

A paper on Koch's researches on tuberculosis, and abstract of a lecture on some of the more recent facts and observations concerning the bacillus of tubercle / by George A. Heron.

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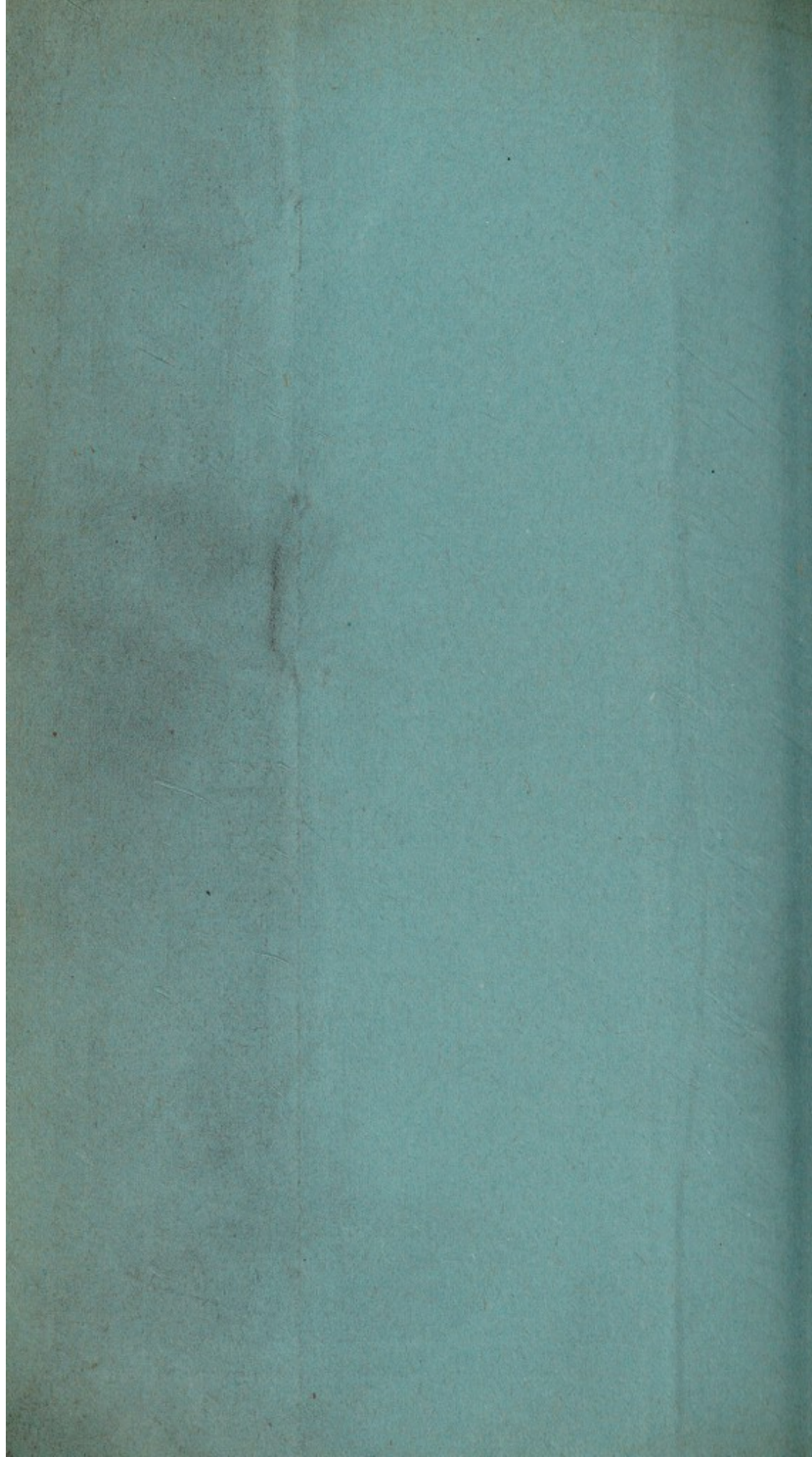
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With the author's comments.

A PAPER
ON
KOCH'S
Researches on Tuberculosis,
AND
ABSTRACT OF A LECTURE
ON SOME OF THE
MORE RECENT FACTS AND OBSERVATIONS
CONCERNING THE
Bacillus of Tubercle.

BY
G. A. HERON, M.D.

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1883.



KOCH'S RESEARCHES ON TUBERCULOSIS.

Read before the Glasgow Medico-Chirurgical Society, on December, 1st, 1882.

Deposited with the President of the Society, November 3rd, 1882.

[*Reprinted from the "Glasgow Medical Journal" for February, 1883.*]

ON the 24th of March, 1882, in a paper read before the Physiological Society of Berlin, Dr. Robert Koch claimed to have established, by experiment and by observation, the existence of a micro-organism which is associated with tubercle, and not only associated with tubercle, but, according to Koch, the cause of all tubercle. This organism is a bacterium of the kind known as a bacillus, and it is, consequently, rod-shaped. In length it varies from about $\frac{1}{3000}$ to $\frac{1}{12000}$ in., and its breadth is about $\frac{1}{3}$ th of its length. In looking at a specimen of these bacilli, it will be seen that certain of them contain spores, two to four, ranged along the length of the organism.

In attempting to give an outline of some of the points on which Koch lays especial emphasis in the lecture referred to above, it is obvious that attention must be given solely to what is there stated. Since that date no observations have been published tending to disprove Dr. Koch's work. On the other hand, the bacillus described by him has been found by several observers in the tissues and in the sputa of persons whose conditions of disease would have suggested to any clinician, of ordinary experience, the probability of the presence of tubercle in the patient. It must, then, be admitted, that we have now to deal with a new fact which characterises, by the presence of these organisms, certain cases of disease of well known type, about the exact clinical significance of which there is, even now, no inconsiderable difference of opinion. For those who find themselves justified in accepting Koch's results as true, all difficulties about the nature of these cases must cease, as soon as it is found that the patients concerned harbour in their tissues, or in their secretions or excretions, this bacillus of tubercle.

The bacillus is demonstrated in tissues by employing the process first described by Professor Ehrlich. Koch has

adopted this process in preference to the one devised by himself, and with the aid of which he worked out all his early experiments. Ehrlich's process will be found fully described in the *British Medical Journal* of 14th October last, and Professor Vignal makes some useful remarks upon the process in the same *Journal* on 28th October. It is, for these reasons, unnecessary here to touch upon the method of investigation required for the detection of the bacillus. There is, however, one error in my remarks as they appear in the *Journal* of 14th October. I ought to have said, that the bacillus of leprosy gives precisely similar results with those shown by the bacillus of tubercle when these two organisms are submitted to the process of staining devised by Ehrlich. There are, however, some differences in form, as Dr. Koch points out, between the two bacilli. The bacillus of leprosy is "more slender and more pointed at the ends" than that of tubercle. They are also distinguished from one another by the colour test of Weigert, to which the bacilli of leprosy respond; those of tubercle, on the contrary, are unaffected by it.

Dr. Koch thus describes the appearance of the bacillus in tuberculous tissues:—In all cases where the tuberculous process is in its early stage and progressing rapidly, the bacilli are to be seen in great numbers. They then lie thickly, and often in groups or small bundles inside the cells, and in some places give the same appearances as the bacilli of leprosy when they are found in cells. Near these (groups or bundles) are found numerous free bacilli. Especially on the borders of large cheesy deposits crowds of bacilli appear, which are not shut up in cells."

"As soon as the highest point of the tubercle eruption is overstepped the bacilli become rarer, or are only to be found in little groups or singly at the edges of the tuberculous deposits, and lying near them are bacilli so faintly coloured as scarcely to be recognisable; these are presumably already dead or in the act of dying. Finally, they can quite disappear, although they are rarely altogether absent, and then only in such places as those in which the tuberculous process has come to a standstill."

In his lecture, Dr. Koch lays emphasis upon the connection which appears to exist between the presence of the bacillus and of the giant cell. "If," he says, "in the tuberculous texture giant cells appear, then the bacilli lie by preference in these structures. In cases of very slowly progressing tuberculous processes, the inside of those giant

cells is generally the only place where the bacilli are to be found."

Dr. Koch has a theory about the connection between the giant cell and the bacillus, and it is this:—"It is to be concluded from the size and position of the giant cells containing bacilli, that these cells are the youngest, while, on the other hand, those cells which are free from bacilli are the oldest, and it is to be assumed that these last originally contained bacilli, and that the organisms have either died or have gone over to that condition which will presently be described. From the observations of Weiss, Friedländer, and Laulamié, according to whom giant cells were formed around foreign bodies, such as vegetable fibres and the eggs of strongylus, we may be able by analogy to realise the relation of the giant cells to the bacilli. We may infer that here also the bacilli, as foreign bodies, are enclosed by the giant cells, and on this account, if the giant cells are found empty, all further relations of the tuberculous process go to shew that the presumption is correct, that the giant cells had formerly harboured one or more bacilli, the organisms having occasioned the origin of the cells." So much for the appearances described by Koch as illustrating the presence of the bacillus of tubercle in tissue, and its peculiarities there. It makes no difference whether the bacillus is seen in a human being or in a monkey, a guinea pig, a mouse, or a hen, the organism is always the same in every detail.

And now as to the facts upon which Koch, on 24th March last, founded his claim for the recognition of this organism as associated with tubercle. He found the bacillus present in the following cases:—

1st. In the human subject—

11 cases of miliary tubercle.

12 cases of cheesy bronchitis and pneumonia. (In six of these cavities had formed.)

1 case of tumour of brain of the size of a hazel nut.

2 cases of freshly extirpated scrofulous glands.

2 cases of synovial degeneration of joints.

Twenty-eight cases in all.

2nd. Amongst the lower animals—

10 cases of perlsucht of the ordinary type.

1 case of caseous cervical gland in a pig.

1 case of a hen which died of tubercle.

3 cases of spontaneous tubercle in apes.

9 cases of spontaneous tubercle in guinea pigs.

7 cases of spontaneous tubercle in rabbits.

Thirty-one cases in all.

"Besides these cases of spontaneous tubercle, I examined," says Koch, "172 guinea pigs, 32 rabbits, and 5 cats, all of them infected with tubercle by the inoculation of the most varied tubercular substances, such as gray and calcified tubercle of human lung, phthisical sputum, tuberculous masses from spontaneously diseased monkeys, rabbits, and guinea pigs, pieces of lung from cattle suffering from perlsucht, cheesy as well as calcified, and, lastly, by inoculation from tubercular affections produced in animals by inoculation." In each of these cases, 268 in all, bacilli were not once wanting, and in many instances they were extraordinarily numerous. So much, then, in proof of the statement that this particular bacillus is found associated with tubercle.

And now comes the second point. It remains still to indicate the line of evidence advanced by Koch in proof of the belief, that this bacillus, and nothing but this bacillus, is the cause of tubercle. To prove this, he carried out a series of experiments in which he took tuberculous particles from animals which had either died of tubercle, or, having tubercle, had been killed for experimental purposes. These particles were about the size of millet seeds, and were removed from the dead body and placed upon the blood serum, prepared in a certain way, of the ox and of the sheep, with scrupulous attention to all those precautions which are familiar, at least in theory, to every one who is acquainted with what are known as "cultivation experiments." The object of these elaborate experiments was to obtain the bacillus of tubercle free from all taint. Dr. Koch believes that he succeeded in attaining this end. After describing how he sowed the tubercular morsels upon the prepared blood serum and watched their slow growth, and noted certain of its peculiarities, he makes a statement which deserves special attention. He says, "The extremely slow growth, which alone is to be obtained at breeding temperature, and the peculiar shovel-shaped, dry, and firm condition of these colonies of bacilli, are not to be found in connection with any other known bacterium, so that, the confounding of the culture of the tubercle bacillus with that of any other bacterium is impossible; and already, with only short experience, nothing is easier than to recognise at once accidental contamination of the culture." This is a very important statement, and it is all the more important when it is made by Koch, one of our best experimenters and observers, and one whose words carry with them that

authority which can be given only to a profound and extensive knowledge, such as his, of the life history of bacteria.

After describing the appearances of the growth of the bacillus under cultivation, he says, "By the help of a low power (30 to 40 diam.) the colonies of bacilli" (undergoing cultivation) "are already visible towards the end of the first week. They appear as very elegant spindle-shaped and S-shaped structures, and also in other similar crooked figures, which, if they are spread out on a cover glass, coloured" (*i.e.*, submitted to Ehrlich's colour test), "and examined with a high power, consist solely of the familiar extremely delicate bacilli." Had any other known organism been present it is hardly within the bounds of possibility that Koch could have failed to observe it, for upon the accuracy of this observation hinges much of the worth of his researches into the nature of tubercle.

These cultivation experiments were carried on for some time. After from ten to fourteen days' cultivation in one test tube containing the prepared blood serum, some of the crop of the bacilli which had grown there was transplanted to another test tube, and after another ten days or so, some of this second crop was sown in a third test tube, and so on, until, in one mentioned instance, the cultivation extended to 178 days.

On such observations and experiments as these rests, in part, the proof that the bacillus of tubercle was obtained free from taint.

Dr. Koch next proceeded to inoculate certain animals with the pure bacillus, obtained by cultivation. The inoculation was always performed with every care against the possibility of contamination. In each series of experiments several animals were used, including rats, mice, guinea pigs, rabbits, a marmot, pigeons, frogs, &c. Some of these animals are, it is well known, difficult to infect with tubercle—a fact which is not without some significance in this connection.

Koch thus sums up the results of these inoculations:—If one looks back upon these experiments, one sees that a not inconsiderable number of animals were experimented upon, on which bacillus culture was brought to bear in very different ways—viz., through simple inoculation into the subcutaneous cellular tissue, through injection into the abdomen or into the anterior chamber of the eye, or direct into the blood stream, without failing, even in one single instance, to develop tubercle; and there had formed in them not solitary nodules, but an extraordinary mass of

tubercle corresponding with the large number of infecting germs introduced." In each of these series of experiments—there were thirteen in all—a certain number of animals were not submitted to the inoculation of the cultivated bacilli. These animals had been bought at the same time, and fed and lodged in the same way and in the same places with those animals which were inoculated with the bacilli, but not one of the former showed any evidence of tubercle, either during life or after they had been killed and examined, *post-mortem*. It must be remembered that these cultivation experiments were made with tubercle taken from the lungs, calcified mesenteric glands, and freshly extirpated scrofulous glands of human subjects, as well as from the lower animals, and that there was no difference whatever in the effects produced by inoculating from these two distinct sources; and the bacilli from these two sources were also identical in appearance.

Dr. Koch makes some very interesting observations about certain distinctions which he draws between tubercle occurring spontaneously in an animal and that type of tubercle which results from inoculation. He bought and examined one hundred guinea pigs, all of which were quite healthy. Several of them were shut up in a room with other guinea pigs which had been inoculated with the tubercle virus. In three or four months, but never before the lapse of that time, spontaneous tubercle began to show itself, and always sporadically, amongst the uninoculated guinea pigs. In them the bronchial glands were "always found unusually large and purulent, particularly, also, in the lung was to be found a large cheesy mass, with very far advanced breaking down in the centre, so that, sometimes, as in human beings, it had reached to actual cavity. The development of tubercle in the organs of the lower part of the body was very far behind that in the lung. The swelling of the bronchial glands, and the commencement of the development of tubercle in the organs of breathing leave it beyond a doubt, that the tubercle of these animals was an inhalation tubercle springing from a few or possibly only one infectious germ, and on that account very slow in its progress."

Contrast that description with what Koch says about inoculated tubercle, and the contrast will be found to be very suggestive. "The place of inoculation was in the belly of the animal, near the inguinal glands." The first sign of the success of the inoculation was the appearance, at the

end of a week, of a nodule over the site of the puncture. About the end of the second week, the inguinal glands beside the wound began to swell, and sometimes also the axillary glands. From that time the animals grew quickly thinner and died in from four to six weeks, with marked tubercular affection of the liver and spleen, those organs having been but slightly affected, as compared with the lungs, in the cases of spontaneous tubercle.

Several animals were inoculated with certain substances which did not contain the bacillus of tubercle; for example, morsels of a scrofulous gland, of degenerated synovial membrane from a joint, of a portion of monkey's lung kept dry for two months, of another portion of the same lung which had been kept in alcohol for one month, and in not one instance did the animals experimented upon with these substances shew any sign of tubercle either during life or *post-mortem*.

Several experiments with sputum from tuberculous individuals are mentioned in Koch's lecture. The sputum was allowed to dry, as it may sometimes be seen drying on a hospital floor, not always in an out of the way corner. Tubercular sputum, dried in this way, was found to be as surely fatal in its results, when an animal was inoculated with it, as had been the case when the cultivated bacillus was used. The specimens of sputa with which these experiments were made, were from two to eight weeks old.

A highly suggestive series of experiments were performed, with the view of ascertaining the effects of varying quantities of bacilli upon animals, into which the organisms were introduced by injection. The anterior chamber of the eye was selected as the site of the experiments. In one case the pure prepared blood serum, used in the cultivation of the bacilli, was injected. It was, however, in this instance, unmixed with the bacillus or any other organism. It was injected; and the animal was killed and examined thirty days after the operation. All its organs were found healthy. No bacilli of tubercle were seen although they were carefully sought for. In another case the injection was made with blood serum mixed with bacilli, which had been cultivated during 132 days. The needle of the syringe was pushed into the anterior chamber of the eye, but the piston of the instrument was not moved. In this way only an extremely small number of the bacilli could have entered the eye. In a fortnight from the day of the puncture, solitary nodules, of a light golden tint, appeared upon the iris near

the site of puncture. From that time tubercular iritis was developed, and the cornea became cloudy. In thirty days the animal was killed, and, besides the changes in the eye, the glands near the jaw and at the root of the ear were swollen and contained yellowish-white deposits. In two other cases the injection was made with blood serum charged with cultivated bacilli; but many drops were introduced into the anterior chamber of the eye. These two animals also developed the local symptoms indicated in the last case, and they rapidly became thin. In thirty days they were killed, and, in addition to the local changes, their lungs contained "innumerable tubercles." The lungs of the animal subjected to the inoculation of a minute portion of the blood serum free from bacilli were free from all sign of tubercle, and so were its other organs.

Experiments exactly similar to the foregoing were repeated again and again, and invariably with like results.

Koch thus begins to sum up and give what he regards as the outcome of his work. He says—"All these facts taken together justify the conclusion that the bacilli present in tubercular substances are not merely the associates of the tubercular process, but the cause of it, and that we have before us, in bacilli, the actual tubercle virus. It is also possible, by this means, to draw the boundary of those diseases regarded as tubercular, which, hitherto, could not be done with certainty. A decided test for tubercle is wanting, and one man considers miliary tubercle, phthisis, scrofula, perlsucht, &c., to be tubercle; another man holds, perhaps with equal right, that all these processes of disease are different. In the future, it will not be difficult to decide what is tuberculous and what is not tuberculous. Not the peculiar structure of tubercle, not its non-vascularity, not the presence of giant cells will decide the question, but the presence of tubercle bacilli—be it in the tissues by the colour test, or be it through culture on prepared blood serum. This criterion, taken as a guide, must, according to my researches, stamp miliary tubercle, cheesy pneumonia, cheesy bronchitis, tubercle of glands and of the intestine, perlsucht in cattle, inoculated and spontaneous tubercle as identical."

Many points of great interest have not been touched upon in this attempt to summarise Dr. Koch's work on tubercle, which received from him, in his lecture, considerable attention. It is hoped, however, that enough has been said to indicate the lines on which this admirable piece of

work has been founded and built. In thinking over it, many questions will suggest themselves to the mind, and answers will be sought for them. If these answers rest upon facts, then only good can follow when medical men come to consider the questions and their answers. If, however, mere personal opinion, founded upon merely personal bias, takes the place of facts, then we shall have discussions which will settle nothing and end nowhere. One question can hardly fail to be amongst the first to suggest itself—How does all this work of Koch's fit in with the hereditary nature of tubercular phthisis? If there has been any fact established in medicine by the evidence of patients, and the practically unanimous opinion of physicians of all countries, it is certain that the hereditary tendency of tubercle has been so established. Of late, however, in Germany, in France, and in America, as well as in our own country, some men have expressed doubts as to the soundness of the evidence upon which rests the all but universal belief in the heredity of tubercle. Of course, this is a perfectly legitimate position, and besides that, it has been taken by men, some of whom are entitled, from their clinical experience, to speak with authority upon the subject. Others have gone still further, and have denied the truth of the hereditary tendency of tubercular phthisis altogether. Koch does not fail to touch upon this point in his lecture. He takes up no definite position in connection with it, but simply indicates the opinion that we must have still further inquiry into this question. I think that, with his views, such an opinion is what might be expected from the man who has done such work as his.

We cannot yet tell what light will be thrown upon disease by Koch's great discovery. I call it a discovery, because whatever may be our attitude with regard to the bacillus of tubercle, it is true that Koch has shown us, in the presence of the bacillus in a certain type of disease, something which we did not know before.

It is only seven months since this discovery was given to the medical world. No doubt, many men have been engaged, since last March, in studying the clinical bearing of the tubercle bacillus. To speak about establishing clinical facts concerning a subject such as this in seven months, would surely be to misuse words. I have, however, had the advantage not only of observing my own cases, but also of receiving from Dr. Bristowe a short statement of some of his observations in his wards in St. Thomas's Hospital,

in this city. In a letter which I received from Dr. Bristowe, dated 22nd October last, and from which he kindly allows me to quote, he says, after detailing some cases under his care in which the bacillus had been found, "My experience, as you see, is limited; but so far as it goes it confirms the belief that a special form of bacillus exists in tubercle, and may be found in the sputa of phthisical patients. It tends, also to show that the examination of the sputa for bacilli is an important method of determining, in doubtful cases, whether we have tubercular or some other disease to deal with. My own experience does not tell me whether the bacilli are chiefly abundant in the sputa, in cases in which the lungs are breaking down. But I may observe that all the phthisis cases examined by me were well marked cases, and probably all had excavations."

At my request Dr. Lawrence Humphry, formerly Resident Medical Officer at the City of London Hospital for Diseases of the Chest, now resident at Cambridge, made a short statement of the results of his observations in connection with the tubercle bacillus in the hospital. It is as follows:—

"I.—*Cases of advanced phthisis with high temperature, &c.*—The sputum, in all cases examined, was highly charged with bacilli.

"*Post-mortem Examination.*—The fluid from the cavities in the lungs, the scrapings of the caseous nodules from different parts of the lung, the caseous parts of the bronchial glands, and in one case the mesenteric glands, contained them in large numbers. I did not find them in the tubercular ulcers of the intestines.

"II.—*Cases of acute secondary tuberculosis.*—In these the sputum contained a larger quantity of bacilli than in any other cases, as did also the fluids from different parts of the lungs. Two or three of them were remarkable for their acute progress and rapid termination.

"III.—*Cases of incipient phthisis.*—In most bacilli were found in small numbers, one or two in a field. In some no bacilli were found after repeated examinations.

"IV.—*Bronchitis, subacute, chronic, and asthmatic.*—No bacilli in the sputum.

"V.—*Chronic fibroid.*—In cases complicated with caseous pneumonia or secondary infective processes, the sputum contained bacilli; also the fluid of the lung cavities."

That is what Dr. Humphrey has to say on this subject. I know that he has taken great care to make his obser-

vations exact, and I am under a debt of gratitude to him for his kindness in supplying me with material for my own work, even, as sometimes happened, at considerable inconvenience to himself.

In the beginning of October I wrote to my friend Dr. Koch, laying before him some of the impressions made upon me by what I had myself seen in practice since last June, when I began to follow this line of observation. I wished to know what he thought about certain points which seemed to me to be worthy of attention. Dr. Koch is not himself in practice, and, therefore, will give no opinion as to clinical matters. He told me, however, in reply to my letter, that the tendency amongst those hospital physicians with whom he had conversed on this subject, was in the direction of the belief that, in the future, the detection of the presence of bacilli will be of more importance than physical diagnosis, because it is a sure sign of the presence of tubercular phthisis.

As regards my own observations:—I have notes of 54 cases, and I hope, by and bye, to publish details of these and of other cases still to be observed. For the present, however, I think that my experience is far too limited for me to speak about it at any length. I will, however, venture to indicate what seems to me to be the tendency of the short clinical experience I have had. I think that we have now a method of investigating lung disease which, standing alone and unsupported by any other method of examination, throws a special light upon a patient's condition. This much I can already say, speaking from my own experience, that bacilli of tubercle are not always present in the sputa of patients whose physical condition would lead anyone who knows something of Dr. Koch's work to expect to find them there. It is also a matter within my own experience, and it has happened to me more than once, to search the sputa for bacilli of tubercle and to fail to find them early in the history of a case of consumption. In the same case, within one or two months (for, as I have said, there were more than one such case) I have found bacilli in the sputum, and in one instance in enormous numbers.

My experience also inclines me to expect to find it established very shortly, that in the prognosis of phthisis we must look to this method of investigating the sputum for valuable information. I think it will be established that, given persistence of a large number of bacilli of tubercle in the sputum early in the history of a case, and that case will

run a short course and end in death. On the other hand, I think it will also be established that, given few bacilli of tubercle in the sputum of a consumptive, and given also, that that condition of fewness of bacilli in the sputum characterises the case for some weeks, then that case will probably run a long course.*

ABSTRACT OF A LECTURE ON SOME OF THE MORE RECENT FACTS AND OBSERVA- TIONS CONCERNING THE BACILLUS OF TUBERCLE.

Delivered at the City of London Hospital for Diseases of the Chest,
March 20th, 1883.

[Reprinted from the "*British Medical Journal*" for April 28th, 1883.]

GENTLEMEN,—As you know, I have undertaken to address you to-day in response to a request made to me by some of your number. I have been asked to speak to you about a part of the work that has been published concerning the bacillus of tubercle. To give you anything like a full review of this subject in one lecture, would be a task which I do not think anyone at all conversant with its literature would attempt. For that reason I asked that I might be told upon what points you wished me to touch, and, in reply to that request, I have received an answer which shews me the line you wish me to follow.

You are, of course, all aware, that the bacillus of tubercle was discovered by Dr. Robert Koch of Berlin. He made his discovery known to the medical world in a lecture, given in Berlin, on March 24th, 1882. As a first step in what I

* Since this paper left my hands, views similar to those indicated in the text have been published by Drs. Balmer and Fraentzel in the *Berliner Klin. Wochenschr.*, No. 45, 1882, so that their observations and mine appear, in some degree to confirm each other. They speak, however, from a more extensive experience than I then had, and their observations go farther than mine.—G. A. HERON.

have to say to you to-day, I shall endeavour to indicate in as few words as I can, an outline of portions of Koch's work. I must confine my remarks to what seem to me to be some of the more important points, which his researches and observations have brought so prominently before students of medicine of all conditions. My object in doing this, is to endeavour to bring clearly before your minds the source whence Koch obtained the bacillus of tubercle. It was whilst searching tuberculous tissues with the view of ascertaining, if possible, what that condition meant, that Koch discovered that a certain rod-shaped bacterium was present, sometimes in enormous numbers, but, also, sometimes in very small numbers, in all tuberculosis tissues. This rod-shaped bacterium, the bacillus of tubercle as it is called, is now familiar to you all. Koch discovered this organism by submitting those diseased tissues to the action of a certain staining fluid, devised by himself. Here I come to a part of the subject on which you have asked me to speak at some length, for you want to hear about the staining of the bacillus. I need not say more about Koch's own method, for he gave it up when Professor Ehrlich told him of another method, which he had discovered, and Koch at once adopted it and has used it ever since. There is, so far as I know, no other method but Ehrlich's now in use for staining the bacillus of tubercle. Various modifications of his process have been suggested; but, in all points of importance, it remains as it was given to us by Ehrlich himself. The modifications which are improvements of this process, aim at giving the staining mixture a uniform composition; and several different formulæ have been suggested for that purpose. The one now in use in this hospital, and I have myself used it for some months past, is Weigert's. Its composition is, saturated alcoholic solution of fuchsin, or methylated violet, or gentian violet, 11 parts; anilin water, 100 parts. (The preparation of the anilin water, and the use of the staining fluids, were described by Dr. Heron in detail).

In warm weather good results are to be obtained when the staining process is carried out at summer temperature, and without the use of artificial heat. I should advise you, however, always to stain your specimens while they are exposed, in an incubator of some kind, to a temperature of 98° to 100° Fahr. Want of attention on my part to this important point caused me much inconvenience when the cold weather set in last autumn.

The process I have just described to you occupies some time. It has, however, certain advantages. Not only does it ensure thoroughly good staining of the bacilli, but the specimens, while being stained, may be safely left from half an hour to ten hours, or even longer, in the fuchsin and anilin mixture, just as the experimenter finds most convenient. There is, however, a more rapid way of staining. The same staining fluids are used. A little of the fuschin dye is filtered into a watch glass; the specimen to be stained is placed in the fluid, and heat is applied. I have been accustomed to apply the heat by lighting a Bunsen burner, not at the top of the funnel, but at the burner itself. The heat, of course, passes up the Bunsen funnel, and so reaches the watch glass, placed at a convenient height upon a tripod. I find that one minute's exposure to the action of the staining fluid, under these conditions is sufficient to ensure excellent colouring of bacilli in sputum or in pus. The rest of the process is identical with what I have already described to you. Following this plan, it is easy to stain and examine with the microscope, a specimen of sputum within ten minutes' time. Most of the specimens of the tubercle-bacillus in sputum and in pus which you see here to-day, have been prepared in this rapid way. In speaking of these staining fluids I have called the red dye fuchsin. That is the name in use on the Continent for the colouring matter which in England we call magenta.

You must not, however, overrate the importance of this colour test. It is not on such a comparatively trivial observation as that that Koch has founded his claim for the special recognition of this organism. Were it shown to-morrow that half a dozen other bacilli, alike in appearance with the tubercle-bacillus, behave in presence of dyes as it does, Koch's reasoning and conclusions concerning this organism would in no way be effected. They are founded upon his cultivation experiments and their outcome, and not upon a mere colour test.

Now, let us turn again to Koch's early researches. Having examined the organs of many animals, including men, known to have died of tubercle, or which, having tubercle, had been killed for experimental purposes, and having found that the bacterium which we now call the bacillus of tubercle was invariably present in greater or less numbers, Koch came to the conclusion that this organism is the constant associate of the tuberculous process. He next set before himself the task of endeavouring to ascertain the

exact relationship of the bacillus to the tuberculous process. With that object in view, he began a series of cultivation experiments. He sowed some tuberculous tissue in a little of the blood-serum, prepared in a certain way, of the ox and of the sheep. The tuberculous morsels thus sown were removed, with every possible precaution against contamination, from the bodies of animals, man included, dead of tubercle. It would be easy to occupy an hour of your time in trying to put before you an outline of Koch's experiments and their results. I can only now state to you, that Koch believes that he has proved that this bacillus of tubercle is not only the associate of tubercle, but that it is the actual virus of tubercle. The last of these two conclusions is, of course, of vast importance when we find it accompanied by the evidence which Koch advances in its support. That evidence is the outcome of the cultivation experiments to which I have just referred. By their means, Koch was able to grow the bacillus of tubercle on the blood-serum of oxen and sheep; and he satisfied himself, by most careful observation, that no known organism was present besides this bacillus. Koch next proceeded to experiment upon animals with this pure bacillus. Every care was taken to insure the introduction of the bacillus of tubercle, and of that organism alone, into the bodies of the animals used. In every instance—and some hundreds of animals were thus experimented upon—tubercular disease followed the injection of the bacillus of tubercle into the animal's body; and, in every case, the bacillus was found in the tuberculous organs of these animals when they were examined after death. The organism injected into these animals, and the organism found in their bodies after death, were identical in appearance; and the bacilli remained the same in appearance, and they retained, apparently, the same virulence, no matter how often they were made to pass from one animal to another.

Gentlemen, that is a very meagre outline of a part of Koch's work. I hope, however, that I have said enough to show you that his work was done with the most laborious care, and that it cannot be set aside by anything short of experimental demonstration of error in its details. Only three days ago, the medical weekly papers contained an abstract of an elaborate series of experiments by Mr. Watson Cheyne, which he has carried out upon the lines laid down by Koch. These experiments and observations confirm Koch's work on tubercle, and even carry the subject beyond the point at which he left it.

Few subjects have raised more discussion amongst medical men than that one which is introduced by the question, "What is tubercle?" Of the many answers which this question has received, probably none has attracted more widespread attention than that given to it by Dr. Koch's researches. Those of us who accept his teaching as true, must look upon every case in which the bacillus of tubercle is found, as tuberculous. During the last twelve months, there has been gradually accumulating a mass of evidence in favour of the view that this bacillus is the constant associate of tubercle. This evidence comes from observers in the Old World and in the New. It comes from men who work in the dead-rooms of hospitals, as well as from those whose observations are made at the bedsides of the sick; and this evidence is already so strong, that it seems to me we are justified in stating it to be a fact, that wherever tubercle is, there the bacillus of tubercle is also. Whether this organism is the cause of tubercle is another question; and it is not to be expected that men who have spent long years in the study of tubercle, and who have their own views about tubercle, will readily accept Koch's teaching as all true—unless, indeed, their own observations have already prepared them for the acceptance of such views. Of one thing we may feel sure, that the subject will not rest where it is, and that every week will add more and more to the weight of the evidence which must, probably very soon, definitively settle the important question—Has Koch discovered the cause of tubercle? Should that question be answered in the affirmative, then every case in which the bacillus of tubercle is found, must be classed under the head of parasitic diseases; and all discussion as to whether miliary tubercle, chronic phthisis, scrofula, perlsucht, &c., are tubercle, or whether each of them is a distinct disease, must end with the establishment of the fact that they are all due to the parasite which Koch has discovered.

And now, gentlemen, let us turn to another part of the subject. Not only is the bacillus of tubercle found in the dead body, but it is also easily obtainable from certain cases of disease in the living man. It has been found in the breath and in the sputa of persons suffering from tubercular disease implicating the lungs; it has been found in the urine in cases of tubercular disease of the kidney; it has been found in the fæces in cases of tubercular ulceration of the intestines, in that connection enabling a diagnosis to be made between tubercular and amyloid disease, in one

published case where, excepting the diarrhoea, the symptoms were not well marked. Lichtheim has recorded the case of a patient who presented the symptoms of acute pneumonia, and in whose sputa the tubercle-bacillus was found. This organism has also been observed in cases of lupus, in freshly-opened scrofulous glands, in synovial degeneration of joints, in the meninges of the brain, in an ulcer of the tongue, and in a previously unopened suppurating knee-joint. These examples suffice for our present purpose; and it is obvious of what vast importance it must be to ascertain the presence or absence of the bacillus of tubercle in such cases. But you have asked me to refer to those cases of lung disease in which we may expect to find the bacillus present in the sputum. The evidence in favour of the belief that this organism is to be found in the sputum of, practically, every case of consumption is now so strong, that I feel warranted in speaking of it as a fact. I have myself found the bacillus in the sputa of one hundred and sixteen patients, all of whom presented, sooner or later, what I regarded as unmistakeable signs of consumption. In the majority of these cases, there could have been no reasonable doubt as to the diagnosis of the disease, for the physical signs of pulmonary phthisis were in them very plainly marked. Now and then, however, I chanced upon a case in which the physical signs were so slight, that I was unable to form a decided opinion about the patient's condition and prospects, until an examination of his sputum showed me that it contained the bacillus of tubercle. With that knowledge in my possession, I cannot now doubt about a patient's condition, for I can but regard the case as one of tubercular disease of the lungs. In certain of these cases, too, an examination of the chest yielded no positive information beyond the fact that the patient was apparently suffering from a pretty sharp attack of bronchitis. The patient's history, and some dulness, more or less marked, over the apex or apices of the lungs, usually suggested to me the probability of the presence of pulmonary phthisis in the majority of such cases; but it happened more than once, that an examination of the sputum and the discovery there of the bacillus of tubercle formed the point in the case which fixed for me its diagnosis.

You all know how difficult it often is to distinguish, with certainty, some cases of bronchiectasis from certain cases of phthisis with lung excavation. An examination of the sputum, by Ehrlich's process, will surely fix the identity

of such cases; and the same remark applies to some cases of empyema. "Is this patient tuberculous?" is a question often asked in such cases, and it used to be by no means always an easy question to answer.

This method of diagnosis is often, as I have already told you, of great use in cases where the physical signs are very indefinite. Litchtheim, Heller, and others, have recorded instances in which, though they could detect no physical signs indicative of disease of the lungs, the bacillus of tubercle was found in the sputum. If the time at our disposal permitted of it, I should like to dwell at some little length upon such cases as these, for they suggest many questions of interest. We must, however, pass on; and I will only now say, upon this part of the subject, that I have not yet seen a case with absolutely no physical signs of lung mischief, in which I have detected the bacillus of tubercle in the sputum. Sputum has been sent to me for examination, taken, I was told, from a patient who, at that time, showed no symptoms of lung-disease, and in it there were tubercle-bacilli. Later on, signs of lung-phthisis became well-marked in the man's chest, and, *post mortem*, extensive tubercular disease was found to have existed. This patient was under the care of two able physicians, who, I hear, intend to publish the case.

Some of you, I think, were present at a lecture I gave, at the London Hospital, last October, at Dr. Andrew Clark's request. You may remember that I then said, that it seemed to me to be probable, that the presence of the bacillus of tubercle in the sputum would be found useful in prognosis as well as in diagnosis. I was speaking then from my observation of fifty-four cases, in whose sputa I had found the organism; and I said that my experience led me to incline to the belief, that the persistence of a large number of these bacteria in the sputa of a patient indicates a case which will run a rapid course; and that a persistence of few bacilli in the sputa would probably come to be regarded as indicative of a very chronic case. In the end of November, Drs. Balmer and Fräntzel published similar views concerning the prognostic value of the bacillus. They had then found the organism in the sputa of one hundred and twenty patients, so that they spoke from a much larger experience than mine. Crämer, and several others, have recorded like conclusions. On the other hand, Lichtheim of Berne, a very careful observer, though he does not distinctly differ from these views about the prognostic

value of the bacillus in cases of phthisis, is doubtful of their correctness. In certain instances of rapidly fatal phthisis, you will find that the sputum is apt to contain little clumps or groups of the bacilli, surrounded by large numbers of these organisms. When this grouping of the bacilli into little masses persistently characterises the specimens of any sputa which you examine, you will, I believe, find that you have to deal with a case which will run a remarkably rapid course, from the time of the appearance of this persistent grouping of the bacilli. My attention was first called to this grouping of the organism by several cases which came under my notice in this hospital, in the summer of last year. Since last November, I have seen only two cases where this peculiarity was persistently present in the sputum. Also, no other observer, so far as I know, has mentioned this point; so that it is, probably, not a common occurrence. All the cases, however, in which I have seen it, have run a very rapid course to death.

And now, let us give a very short time to summarising the results of observations bearing upon the habitat of the bacillus of tubercle in the lungs of the human subject. In cases of phthisis, it is found in the lining of the walls of lung-cavities, and in and around caseous masses scattered here and there throughout the lung, usually with some evident relation to centres of active disease, but sometimes, apparently, more or less isolated. The organism is not found to infest the lung-tissue itself in great numbers, and you may examine section after section of lung without finding a single bacillus. As a rule, all these centres of bacillus-life communicate with the air tubes; but to that rule there seem to be marked exceptions. That bacillus life may flourish when entirely cut off from all communication with the external air, is a fact which is demonstrated by some of the cases alluded to at the beginning of this lecture.

I cannot do better than give you, in brief, what Mr. Watson Cheyne has said about the appearances in the lung which go along with, and result from phthisis. We have here, under the microscope, a few specimens illustrating some of his results in this line of research. Those specimens have been prepared by Mr. Watson Cheyne, and he has most kindly lent them to me for your inspection (A short *résumé* of Mr. Watson Cheyne's recent work and views in relation to phthisis was then given.)

And now, gentlemen, I must bring these remarks to a close. No one can be more conscious than I am how im-

possible it is to give, within an hour's time, more than a mere summary of even those points which have occupied our attention to-day. We must leave almost untouched the burning question, for it has now assumed that shape—"Is phthisis an infectious disease?" The consequences involved in an answer to that question are so grave, that every piece of evidence tending to settle it, one way or the other, must be looked at with the closest scrutiny. There are not wanting records of observations tending to answer the question in the affirmative, and, certainly, there is no lack of evidence which is regarded by many as proving that phthisis is not infectious. It seems to be established as true, that this disease does not readily pass from man to man, under the ordinary conditions of life. All our clinical experience goes to prove the truth of that belief. But it does not follow from this that there are not men who possess, in some peculiarity of their physical life, a factor which, under certain conditions, may favour in them the development of phthisis. If that be true, it would follow that at least two factors are necessary to the production of phthisis; one peculiar to the individual man, and, therefore, always present with him in possibly a varying degree of intensity, the other, coming from without, and probably present only under certain conditions. According to the view which now seems to be gaining most adherents, the former of these two factors would be what constitutes the hereditary tendency to phthisis. What physical condition these words imply, is to-day an unsolved problem. Of the second factor, that one which comes from without the body, we are surely amply justified in asking: Is it not this bacillus of tubercle which Koch has discovered? Whatever may be our answer to that question, if it be admitted that two such factors exist and are necessary to the development of phthisis, then it seems to me, that we cannot shut out the conclusion, that for a large proportion of mankind, phthisis is an infectious disease.

