The Aetiology of Tuberculosis

By
Dr. Robert Koch

Introduction

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The World Health Organization estimates that approximately 2-3 million people die from tuberculosis (TB) each year. Most of these deaths occur in developing countries. Although there has been a steady decline in the number of persons with active TB in the United States, TB is still a problem in this country. Robert Koch (1843-1910) recipient of the Nobel Prize for Physiology or Medicine in 1905 is famous for the development of research techniques that have since been used by researchers throughout the world. Koch's skilled and meticulous research methodology led to the discovery of the organism responsible for causing tuberculosis and dispelled the belief that "bad air" (miasma) was responsible for the dreaded infection.

Koch's tenaciousness and intelligence was apparent from a very young age. Born the son of a mining engineer, he taught himself to read. In 1862 he attended medical school at the University of Göttingen and is believed to have been influenced by Jacob Henle, who published in 1840, that infectious diseases were caused by living organisms. In 1866, after completing his M.D. degree, Koch studied chemistry in Berlin.

In 1872, at the age of 29, Koch became District medical Officer for Wollstein, a rural area near Berlin. It was here that he began his experiments with microbes in the small laboratory that was also his home. Although the anthrax bacillus had previously been discovered by Pollender, Rayer and Davaine, Koch was able to isolate the anthrax organism and prove that the anthrax bacillus was indeed the cause of disease. Koch became famous when the results of his work with the anthrax bacillus were published in a botanical journal "Beitrage" which was then edited by Ferdinand Chon, professor of Botany at the University of Breslau.

In 1880, Koch was appointed a member of the Imperial Health Bureau in Berlin. Here, he invented new methods of cultivating pure cultures of bacteria and developed new media such as potato and agar, which he used in a flat dish newly invented by Petri. He also invented new methods of staining bacteria which made them more easily visible and helped to identify them. In 1882, Koch announced that he and his team had found the Mycobacterium tuberculosis organism, which caused what was then known as "consumption".

In 1882, Koch published his classical work on the tubercle bacillus. He presented his findings during the meeting of the Berlin Psychological Society on March 24, 1882. Koch stunned his audience with his presentation on the "Etiology of Tuberculosis". He related with detail the exacting methodology with which his numerous experiments were carried. He considered all possibilities during the experimentation process and was able to account for possible alternate explanations. Koch's detailing of the discovery of the bacteria that was the cause of tuberculosis, left the crowd speechless. The discovery of the tuberculosis bacteria by Koch was very important first step in the attempt to control the infectious disease. Knowing the pathogenesis of an organism gives way to finding measures of controlling its communication.

Koch's patience as a researcher is mentioned as being one of the important factors behind his successful attempt to isolate the tubercle bacillus. It has been posited that due to the slow growth of the bacteria, an impatient researcher might have mistakenly made an assumption that either the bacteria did not exist or was not able to be grown in the available media.

His methods inspired other researchers to follow suit and after his report on the etiology of tuberculosis, 21 disease-causing germs had been identified within 21 years. Koch is also credited with the establishment of four criteria that must be demonstrated in order to prove that a specific microorganism causes a particular disease. These criteria, known as "Koch's Postulates" are still used today in order to determine the pathogenicity of current infectious diseases such as SARS, Ebola and HIV.

Koch's Postulates:

1. The micorooganism must be found in all cases of the disease.
2. It must be possible to isolate the microorganism from the host and grow it in pure culture.
3. The microorganism must reproduce the original disease when introduced into an experimental animal.
4. The microorganism must be recoverable from that animal.

In 1891, Koch became an honorary professor of the Medical Faculty of Berlin and director of the new Institute for Infectious Diseases. During this time, Koch continued his work on tuberculosis. In an attempt to find a cure for tuberculosis, Koch developed a preparation which he called "tuberculin" made from cultures of tubercle bacilli. Although the preparation did not prove successful as a cure, it did lead to the discovery of a diagnostic substance which is used today. Koch went on to work in other countries such as India and Africa, and published work on infectious diseases such as malaria, and plague.

Koch's innovative research is more relevant today than it was in the late 1800's. Tuberculosis is the most common infection in the world. Almost one third of the world's population is infected with TB. Of those infected with the tuberculosis bacillus, approximately 350 million have active tuberculosis. It is estimated that some 7-8 million new cases and 2-3 million deaths occur annually throughout the world. Until 50 years ago, there were no medicines to cure TB. Now, strains that are resistant to a single drug have been documented in every country. A particularly dangerous form of drug-resistant TB is multidrug-resistant TB (MDR-TB), which is prohibitively expensive (often more than 100 times more expensive than treatment of drug-susceptible TB), and is also more toxic to patients. The WHO has recommended an effective and inexpensive approach to TB control known as DOTS (Directly Observed Therapy-Short Term). The DOTS strategy produces cure rates of up to 95% even in the poorest countries. The World Bank has ranked the DOTS strategy as one of the "most cost-effective of all health interventions".

Robert Koch died on May 27, 1910. He had been married twice and was the father of one daughter. Koch's work was a benefit to human kind. The world remembers his important gift each year on World TB Day, which occurs on March 24th, the anniversary of his historic presentation.

The Aetiology of Tuberculosis

Villemin's discovery that tuberculosis is transmissible to animals has, as is well known, found varied confirmation, but also apparently well grounded opposition, so that it remained undecided until a few years ago whether tuberculosis is or is not an infectious disease. Since then, however, inoculations into the anterior ocular chamber, first performed by Cohnheim and Salomonsen, and later by Baumgarten, and furthermore the inhalation experiments done by Tappeiner and others have established the transmissibility of tuberculosis beyond any doubt, and in future tuberculosis must be classed as an infectious disease.

If the number of victims which a disease claims is the measure of its significance, then all diseases, particularly the most dreaded infectious diseases, such as bubonic plague, Asiatic cholera, etc., must rank far behind tuberculosis. Statistics teach that one-seventh of all human beings die of tuberculosis, and that, if one considers only the productive middle-age groups, tuberculosis carries away one-third and often more of these. Public hygiene has therefore reason enough to devote its attention to so destructive a disease, without taking into any account that still other conditions, such as the relations of tuberculosis to Perlsucht, engage the interest of Public Health. Since it is part of the task of the Gesundheitsamt to investigate infectious diseases from the point of view of public health, that is, primarily as regards their aetiology, it seemed an urgent duty to make thorough studies on tuberculosis particularly. There have been repeated attempts to fathom the nature of tuberculosis, but thus far without success.

The so frequently successful staining methods for the demonstration of pathogenic microorganisms have failed in regard to this disease, and, to date, the experiments designed to isolate and cultivate a tubercle virus cannot be considered successful, so that Cohnheim, in the recently published and newest edition of his lectures on general pathology had to designate "the direct demonstration of the tuberculous virus as a still unsolved problem." In my studies on tuberculosis I first used the known methods without elucidating the nature of the disease. But by reason of several incidental observations I was prompted to abandon these methods and to follow other paths, which finally led to positive results.

The aim of the study had to be directed first toward the demonstration of some kind of parasitic forms, which are foreign to the body and which might possibly be interpreted as the cause of the disease. This demonstration became successful, indeed, by means of a certain staining process, which disclosed characteristic and heretofore-unknown bacteria in all tuberculous organs. It would take us too far a field to tell of the road by which I arrived at this new process, and I shall therefore immediately give its description. The objects for study are prepared in the usual fashion for the examination for pathogenic bacteria. They are either spread on the cover-slip, dried and heated, or they are cut in sections after being hardened in alcohol.

The cover-slips or sections are put in a staining solution of the following formula: 200 cc. of distilled water are mixed with 1 cc. of a concentrated alcoholic methylene-blue solution, and with repeated shaking 0.2 cc. of a 10 per cent potassium-hydrate solution is added. This mixture should not produce a precipitate even after standing for several days. The objects to be stained remain in it from 20 to 24 hours. By heating the staining solution to 40°C. in a water-bath this time can be shortened to from one-half to one hour. The cover-slips are then covered with a concentrated aqueous solution of vesuvin, which must be filtered each time before use and rinsed after one to two minutes with distilled water. When the cover-slips are removed from the methylene-blue the smear looks dark blue and is much overstained, but upon the treatment with vesuvin the blue color disappears and the specimen appears faintly brown.

Under the microscope all constituents of animal tissue, particularly the nuclei and their disintegration products, appear brown, with the tubercle bacilli, however, beautifully blue. With the exception of leprosy bacilli, all other bacteria which I have thus far examined in this respect assume a brown color with this staining method. The color contrast between the brown-stained tissue and the blue tubercle bacilli is so striking, that the latter, which are frequently present only in very small numbers, are nevertheless seen and identified with the greatest certainty. Sections are treated quite similarly. They are transferred from the methylene-blue solution into the filtered vesuvin solution, in which they remain from fifteen to twenty minutes, and are then rinsed in distilled water until the blue color has disappeared and a more or less distinct brown stain remains. They are then dehydrated with alcohol and cleared in oil of cloves, and are either at once microscopically examined directly in this fluid or are finally embedded in canada-balsam.

In these preparations the tissue constituents appear brown and the tubercle bacilli a vivid blue. Incidentally, the bacteria can be stained not only with methylene-blue, but they take also other aniline dyes, with the exception of brown dyes, under the simultaneous action of an alkali; but their staining is not so beautiful by far as with methylene-blue. In the staining process mentioned the potassium-hydrate solution can be substituted by sodium hydroxide or ammonia water, from which one may conclude that the potassium does not play an essential role, but it is the strongly alkaline reaction of the solution, which counts. This is further confirmed by the fact that a stronger addition of potassium will stain bacteria in such places where a weaker potassium solution fails. But the tissues in sections shrink and change so much under the influence of stronger potassium solutions that the latter are only exceptionally of advantage. In several respects the bacteria made visible by this process exhibit a characteristic behavior. They are rod-shaped, and they belong to the group of bacilli. They are very thin and one-fourth to one-half as long as the diameter of a red blood-corpuscle, although they may sometimes reach a greater length, up to the full diameter of an erythrocyte. In shape and size they bear a striking similarity to leprosy bacilli. They are differentiated from the latter by being a bit more slender and by having tapered ends.

Further, leprosy bacilli are stained by Weigert's nuclear stain, while the tubercle bacilli are not. Wherever the tuberculous process is in recent evolution and is rapidly progressing, the bacilli are present in large quantities; they usually form, then, densely bunched and frequently small braided groups, often intracellular; and they present at times the same picture as leprosy bacilli accumulated in cells. In addition, numerous free bacilli are found. It is particularly at the margin of larger caseous foci that there occur practically only shoals of bacilli, which are not enclosed in cells. As soon as the height of tubercle-development is passed the bacilli become rarer, and occur only in small groups or quite singly, in the margin of the tuberculous focus and side by side with weakly stained and sometimes hardly recognizable bacilli, which are presumably dying or dead.

Finally, they may disappear completely; but they are but seldom entirely absent and, if so, only in such places in which the tuberculous process has come to a standstill. If giant cells occur in the tuberculous tissue the bacilli are by predilection within these formations. In very slowly progressing tuberculous processes, the interior of giant cells is usually the only place in which bacilli .are to be found. In this case the majority of giant cells enclose one or a few bacilli; and it produces a surprising impression to find repeatedly in large areas of the section groups of giant cells, most of which contain one or two tiny blue rods in the center, and within the wide space enclosed by brown-stained nuclei. Frequently, the bacilli are seen only in small groups of giant cells, sometimes only in single cells, while simultaneously many other giant cells are free from them. Then, by their size and position, the bacilliferous cells are recognized as the younger ones, while those free from bacilli are the older ones; and it may be assumed that originally the latter also enclosed bacilli, which have died or changed into a resting state, soon to be mentioned. Analogous to the formation of giant cells around foreign bodies, such as vegetable fibres and strongylus eggs, observed by Weiss, Friedländer and Laulamié, it may be assumed that the bacilli, acting as foreign bodies, are enclosed by giant cells; therefore it seems justifiable to assume that, even when the giant cell is found empty while all other features indicate processes as tuberculous, the giant cell was formerly the host of one or several bacilli, and that the latter have been responsible for their formation. The bacilli are also observable unstained in unprepared specimens.

For this it is necessary to take a little material from such places as contain considerable numbers of bacilli, for example, from a gray tubercle from the lung of a guinea pig, dead of inoculation tuberculosis. This material must be examined after the addition of a little distilled water or, preferably, blood-serum, and best in a hollow slide, in order to avoid streaming in the fluid. The bacilli appear then as very fine rods which show only molecular, but not the slightest trace of intrinsic movement. Under certain conditions to be mentioned later the bacilli form spores even in the animal body. Individual bacilli contain several, usually 2 to 4 spores, oval in shape, and distributed at even intervals along the entire length of the bacillus. In regard to the occurrence of bacilli in the various tuberculous manifestations in human beings and animals it has been possible to examine the following material thus far:

(A) From Human Beings: Eleven cases of miliary tuberculosis:

The bacilli never failed of demonstration in miliary tubercles of the lungs; frequently, however, they could not be found any more in those tubercles whose center no longer stained with nuclear dyes. However, they were then still present, and all the more numerous, in small groups in the margin of the tubercle and in younger nodules as yet without central caseation. They were demonstrable, also, in miliary tubercles of the spleen, liver and kidneys, and quite numerous in the gray nodules of the pia mater in basilar meningitis. The caseated bronchial lymph nodes which were examined in several cases contained, in part, dense shoals of bacilli and among them many spore-bearing ones. Tubercles, 'embedded partly in the lymphoid tissue with a central giant cell surrounded by epithelioid cells, showed some tubercle bacilli within the giant cells. Twelve cases of caseous bronchitis and pneumonia (in 6 cases cavity formation); the presence of bacilli was usually limited to the margin of the caseously infiltrated tissue, where several times, however, they were very numerous. Also, within the infiltrated portions of the lung one occasionally encounters nests of bacilli. In most cavities the bacilli are abundant, and the well-known small caseous particles in the cavity contents consist almost completely of bacillary masses. Among those bacilli found in soft caseous foci and in cavities there were, now and then, numerous spore-bearing bacilli. In larger cavities the bacilli occur mixed with other bacteria. However, they were easily distinguishable because, with the staining-method mentioned, only tubercle bacilli stain blue while other bacteria assume a brown color. One case of solitary tubercle in the brain, larger than a hazelnut:

The caseous part of the tubercle was enclosed by a cellular tissue in which were embedded many giant cells. Most of these did not contain any parasites, but here and there were encountered groups of giant cells, each of which contained one or two bacilli. Two cases of intestinal tuberculosis: In tuberculous nodules, which were grouped around the intestinal ulcers, the bacilli were demonstrable with particular ease. Here again they were predominantly numerous in the youngest and smallest nodules. In the mesenteric lymph nodes of these two cases bacilli were present in great numbers. Three cases of freshly excised scrofulous lymph nodes: In only two of them could bacilli be demonstrated in giant cells. Four cases of fungoid arthritis: In two cases separate small groups of giant cells contained bacilli.

(B) From Animals:

Ten cases of Perlsucht with calcified nodules in the lungs, in several cases also in the peritoneum and once on the pericardium: In all cases bacilli were found predominantly within giant cells in the tissue surrounding the calcareous masses. The distribution of the bacilli is most frequently so even that among numerous giant cells there is hardly one which does not contain one or several bacilli, and sometimes as many as twenty. In one of these cases the bacilli could also be demonstrated in the bronchial lymph nodes and in a second case in the mesenteric lymph nodes. Three cases in which the lungs of cattle contained, not the well-known calcified nodules with knobby surface, as usually seen in Perlsucht, but smoothwalled, spherical nodes, filled with a thick, cheesy material: Usually this form is not regarded as tuberculosis but is interpreted as bronchiectasis. In the neighborhood of these nodules were found giant cells containing tubercle bacilli.

A caseated cervical lymph node from a hog likewise contained the bacilli. Large amounts of tubercle bacilli were found in the organs of a chicken dead of tuberculosis, both in tubercles in the bone-marrow and in the peculiar large lymph nodes of the intestines, the liver, and the lungs. Of three monkeys which had died spontaneously of tuberculosis, the lungs, spleen, liver and omentum, all studded with innumerable nodules, and the caseated lymph nodes were examined; and bacilli were found everywhere in the nodules or in immediate proximity to them. Of spontaneously diseased animals, nine guinea pigs and seven rabbits were examined; all showed bacilli in the tubercles. In addition to these cases of spontaneous tuberculosis, I could avail myself of a not inconsiderable number of animals which had been infected by inoculation with the most varied tuberculous materials: as, for instance, with gray and caseated tubercles from human lungs, with sputum from consumptives, with tuberculous masses from spontaneously diseased monkeys, rabbits and guinea pigs, with masses of calcified or caseated lesions from Perlsucht in cattle, and finally with material from lesions obtained by animal-passage.

The number of animals so infected amounted to 172 guinea pigs, 32 rabbits and 5 cats. In the majority of these cases the demonstration of bacilli had to be limited to the examination of tubercles in the lungs, which were always present in large numbers. Here bacilli never failed to be found: frequently they were extraordinarily numerous, and sometimes spore-bearing, but in some preparations only a few yet unmistakable individual forms were observed.

Considering the regularity of the presence of tubercle bacilli it is striking that so far they have not been seen by anyone. But this is explained by the fact that the bacilli are extraordinarily small formations, and are usually so scanty in number, particularly when their occurrence is limited to the interior of giant cells, that for this reason alone they are not detectable by the most attentive observer without the use of quite specific staining-reactions. When present in larger numbers, they are mixed with a finely granular detritus, and obscured by it in such a manner that their visualization is made difficult in the highest degree. Incidentally, there exist some reports about the finding of microorganisms in tuberculous tissue. For example, Schüller, in his paper on scrofulous and tuberculous arthropathies, mentions that he has constantly found micrococci. Just as the very small motile granules which were found in tubercles by Klebs, these micrococci are undoubtedly something entirely different from the tubercle bacilli seen by me, which are nonmotile and rod-shaped.

Furthermore, in the first issue of his pathological reports Aufrecht states that, besides two different types of micrococcus, he has seen short, rod,.like formations whose length was twice their breadth. He saw these rods in the centre of tubercles in three of a series of rabbits which he had infected with Perlsucht and tuberculous material. But tubercle bacilli are at least five times as long as they are thick, and often much longer yet in relation to their thickness; furthermore, in cases of uncomplicated tuberculosis they never occur mixed with micrococci or other bacteria in the tubercles. For this reason it is extremely unlikely that Aufrecht saw the real tubercle bacilli; had he done so, he would then have necessarily demonstrated their occurrence in human tubercles and in lungs with Perlsucht, and he could not have escaped noticing the conspicuous relationship between the bacilli and the giant cells. On the basis of my numerous observations I consider it established that, in all tuberculous affections of man and animals, there occur constantly those bacilli which I have designated tubercle bacilli and which are distinguishable from all other microorganisms by characteristic properties.

However, from the mere coincidental relation of tuberculous affections and bacilli it may not be concluded that these two phenomena have a causal relation, notwithstanding the not inconsiderable degree of likelihood for this assumption that is derivable from the fact that the bacilli occur by preference where tuberculous processes are incipient or progressing, and that they disappear where the disease comes to a standstill. To prove that tuberculosis is a parasitic disease, that it is caused by the invasion of bacilli and that it is conditioned primarily by the growth and multiplication of the bacilli, it was necessary to isolate the bacilli from the body; to grow them in pure culture until they were freed from any disease product of the animal organism which might adhere to them; and, by administering the isolated bacilli to animals, to reproduce the same morbid condition which, as known, is obtained by inoculation with spontaneously developed tuberculous material. Disregarding the many preliminary experiments, which served for the solution of this task, here again the finished method will be described. Its principle rests on the use of a solid transparent medium, which retains its solid consistence at incubator temperature.

The advantages of this method of pure culture, which I have introduced into bacteriology, I have explained in detail in an earlier publication. That the really complicated task of growing tubercle bacilli in pure culture was achieved by this method is to me a new proof of its efficiency. Serum from sheep- or cattle-blood, separated as pure as possible, is put into test-tubes closed with a cotton stopper and heated every day to 58°c. for six subsequent days. It is not always possible to sterilize the serum completely by this process, but in most cases it suffices. Then the serum is heated to 65°C. during several hours, or sufficiently long for it to be just coagulated and solidified. After this treatment it appears as an amber-yellow, completely transparent or only slightly opalescent, solid, jelly-like mass; and after several days at incubator temperature it must not show the slightest development of bacterial colonies. If the heating exceeds 75°c. or if it lasts too long, the serum becomes opaque. In order to obtain a large surface for the preparation of the cultures the serum is solidified in test-tubes slanted as much as possible. For those cultures intended for direct microscopical examination the serum is solidified in flat.

Upon this solidified blood-serum, which forms a transparent medium that remains solid at incubator temperature, the tuberculous materials are applied in the following manner: The simplest case in which the experiment is successful is presented, almost without exception, when an animal which has just died of tuberculosis, or a tuberculous animal which has just been killed for this purpose, is at one's disposal. First, the skin is deflected over the thorax and abdomen with instruments flamed just before use. With similarly prepared scissors and forceps, the ribs are cut in the middle, and the anterior chest wall is removed without opening the abdominal cavity, so that the lungs are to a large extent laid free. Then the instruments are again exchanged for freshly disinfected ones, and single tubercles or particles of them, of the size of a millet-seed, are quickly excised with scissors from the lung tissue, and immediately transferred to the surface of the solidified blood serum with a platinum wire, which has been melted into a glass rod which must be flamed immediately before use. Of course, the cotton stopper may be removed for only a minimal time. In this manner a number of test-tubes, about six to ten, are implanted with tuberculous material, because, with even the most cautious manipulation, not all test-tubes remain free from accidental contamination.

Lymph nodes in a state of incipient caseation are as well suited for this experiment as are pulmonary tubercles; less so, however, the pus from liquefied lymph nodes which usually contains very few bacilli or none at all. The direct isolation of bacilli from tuberculous human organs or from lungs with Perlsucht is more difficult. Objects of this kind, whose excision from the body I could not attend to with all the precautions just mentioned, I have washed carefully and repeatedly with a solution of bichloride of mercury, and have then removed their superficial layers with flamed instruments and taken the substance for inoculation from a depth which putrefactive bacteria had presumably not yet invaded.

The test-tubes, provided with tuberculous substance in the described manner, are kept in the incubator at a constant temperature of 37° or 38°c. In the first week no noticeable alteration occurs. If some change does occur and if, already during the first days, bacterial growth develops, starting from the inoculation material or even remotely from it and spreading, and appearing usually as whitish-gray or yellowish drops, and often liquefying the solid serum, then one is dealing with contaminations and the experiment has failed. Cultures that result from a growth of tubercle bacilli do not appear to the naked eye until the second week after the seeding, and ordinarily not until after the tenth day. They come into view as very small points and dry-looking scales.

Depending upon whether the tuberculous material was more or less crushed in seeding and whether it was brought into contact with a large surface of the medium by rubbing motions, the colonies surround the explanted bit of tissue in smaller or larger areas. If only very few bacilli were present in the inoculum it is hardly possible to free the bacilli from the tissue and bring them into immediate contact with the medium. In this case the colonies develop in the fragments of explanted tissue; and one sees, if the tissue is transparent enough (for example, in bits from scrofulous lymph nodes), dark points in transmitted light and white points in direct light. With the aid of a 30 - to 40-times magnification one can perceive the bacterial colonies as soon as toward the end of the first week. They appear as very neat spindle- and usually S-shaped or similarly curved formations, which consist of the well-known most tenuous bacilli when spread on a coverslip, and stained and examined with high magnifications. Up to a certain degree their growth proceeds for a period of 3 to 4 weeks, as they enlarge to flat scale-like bits, usually not reaching the size of a poppy seed, and lie loosely on the medium, which they never invade or liquefy.

Furthermore, the bacillary colony forms such a compact mass that its small scale can easily be removed with a platinum wire from the solidified blood-serum as a whole, and can be crushed only upon the application of a certain pressure. The exceedingly slow growth which can be obtained only at incubator temperature, and the peculiar scale like dry and firm texture of these bacillary colonies are not met with in any other known bacterial species, so that it is impossible to confuse cultures of tubercle bacilli with those of other bacteria; and, even with but little experience, nothing is simpler than to recognize accidental contaminations of the cultures immediately. As mentioned, the growth of the colonies is finished after a few weeks; and a further enlargement does not occur, because the bacilli are devoid of any intrinsic motility, and because they are moved along the medium only by the process of growth, which, on account of the slow multiplication of the bacilli, may, of course, occur within very small dimensions only.

In order to keep such a culture going, it is necessary to transplant it to a new medium some time after the first seeding, approximately after 10 to 14 days. This is done by removing a few scales with the flamed platinum wire and by transferring these into a fresh test-tube of sterilized coagulated blood serum, where they are crushed on the surface of the medium and spread as widely as possible. Within the same interval there again develop scale-like, dry masses, which coalesce and, depending upon the extent of their seeding, cover a larger or smaller part of the surface of the blood serum. In this manner are the cultures continued. The tubercle bacilli can also be cultivated on other nutritive media, provided the latter possess properties similar to those of the solidified blood serum. For example, they grow on agar-agar, which remains solid at incubator temperature and which contains an addition of meat infusion and peptone. But on this medium there take form only amorphous small crumbs, and never, as on blood serum, the characteristic vegetations.

Originally I cultivated tubercle bacilli from only the pulmonary tubercles of guinea pigs that had been infected with tuberculous material. Accordingly, the cultures derived from various sources had to pass a sort of intermediary stage, namely, in the body of a guinea pig. This method could, however, have led to the same errors as accompanied the transfer of a culture from one test-tube to another if, accidentally, other bacteria had been inoculated with the tubercle bacilli, or if, as is not rare, spontaneous tuberculosis had occurred in the experimental animal. To avoid these sources of error, special precautions were necessary; they were derived from observations of the behavior of spontaneous tuberculosis, which endangered these experiments most.

Among hundreds of recently bought guinea pigs, which were autopsied in the course of other experiments, I have not found a single tuberculous one. Spontaneous tuberculosis occurred only in single instances and never before three or four months after the animal had been kept in the same room with tuberculous animals. In spontaneously tuberculous animals the bronchial lymph nodes were without exception excessively enlarged and purulent, while in most cases the lungs contained a large caseous focus with far advanced central necrosis, so that several times there had occurred true cavity-formation, as in human lungs. The development of tuberculosis was much slighter in the abdominal organs than in the lungs. The swelling of the bronchial lymph nodes and the beginning of the process in the respiratory organs leave no doubt that spontaneous tuberculosis of these animals is an inhalation infection, that originates from the invasion of a few or possibly only a single infectious germ and which therefore develops very slowly. Inoculation tuberculosis behaves quite differently.

The site of inoculation was in the abdomen near the inguinal lymph nodes. These swelled first, and so presented an early and unmistakable sign of a successful inoculation. The tuberculosis proceeded much more rapidly than does spontaneous tuberculosis, because a larger amount of infectious material was involved, and at autopsy the spleen and liver were found more tuberculous than the lungs. It is therefore not at all difficult to differentiate spontaneous tuberculosis from inoculation tuberculosis in the experimental animal. Considering all these conditions, it could well be assumed that, if several recently bought guinea pigs, inoculated in the same manner and with the same material and kept in separate cages removed from other animals, all simultaneously and after a brief period developed inoculation tuberculosis in the characteristic fashion, then the occurrence of the tuberculosis was caused by the action of the inoculated material.

Events proceeded in the indicated manner; and with all precautions (disinfection of the site of inoculation, use of flamed instruments) the substance to be tested for its virulence was inoculated each time into from four to six guinea pigs. The result was uniform throughout: in all animals which were inoculated with fresh material containing tubercle bacilli the slight inoculation wound was usually scabbed on the following day, and the site remained unchanged for about eight days. Then a nodule formed, which enlarged without rupturing or, in most cases, developed into a flat and dry ulcer.

After two weeks the inguinal lymph nodes on the side of inoculation, and sometimes also the axillary nodes, were already swollen to pea size. From this time on, the animals became emaciated rapidly, and died after four to six weeks; or they were killed, in order to exclude any possible combination with a later-developing spontaneous tuberculosis. In the organs of all these animals, but chiefly in the spleen and liver, were found the characteristic and well-known tuberculous alterations. That the infection of the guinea pigs in this procedure was caused only by the inoculated material is evident from the fact that, in several experimental series, the inoculation of material which did not contain living tubercle bacilli did not produce tuberculosis in a single inoculated animal. The material used in these series consisted of a scrofulous lymph node and fungoid masses from a joint, in both of which no tubercle bacilli were demonstrable, and pulmonary tubercles from a monkey, dried for two months and in another case kept in alcohol for two months. Without exception, animals injected with bacilliferous material had far-advanced tuberculosis, four weeks after inoculation.

From such guinea pigs as were infected with tubercles from the lungs of apes, with miliary tubercles from the brain and lungs of human beings, with caseous materials from phthisical lungs, and with nodules from the lungs and the peritoneum of cattle with Perlsucht, cultures of tubercle bacilli were isolated in the manner described above. It became evident that, just as the picture of the disease is the same, whether produced by all the enumerated different substances, so do the bacilliary cultures obtained differ not in the slightest from one another. Altogether, there were secured fifteen such pure cultures of tubercle bacilli, four from guinea pigs infected with tuberculous products from a monkey, four from guinea pigs infected with Perlsucht material, and seven from guinea pigs infected with tuberculous formations from human beings.

In order to exclude the possible criticism that the inoculation of tuberculous material into guinea pigs causes an alteration, or possibly a disappearance, of the differences characterizing the previously different microorganisms, an attempt was made to cultivate the tubercle bacilli directly from the spontaneously tuberculous organs of human beings and animals. This attempt succeeded repeatedly, and pure cultures were obtained from two human lungs with miliary tuberculosis, from a human lung with caseous pneumonia, from the contents of small cavities in phthisical lungs twice, from caseated mesenteric lymph nodes once, and from specially excised scrofulous lymph nodes twice; further, twice from pulmonary Perlsucht in cattle, and three times from the lungs of spontaneously diseased guinea pigs. These cultures likewise resembled one another completely, as did those, which were obtained by the intermediation of inoculated guinea pigs, so that the identicalness of the bacilli present in various tuberculous processes cannot be doubted.

In regard to these pure cultures I must mention that Klebs, Schüller, and Toussaint have also cultivated microorganisms from tuberculous masses. All three investigators found that, after their infection with tuberculous material, the nutritive-media fluids became cloudy as early as within two to three days, and contained numerous bacteria. In Klebs's experiments small motile rods developed rapidly, while Schüller and Toussaint obtained micrococci. I have convinced myself repeatedly that tubercle bacilli grow only very sparsely in liquids, that they never cloud the latter because they are totally nonmotile and that, if growth occurs, it becomes recognizable only after three or four weeks.

The authors mentioned must therefore have dealt with organisms other than tubercle bacilli. Up to this point it was established by my studies that the occurrence of characteristic bacilli is regularly coincidental with tuberculosis and that these bacilli can be obtained and isolated in pure cultures from tuberculous organs. It remained to answer the important question whether the isolated bacilli when again introduced into the animal body are capable of reproducing the morbid process of tuberculosis. In order to exclude every error in the solution of this question, which contains the principal point in the whole study of the tubercle virus, many different series of experiments were done, which, on account of the significance of the point at issue, will be enumerated. First, were done experiments involving the simple inoculation of bacilli in the previously described manner.

<u>First Experiment:</u>

Of 6 recently bought guinea pigs which were kept in the same cage, four were inoculated on the abdomen with bacillary culture material derived from human lungs with miliary tubercles and grown in five transfers for fifty-four days. Two animals remained uninoculated. In the inoculated animals the inguinal lymph nodes swelled after fourteen days, the site of inoculation changed into an ulcer, and the animals became emaciated. After thirty-two days one of the inoculated animals died, and after thirty-five days the rest were killed. The inoculated guinea pigs, the one that had died spontaneously as well as the three killed ones, showed far-advanced tuberculosis of the spleen, liver and lungs; the inguinal nodes were much swollen and caseated; the bronchial lymph nodes were but little swollen. The two noninoculated animals displayed no trace of tuberculosis in lungs, liver or spleen.

<u>Second Experiment:</u>

Of 8 guinea pigs, six were inoculated with bacillary culture material, derived from the tuberculous lung of an ape, and cultivated in eight transfers for ninety-five days. Two animals remained uninoculated as controls. The course was exactly the same as in the first experiment. At autopsy the 6 inoculated animals were found with far advanced tuberculosis, while the two noninoculated ones were healthy when they were killed, after thirty-two days.

<u>Third Experiment:</u>

Of 6 guinea pigs, five were inoculated with culture material, derived from a Perlsucht lung, and seventy-two days old and transferred six times. After thirty-four days all animals were killed. The five inoculated ones were tuberculous, the non inoculated one was healthy.

Fourth Experiment:

A number of animals (mice, rats, hedgehogs, hamsters, pigeons, frogs), whose susceptibility to tuberculosis is not known, were inoculated with cultures derived from the tuberculous lung of a monkey which had been cultivated for 113 days outside the animal body. Four field mice, killed 53 days after the inoculation, had numerous tubercles in the spleen, liver and lung; a hamster, killed 53 days after inoculation, showed the same result. In these four experiments the inoculation of bacillary cultures on the abdomen of the experimental animals had, then, produced exactly the same kind of inoculation tuberculosis as if fresh tuberculous materials had been inoculated. In the next experiment the inoculum was introduced into the anterior chamber of rabbits' eyes, in order to find out whether, in the so modified inoculation method, the same effect would be obtained by the artificially cultivated tubercle virus as with the natural virus.

Fifth Experiment:

Three rabbits were inoculated with a small crumb of a culture (derived from a caseous pneumonia in a human lung and cultivated for 89 days) in the anterior ocular chamber. An intense iritis developed after a few days, and the cornea soon became clouded and discolored to a yellowish-gray. The animals rapidly became emaciated. They were killed after 25 days and their lungs were found studded with countless tubercles.

Sixth Experiment:

Of three rabbits, one received an injection of pure blood-serum into the anterior chamber of the eye, and the two others an injection of the same blood-serum; in which, however, a small crumb of a culture (originating from a lung with Perlsucht and cultivated 91 days) had been suspended. In the latter two rabbits, the same phenomena occurred as in the preceding experiment-rapidly progressing iritis and clouding of the cornea. After 28 days the animals were killed. The first rabbit, injected with pure blood serum, was completely healthy, while the lungs of the other two were studded with innumerable tubercles.

Seventh Experiment:

Of 4 rabbits, the first received pure blood serum in the anterior eye chamber; in the case of the second the needle, which contained blood-serum with a bacillary culture (from monkey tuberculosis, cultivated 132 days), was introduced into the anterior chamber of the eye, but the plunger was not moved, so that only a minimal amount of the fluid could get into the aqueous humor. The third and fourth rabbits were injected in the anterior chamber with several drops of the blood-serum with bacillary culture. Iritis and panophthalmitis developed in the latter two animals, and very rapid emaciation followed. In the case of the second rabbit, on the other hand, the eye remained at first unchanged, but in the course of the second week single whitish yellow nodules appeared on the iris near the site of the puncture, and there developed, growing out from this center, a typical tuberculosis of the iris. New nodules kept forming on the iris, which became wrinkled, while the cornea clouded slowly and the further changes were obscured to further observation. After 30 days these four animals were killed. The first was entirely healthy; in the second, besides the formerly noted changes in the eye, the lymph nodes near the mandible and beside the root of the ear were swollen and studded with yellowish-white foci. The lungs and the other organs were still free from tuberculosis. The two latter rabbits, again, had countless tubercles in the lungs.

Eighth Experiment:

Six rabbits were infected in the same manner as in the preceding experiment, using culture from a human lung with miliary tuberculosis, which had been cultivated 105 days. The second animal was infected only by a prick in the anterior chamber of the eye, without injection. All six developed tuberculosis of the iris, while some developed also a slowly spreading infiltration with tubercles on the conjunctiva near the site of inoculation. The results of these experiments with inoculation into the anterior eye chamber, when as small a number of tubercle bacilli as possible was introduced, corresponded entirely with those obtained by Cohnheim and Salomonsen, and Baumgarten. I did not content myself with this, but began further experiments, comprising injections of bacillary cultures into the abdominal cavity or directly into the blood stream, and attempted, finally, to make tuberculous, with the artificially grown virus, such animals whose infection with tuberculosis was not easily accomplished.

Ninth Experiment:

Of 12 guinea pigs, 10 were injected in the abdominal cavity with blood serum containing a bacillary culture, originating from monkey tuberculosis and cultivated 142 days. The eleventh animal was injected with pure blood serum in the abdominal cavity, while the twelfth, which had a fresh, considerable wound from a bite on the abdomen, was not injected. The animals injected died on the 10th, 13th, 16th, 17th and 18th days respectively. On the 25th day, the remainder, together with the control animals, were killed. Of those that died first, the omentum was markedly thickened and rolled together, and was infiltrated with a firm, yellowish mass. Under the microscope, this mass was seen to be composed of countless tubercle bacilli, almost all of which had very definite spores. Those that died later and also the killed animals of this group had already had, in addition to the infiltration of the omentum, eruptions of tubercles in the spleen and liver. The control animals were found entirely healthy.

Tenth Experiment:

A number of white rats were fed for two months almost entirely with the bodies of tuberculous animals. From time to time one was killed and examined. A few times a few single small gray nodules were found in the lungs of these animals, but the majority remained entirely healthy. Also, simple inoculation with tuberculous substances and with cultures from these substances had no effect on these animals, although such inoculations were repeatedly done. After the feeding with tuberculous masses had been stopped for several weeks, five of these rats received an intraperitoneal injection of bacillary culture (from monkey tuberculosis, cultivated 142 days). Five weeks later these animals were killed, and in the lungs, as well as in the much-enlarged spleen, countless tubercles were found. This experiment is not clear-cut, since the feeding with tuberculous masses had been done before, but I refer to it because it was successful in creating a typical tuberculosis through the injection of bacillary culture, in rats, which are as resistant to all infectious material as dogs.

Eleventh Experiment:

Of 12 rabbits, 2 received 0.5 cc. of pure blood serum in the ear-vein. Four rabbits received in the same manner blood serum with culture (originating from monkey tuberculosis and cultivated 178 days). Three rabbits were injected with culture from a phthisical human lung, cultivated 103 days, and the last three received blood serum with culture from a Perlsucht lung, cultivated 121 days. For each of these groups a separate syringe was used. The first two rabbits remained lively and strong, but all the rest grew thin rapidly and began to breathe with difficulty in the second week. The first animal died after 18 days (injection with culture from phthisical lung); the second and third (both had received culture from monkey tuberculosis) after 19 days; the fourth (injection with culture from Perlsucht) after 21 days; the fifth (infected with culture from phthisis) after 25 days; the sixth and seventh (infected with culture from monkey tuberculosis) after 26 and 27 days; and on the thirtieth and thirty-first days two more animals died. The last animal and the two controls were killed on the thirty-eighth day after the injection. No difference could be discerned in the lung and the rest of the organs of the animals infected with different cultures. Countless miliary tubercles were found in the lungs of all the animals. The livers and spleens of all these animals also contained remarkably numerous tubercles, but these were, in the case of those that died first, microscopical in size; in the case of those that died later, the tubercles had developed so far as to be visible macroscopically; and one rabbit showed many miliary tubercles visible to the naked eye also in the omentum, the diaphragm and the mesentery as well. The two control animals were found at autopsy to be without deposit of tubercles in any organ whatever.

Twelfth Experiment:

Two strong, full-grown cats received an injection in the abdominal cavity with blood serum, which had been triturated with a culture from monkey tuberculosis, cultivated for 162 days. One died in 19 days. The omentum was infiltrated with a firm whitish mass, and was more than a centimetre thick in places. The serous lining of the intestines and peritoneum had lost its lustre; the spleen was much enlarged. The infiltration of the omentum consisted (just as in the case of the guinea pigs that had received an injection with bacillary culture in the abdominal cavity) of densely packed tubercle bacilli, for the most part embedded in cells. There was as yet no macroscopically visible eruption of tubercles; but, microscopically, countless tubercles were visible in the lungs, liver and spleen. The second cat was killed after 43 days, and numerous tubercles, of the size of a millet-seed, were found in the lungs, spleen and omentum, with relatively few in the liver.

Thirteenth Experiment:

Two cubic centimeters of blood serum, mixed with culture from human miliary tuberculosis, which had been cultivated 94 days, was injected into the abdominal cavity of a bitch several years old. No change was visible in the animal during the first 2 weeks after the injection; then she lost spirits, ate less, and, from the end of the third week on, she showed a definite distention of the abdomen. At the beginning of the fifth week she was killed. A fairly massive, clear, pale exudate was found in the abdominal cavity. The omentum, mesentery and the round ligaments were studded with many tubercles, as were also the surfaces of the intestines and the bladder. The enlarged spleen, the liver and the lungs contained innumerable miliary tubercles. The site of injection was not recognizable, and there was no trace of caseous pus. It is scarcely necessary to mention that the syringes used in all these experiments were always safely disinfected before use, through heating for one hour at a temperature of 160° to 170°c. The tubercles obtained by inoculation or injection of bacillary cultures were examined microscopically many times, and found entirely identical with the ordinary tubercles formed in the same animal species spontaneously or after infection with tuberculous masses. They had absolutely the same arrangement of cellular elements, and frequently contained giant cells which, just as in the case of the spontaneous tubercles, enclosed bacilli. Furthermore, from these tubercles, which were derived by means of the bacillary culture, the bacilli were again isolated in pure culture, and with these, as well as with the tubercles, inoculation experiments were done, which had entirely the same result as infection with human tubercles or with Perlsucht. Therefore, in this regard also, the tubercles obtained through infection with cultures behaved like those occurring naturally.

Looking back on these experiments, it is seen that a not inconsiderable number of experimental animals that received the bacillary cultures in very different ways-namely, through simple inoculation in the subcutaneous tissues, through injection into the abdominal cavity or the anterior chamber of the eye, or directly into the blood-stream-became tuberculous without exception. Not only were single nodules formed, but the extraordinary number of tubercles was in proportion to the large number of bacilli introduced. It was successful with other animals, through infection in the anterior ocular chamber with as small a number of bacilli as possible, to give rise to the very same tuberculous iritis as in the well known experiments of Cohnheim and Salomonsen, and Baumgarten, which were so decisive on the question of inoculation tuberculosis and which were performed with true tuberculous material only.

A confusion with spontaneous tuberculosis, or a chance undesigned infection with tuberculous virus is impossible in these experiments for the following reasons: In the first place, neither a spontaneous tuberculosis nor a chance infection could cause such massive eruptions of tubercles in so short a time. In the second place, the control animals, which were treated in exactly the same way as the infected animals, with only the single difference that they received no bacillary culture, remained healthy. In the third place, in the case of numerous guinea pigs and rabbits, infected and injected with other substances in the same way, for other purposes of research, there never occurred this typical picture of miliary tuberculosis, which can only exist when the body is suddenly overwhelmed with a large number of bacilli. All these facts, taken together, justify the statement that the bacilli present in tuberculous substances are not only coincidental with the tuberculous process, but are the cause of the process, and that we have in the bacilli the real tuberculous virus. This establishes the possibility of defining the boundaries of the diseases to be understood as tuberculosis, which could not be done with certainty until now. A definite criterion for tuberculosis was lacking.

One author would reckon miliary tuberculosis, phthisis, scrofulosis, Perlsucht, etc., as tuberculosis; another would hold, perhaps with quite as much right, that all these morbid processes were different. In future it will not be difficult to decide what is tuberculous and what is not tuberculous. The decision will be established, not by the typical structure of the tubercle, nor its avascularity, nor the presence of giant cells, but by the demonstration of tubercle bacilli, whether in the tissues by staining-reactions or by culture on coagulated blood-serum. Taking this criterion as decisive, miliary tuberculosis, caseous pneumonia, caseous bronchitis, intestinal and lymph-node tuberculosis, Perlsucht in cattle, spontaneous and infectious tuberculosis in animals, must, according to my investigations, be declared identical.

My investigations of scrofulosis and fungoid joint affections are not numerous enough to make a decision possible. In any event, a large number of scrofulous lymph nodes and joint affections belong to true tuberculosis. Perhaps they belong entirely to tuberculosis. The demonstration of tubercle bacilli in the caseated lymph node of a hog, or in the tubercles of a hen, permits the inference that tuberculosis has a wider dissemination among domestic animals than is commonly supposed. It is very desirable to learn exactly the distribution of tuberculosis in this respect.

Since the parasitic nature of tuberculosis is proved, it is still necessary for the completion of its aetiology to answer the questions of where the parasites come from and how they enter the body. In regard to the first question it must be decided whether the infectious materials can propagate only under such conditions as prevail in the animal body or whether they may undergo a development independent of the animal organism, somewhere in free nature, such as, for example, is the case with anthrax bacilli. In several experiments it was found that the tubercle bacilli grow only at temperatures between 30° and 41°c. Below 30° and above 42° not the slightest growth occurred within three weeks, while anthrax bacilli, for example, grow vigorously at 20° and between 42° and 43°C.

The question mentioned can already be decided on the basis of this fact. In temperate climates there is no opportunity offered outside the animal body for an even temperature of above 30°c. of at least two weeks' duration. It may be concluded that, in their development, tubercle bacilli are dependent exclusively upon the animal organism; that they are true and not occasional parasites; and that they can be derived only from the animal organism. Also the second question, as to how the parasites enter the body, can be answered. The great majority of all cases of tuberculosis begin in the respiratory tract, and the infectious material leaves its mark first in the lungs or in the bronchial lymph nodes. It is therefore very likely that tubercle bacilli are usually inspired with the air, attached to dust particles. There can hardly be any doubt about the manner by which they get into the air, considering in what excessive numbers tubercle bacilli present in cavity-contents are expectorated by consumptives and scattered everywhere. In order to gain an opinion about the occurrence of tubercle bacilli in phthisis sputum I have examined repeatedly the sputum of a large series of consumptives and have found that in some of them no bacilli are present, and that, however, in approximately one-half of the cases, extraordinarily numerous bacilli are present, some of them sporogenic. Incidentally, it may be remarked that, in a number of specimens of sputum of persons not diseased with phthisis, tubercle bacilli were never found.

Animals inoculated with fresh bacilliferous sputum become tuberculous as certainly as following inoculations with miliary tubercles. Also, such infectious sputa did not lose their virulence after drying. Four guinea pigs were inoculated with two-weeks-old dried sputum, and 4 guinea pigs with sputum kept in the same way for 8 weeks; they all became tuberculous in the same manner as following infection with fresh material. It can therefore be assumed that phthisical sputum dried on the floor, clothes, etc., retains for a considerable time its virulence, and that, if it enters the lung in a pulverized state, it can produce tuberculosis there. Presumably the durability of its virulence is dependent upon the spore-formation of the tubercle bacilli, and it must be considered in this regard that the spore-formation, as we have seen in several examples, occurs already in the animal organism, and not, as in anthrax bacilli, outside of it.

It would lead too far into the realm of hypothesis to attempt to discuss here the conditions of acquired and inherited disposition, which undoubtedly playa significant role in the aetiology of tuberculosis. In this connection thorough studies are still required before a judgment is warranted. I wish to draw attention only to one point, which may serve as explanation for many puzzling phenomena: that is, the exceedingly slow growth of the tubercle bacilli. This is most probably the reason why the bacilli cannot infect the body through every little wound in such a way as do the unusually fast-growing anthrax bacilli. If one wishes to render an animal tuberculous with certainty, the infectious material must be brought into the subcutaneous tissue, into the peritoneal cavity, into the ocular chamber; in brief, into a place where the bacilli have the opportunity to propagate in a protected position and where they can focalize. Infections from superficial skin wounds not penetrating into the subcutaneous tissue, or from the cornea, are only exceptionally successful.

The bacilli are eliminated again before they are able to implant themselves. This explains why autopsies on tuberculous bodies do not cause infection, even when small cuts on the hand come in contact with tuberculous masses. Small superficial cuts are not suitable inoculation wounds for the invasion of bacilli. Similar conditions prevail probably for the implantation of bacilli which have reached the lungs. It is probable that certain peculiar factors favoring the implantation of bacilli, such as stasis of secretions, desquamation of epithelium, etc., must aid to make infection possible. It would be hardly understandable otherwise that tuberculosis is not much more frequent than it really is, since practically everybody, particularly in densely populated places, comes more or less in contact with tuberculosis. If we ask further what significance belongs to the results gained in this study of tuberculosis it must be considered a gain for science that it has been possible for the first time to establish the complete proof of the parasitic nature of a human infectious disease, and this of the most important one. So far such proof was established only for anthrax, while in a number of other infectious diseases in human beings, for example, relapsing fever, wound infections, leprosy, gonorrhea, it was only known that parasites occur simultaneously with the pathological process, but the causal connection between the two has not been established.

It may be expected that the elucidation of the aetiology of tuberculosis will provide new viewpoints for the study of other infectious diseases, and that the research methods which have stood the test in the investigation of the aetiology of tuberculosis will be of advantage for the work in other infectious diseases. Quite particularly may this hold true for studies of those diseases, which, like syphilis and glanders, are most closely related to tuberculosis, and form with it the group of infectious tumors.

How far pathology and surgery can utilize the knowledge about the properties of the tuberculosis parasite it is not my duty to define. It remains to be seen whether, for example, the demonstration of tubercle bacilli in the sputum can be used for diagnostic purposes, or whether the certain diagnosis of many localized tuberculous affections will be of influence in their surgical treatment, and whether therapy may profit from further experiences about the living conditions of the tubercle bacilli.

My studies have been done in the interest of public health, and I hope that this will derive the largest profit from them. Tuberculosis has so far been habitually considered to be a manifestation of social misery, and it has been hoped that an improvement in the latter would reduce the disease. Measures specifically directed against tuberculosis are not known to preventive medicine. But in future the fight against this terrible plague of mankind will deal no longer with an undetermined something, but with a tangible parasite, whose living conditions are for the most part known and can be investigated further. The fact that this parasite finds the conditions for its existence only in the animal body and not, as with anthrax bacilli, also outside of it under usual, natural conditions, warrants a particularly favorable outlook for success in the fight against tuberculosis.

First of all, the sources from which the infectious material flows must be closed as far as this is humanly possible. One of these sources, and certainly the most essential one, is the sputum of consumptives, whose disposal and change into a harmless condition has thus far not been accomplished. It cannot be connected with great difficulties to render such phthisical sputum harmless by suitable procedures of disinfection, and to eliminate thereby the largest part of the infective tuberculous material. Besides this, the disinfection of clothes, beds, etc., which have been used by tuberculous patients, must certainly be considered. Another source of infection with tuberculosis is undoubtedly tuberculosis of domestic animals, in the first rank, Perlsucht. Herewith, too, is indicated the position which public health has to assume in future on the question of the danger of meat and milk from animals with Perlsucht.

Perlsucht is identical with tuberculosis in man, and is therefore a disease transmissible to man. It must therefore be treated exactly the same way as other diseases transmissible from animals to man. Be the danger of meat and milk from animals with Perlsucht ever so great or ever so little, it is present, and it must therefore be avoided. It is sufficiently known that anthrax-infected meat has been eaten by many persons, and often for a long time, and without any ill effects, and still no one will conclude therefrom that the trade in such meat should be permitted. In regard to milk from cows with Perlsucht it is noteworthy that the extension of the tuberculous process to the mammary gland has been observed not rarely by veterinarians, and it is therefore quite possible that in such cases the tuberculous virus may be mixed directly with the milk.

Still further viewpoints might be mentioned in regard to measures which could serve to limit the disease on the basis of our present knowledge of the aetiology of tuberculosis but the discussion here would lead too far. When the conviction that tuberculosis is an exquisite infectious disease has become firmly established among physicians, the question of an adequate campaign against tuberculosis will certainly come under discussion and it will develop by itself.