Discharge. The organisms causing influenza, leprosy, glanders, infantile paralysis and meningitis are found in such discharges.

III. Intestinal Discharge. This is often the chief and only avenue of exit. It is primarily of importance when the organism is multiplying in the intestine, but also when the intestine is penetrated, ulcerated, or the growth is localized as may be the case in anthrax, bacillary as well as amoebic dysentery, typhoid and para-typhoid fever.

IV. Urine. It is almost axiomatic that infections of the blood settle in the organs and may remain there for some time and then finally pass out through the urine. It usually is secondary to the intestinal route but still very important. This is true of malta fever and may be of tuberculosis, typhoid fever and a host of other diseases. This concerns mostly the kidney.

V. Scaling. Although we do not yet know the specific organism for smallpox and chickenpox, still there is now absolutely no doubt of these diseases being spread from the scabs.

VI. Blood. The blood may harbor bacteria, protozoa (malaria, trypanosomes, etc.), spirochaetes or even invisible unknown organisms (foot and mouth disease). Such blood leaving by hemorrhages or abscesses may spread plague, glanders, anthrax, etc. When a blood sucking insect (fly, tick, flea, mosquito), absorbs infective blood it becomes capable of transferring the infection to other animals. Usually there is a specific carrier for each disease and organism (one species and one genus).

INDIVIDUAL CARRIERS.

The first recognition of an individual carrier was by Pasteur and Sternberg, 1881, in pneumonia. Now it is known that all of us often have some dangerous organism in our mouth. It causes us no harm but later it may reach a susceptible person and start the disease.

Later (in the early nineties) in the study of diphtheria, it was found that convalescents could carry the organism in their mouths for months. Moreover, typhoid fever patients may continue to excrete the bacillus for months and years through the feces and the urine. The same is true of cholera, but usually the dangerous period is much shorter than that of typhoid fever; only a matter of a few weeks.

Again, in spinal meningitis and infantile paralysis, many apparently healthy persons have been shown to have infected nasal discharges.

In the same class is Texas fever of cattle. The animal recovers from the disease but remains a carrier for life.

This principle is nicely illustrated in malta fever. The organism was known for 15 years (1885) before its life cycle was worked out. Investigation proved that nearly all the goats on the island of Malta were infected and the organism was isolated from the goat's milk. Needless to say the disease is prevented by simply heating the milk.

Many of the infectious diseases may be prevented by other means than those referred to. Experience has taught us that often an individual who has had one attack of a disease is immune from a second attack. This fact was observed from the earliest times especially in relation to the plague at Athens and smallpox in China.

The very first example of practical application of this was noted in China at least 1100-1200 B. C. Here children were exposed to smallpox or actually inoculated with the serous exudate or dried lymph. It was hoped that the disease which ensued would be mild in form. They then usually survived and were rendered immune, that is refractory to the disease. There was no change in this method for 3,000 years. This variolation—to produce a mild form of the disease—was introduced into Europe by Lady Montague about 1720.

Another phase of this came up in 1795 when Jenner, who was trained by John Hunter, noticed the absence of smallpox among those having had cowpox. He mentioned it to Hunter whose famous reply was "don't talk, try". This led to our modern practice of vaccination against smallpox, a blessing with which we are all familiar.

This principle of protecting against disease (vaccination) was advanced by Pasteur almost a century later; a little over 40 years ago. It was discovered quite accidentally in 1880 by Pasteur and his assistants while they were working with the germ of chicken cholera. The experiments were set aside during the summer vacation after which the cultures were found to be markedly changed as to their disease-producing qualities.

Since cowpox, which is a modified or weakened (attenuated) form of smallpox, protects against the disease of smallpox, Pasteur reasoned that immunity to other diseases might be likewise brought about. Acting upon this assumption, Pasteur attempted to protect fowl against chicken cholera by first inoculating them with an attenuated specific culture. He was able not only to induce immunity against this diseases but later successfully vaccinated against other diseases such as anthrax, and swine erysipelas.

Pasteur discovered that the pathogenic properties of a parasite toward its natural host might also become changed by serial passage through other animals; by desiccation as well as by other means.

He utilized these two principles to protect man against the dreadfully fatal disease of rabies. This often is spoken of as the crowning achievement of his 30 years of constant work. By repeated passage (270) through the rabbit of the "street virus" type of the disease, which had a marked varying period of incubation, he was able to standardize the rabic virus so that it killed this animal uniformly in six to seven days. Immunity was produced by several injections of a suspension made of the spinal cord which had been previously attenuated by drying over caustic soda.

Soule, aware of the fact that in the early times in India and Africa, natives were protected against the ill effects of snake bites with small amounts of snake venom, in 1885 found that when susceptible animals were repeatedly injected with sub-lethal doses of the venom that an increased tolerance for the poison and a relative immunity was gradually built up. This was the first experimental evidence of such protection.

In the following year Smith and Salmon first demonstrated that dead cultures upon inoculation induced immunity also.

In the same year Roux and Chamberlain used dead cultures of symptomatic anthrax and obtained protection.

It was also found that in some cases equally good results ensued by injecting filtered culture fluids devoid of bacteria (filtrate).

In 1888 Roux, Yersin and Martin made a classical study of diphtheria. They showed the exact relation of the bacillus to the disease and demonstrated the existence of the soluble toxin. This work led directly to antitoxic immunity.

Kitasato and von Behring used tetanus and later diphtheria toxin to protect against the respective diseases. They further discovered that the blood serum of an animal actively immune against the diphtheria toxin would in turn protect (passively) other animals against fatal results. This is the basis of our present day antitoxic treatment which von Behring 1893 first introduced for human use. Roux, '94, used the horse to produce antitoxin on a large scale.

A practical application of determining the susceptibility of a person to diphtheria was made quite recently by Schick. In a susceptible person a local irritation ensues upon the injection of a small amount of diphtheria toxin. In the case of a positive Schick test the individual should be immunized either with antitoxin (passively) or with mixtures of harmless toxin-antitoxin (actively).

Innumerable attempts have been made to apply this means to protect against various other diseases. The anti-bacterial sera of which anti-meningococci of Flexner and anti-pneumonic which have proved to be helpful in certain types of these diseases are also available.

Recently Roux, the successor of Pasteur and at present director of the Pasteur Institute, Nicholle and Conseille have developed a sero-vaccination for protection against measles. The serum is drawn from the convalescent between the sixth and tenth day after the subsidence of the fever.

These scientists recommend, in view of the fact that the immunity lasts but a short time, that one day after the child receives the inoculation an injection of blood serum (infective) drawn from a person sick (fever) with measles be made. This confers not only a longer but a higher degree of immunity. It has been conservatively estimated that "tens of thousands" of children have been saved from measles by this procedure.

Haffkine, '92, in the Hamburg cholera epidemic, vaccinated with living spirilla attenuated by long culture and later introduced it into India on a large scale.

A few years later ('96), Kohle introduced prophylactic vaccination against cholera by using cultures killed by heat or by chemicals.

This work led Wright to try out a typhoid vaccine. It was quite unsuccessful in the Boer war and it was dropped in the British army. Then Leishman also of the British army took up the work. Soldiers were treated and men in the same company living under similar conditions were used as controls. The results were quite conclusive.

After our bitter experience in the Spanish-American war, our army board took up the matter. During the Texas manoevures in 1909 hardly a case of typhoid fever resulted and the treatment was extended to the entire army with marvelous results.

Today we can positively say that typhoid fever is a disease that need not exist and can be avoided by simply applying our knowledge of how it is transmitted (water and milk borne) and by vaccination.

The same treatment was applied by Shiga, '98, to dysentery with success.

Wright urged vaccines for all germs and as we know the idea has been seized upon by manufacturers with their list of shotgun vaccines and bacterines.

Shortly after von Behring, '90, discovered that immune serum possessed antitoxic properties it was noted that it had other specific reactions which bear a very practical significance from the standpoint of clinical diagnosis.

In setting forth the reasons for the reactions of immune sera, it was conceived that various body fluids possessed anti-microbic properties or were anti-infectious due to cytolytic (cell dissolving) action. This was nicely illustrated by Pfeiffer's work in 1894. He showed that when virulent cholera germs are injected into cholera immune animals that the vibrio finally fell into granules and dissolved apparently "like sugar in water". This lytic or cytolytic action is spoken of as Pfeiffer's phenomenon.

This led directly to the demonstration that as a general proposition when any foreign protein is introduced into the animal body certain reactions are set up.

Among such immune bodies generated are agglutinins, precipitins and lysins. The phenomenon of agglutination, which is the clumping together of micro-organisms by a specific serum, was first noticed by Pfeiffer but no attention was paid to it.

Through the efforts of Widal, Gruber and Krause it was noted that its practical application was twofold: (1) the recognition of disease and (2) the identification of the organism. In the former case the serum of the suspected typhoid fever patient is brought in contact with a known typhoid fever bacillus and if the phenomenon (Widal test) occurs a positive diagnosis is made. While in the latter instance the blood serum is known to cause agglutination with a specific organism.

Precipitation is the combination of a soluble protein substance such as blood, serum, egg white, meat extract, bacterial filtrates, etc., and the corresponding immune serum, resulting in the formation of a flocculent precipitate. And thus it too can be used to identify disease and various soluble protein substances, such as may appear in blood stains. This may be important from a legal medical standpoint or in determining the source of meat as in the case of sausage suspected of containing horse or even dog flesh.

Lysis is the disintegration of organized cells (plant or animal) by specific immune serum. Bordet and Gengou first noticed this lytic action of immune serum. It was observed that it was comparable to gastric digestion in that there is a substance (immune body, sensitizer, amboceptor) which is not easily destroyed by heat (thermostable) and in that respect resembles the hydrochloric acid. Another substance (alexin, complement) is readily removed (thermo-labile, 56° C.) and is similar to the pepsin of the gastric fluid. The latter is present in all normal blood. When bacteria are thus dissolved it is referred to as bacteriolysis; when red blood cells are destroyed it is known as hemolysis, etc.

These reactions are specific. Consequently injections of red blood cells of human source or typhoid fever germs, etc., into animals produce the development of antibodies (lysins) which have the property of dissolving only the substance (antigen) which caused their appearance.

Thus the various red blood cells may be identified and one may positively say that this blood is or is not human in nature. Such findings have proven to be very valuable in fixing guilt in the case of murder.

The various other body cells and tissues, as of the spleen, liver, kidney, brain, placental as well as others, may be recognized by the application of this serological test.

Bordet and Gengou also found that when red blood or bacterial cells were treated with immune serum from which the complement had been removed by heating (56° C.), that they become susceptible (sensitized) to the action of the normal constituent in the blood (complement). And that if now these sensitized cells were added to fresh serum all the complement present in this serum would be taken up (fixed) by them so that the fluid no longer dissolved cells.

Thus the Bordet-Gengou phenomenon is also known as the complement-fixation test and is important in identifying diseases. It finds wide practical application in serology and when it is used to diagnose syphilis it is referred to as the Wassermann reaction.

The phenomena of agglutination, precipitation and lysis and their various modifications have a very great importance and practical significance in immunology and are used in the daily routine in all clinical and public health laboratories where they have become indispensable.

IDIOSYNCRASY.

In 1835, the effect of reinjection of protein substances was noted. In the early nineties this subject was again brought forth in serological work with tetanus and diphtheria.

In 1902 Richet, while studying poisons in sea animals, also observed this effect of reinjection of protein material. He proposed the name now used, anaphylaxis (without or no protection). Von Pirquet and Schick used the term allergie, meaning "off the normal". Hyper or supersensitiveness are different names for the same condition.

Arthur, '04, following up Richet's work on the suggestion of Chauvei used horse serum on rabbits and obtained the same results. Accumulative poisoning following repeated injection of protein is known as the Arthus phenomenon.

In 1904 and 1905 clinicians began to observe certain results following serum treatment, (tetaus and diphtheria antitoxin) e. g., restlessness and peripheral irritation perhaps skin eruption followed by paralysis, convulsions and even suffocation and death.

Von Pirquet and Schick collected a number of such reports into a book entitled—"Serum Diseases".

Theobald Smith, '05, called Ehrlich's attention to this strange phenomenon. Ehrlich turned this problem over to Otto who in 1906 published a paper on the Theobald Smith phenomenon.

About the same time Rosenau and Anderson, while working on the standardization of toxins and antitoxins, published a paper on the behavior of guinea-pigs to serum. Literally thousands of articles have since been published on this subject.

Summing up all the experimental evidence shows this to be a specific protein phenomenon and occasioned by any protein whether plant or animal.

Along the line of such protein sensitization we have certain diagnostic applications.

Koch's tuberculin which is prepared from the tubercle bacillus or its products of growth, which are protein in chemical nature, reacts markedly when persons or animals affected with active and masked or incipient forms of the disease. The von Pirquet or cutaneous; the Calmette or ophthalmo; the Moro, percutaneous or ointment; the thermal and the Detre differential are tests of this type for tuberculosis.

Mallein which is prepared in much the same way as tuberculin is used in the diagnosis of glanders.

Similarly luetin, a filtered culture of the syphilis spirochaete, is used to test for syphilis and gives a local reaction in 24 hours in an individual afflicted with the disease.

Hay fever, in many cases, at least, seems to be a sensitization from certain vegetable proteins (pollens) followed by a reaction during the pollen season. The practicability and clinical value of pollen extracts in diagnosis, prophylactic and as a curative means is well known.

Idiosyncrasy or charactertistic symptoms of poisoning due to foods, such as eggs, fish, oysters, milk, cheese and cereals, among certain individuals may be explained along these same lines of hypersensitiveness or anaphylaxis.

CHEMOTHERAPY.

Just as the application of antitoxins and anti-infectious sera, vaccines, and the various tests used in clinical diagnosis are bacteriological problems, so is the combating of microbic disease by use of chemicals. We are here also concerned with the micro-organic cause of disease, its prevention and cure.

Before the days of bacteriology man had successfully combated only two diseases: malaria with quinine and syphilis with mercury. The laboratory has already accomplished wonders. Emetin, the active principle of ipecac, has been found to be specific for amoeba.

The injection of pure chemical substances into the body in curing disease was early thought of. Most everything under the sun was tried sooner or later. An example of this chemical work was the injection of sodium carbonate in an effort to so change the reaction of the body that the organism could not grow.

The discovery of anti-sera sidetracked this work but it was revived in a different spirit in 1900 when investigation of protozoal forms became important as pathogenic organisms. The "ultima thule" was Ehrlich's "Therapia sterilisans magana", that is, to kill everything at once—complete sterilization.

In the treatment of humans different conditions are involved and one cannot always use one large sure-cure dose. It, therefore, is most desirable and is the aim of this whole line of therapy to select a drug which has specific and parasitotropic properties (having greater affinity for the parasite than for the tissue of the host). It was noted that if a large enough dose cannot be injected so as to kill all the micro-organisms at once, some forms, especially trypanosomes, can tolerate the chemical used (chemofast) until finally the drug has no effect whatsoever on the parasite. In such cases, however, the rotation of chemicals of a widely different chemical nature have proven beneficial.

Arsenic was first used quite empirically. Livingston, a missionary in South Africa in the early fifties, administered arsenic in the form of Fowler's solution (potassium arsenite) to his animals sick of tick fever. A temporary improvement was noted but this was soon followed by a decline and they finally died. Lingard used arsenic, again quite empirically in India, to combat surra, a trypanosomal disease (*Trypanosoma equium*) which attacks horses, elephants, etc., but with no marked results. There was usually death after temporary improvement.

In 1905 Thomas tried other arsenic compounds. He used atoxyl (sodium p-arsanilate), a proprietary arsenic compound, with fair results. Koch used atoxyl on humans and animals in Africa and again it was the same old story—a temporary improvement but eventually death.

Arsenic in the organic combinations of arsphenamine, commonly known as salversan or 606, and neo-arsphenamine are intensely destructive to spirochaetes in general and are universally used in combating the spirochaetes causing syphilis and yaws. They are specific for the spirochaetes, responsible for the relapsing fevers; are used in the treatment for trypanosomiasis and are beneficial in certain cases of malaria where quinine seems to make no headway.

Antimony compounds were also tried out and tartar emetic (potassium antimonyl tartrate) was especially successful when used with animals. But a suspension of fine electrolytic antimony injected intravenously is the best of all. Antimony seems good in cases of Leishmania of the skin and with Granuloma (venereal) it is marvelously effective, While in Framboesia (yaws), a disease resembling syphilis and also due to a spirochaete, very successful results are noted with the cutaneous type of the disease. It is a specific for filaria.

The active agents used in chemo-therapy are now narrowed down to arsenic and antimony and their compounds in treating blood parasites.

These are some of the many practical applications accomplished in bacteriology which, remindful of the fact that the subject as an exact science has been established less than one-half century, are indeed quite marvelous.

Incalcuable benefits ensue to mankind and his onward movement are made possible by the utilization of those micro-organisms which are useful and the destruction of those which are harmful either before or after they enter the body of man, lower animals and plants.