Indian J Med Res 157, February and March 2023, pp 169-173
DOI: 10.4103/0971-5916.373948

PROFESSOR KOCH'S REMEDY FOR TUBERCULOSIS.

A FURTHER COMMUNICATION ON A REMEDY FOR TUBERCULOSIS:

By Professor Dr. ROBERT KOCH,
Berlin.

[*The German Text from which this is translated is published in the Deutsche Medicinische Wochenschrift, January 15th, 1891.*]

[*Continued from page 1195, volume II, 1890.*]

Results of Recent Therapeutic Experience.

Since the publication of my experiences with a new remedy for tuberculosis two months ago, many doctors have been put in possession of the remedy, and have thus been enabled to make themselves acquainted with its qualities by their own experiments. As far as I can judge by the publications that have appeared on the subject, and the letters addressed to me, my statements have, on the whole, found full confirmation. That the remedy exercises a specific action on tuberculous tissue, and can in consequence be employed as a very delicate and certain reagent in searching out hidden, and diagnosing doubtful, tuberculous processes, is agreed on all sides. And in regard also to the therapeutic effect of the remedy, most accounts agree that, in spite of the relatively short duration of the treatment, many patients show improvement, varying only in degree. In not a few cases I am informed that cure even has been attained. Only in some exceptional cases has it been affirmed that the remedy may not only be dangerous in too far advanced cases—which is freely admitted—but that it directly hastens the tuberculous process, that it is in fact harmful *per se*. I myself have had the opportunity during a month and a half of collecting further experiences regarding the therapeutic effect and the diagnostic value of the remedy in about 150 cases of various forms of tuberculosis, and I can only say that all I have lately seen is in harmony with my former observations, and that I have nothing to retract of what I have before stated.[1] So long as the only point of importance was to judge of the correctness of my statements it was not essential to know what the remedy contains, and what its origin is. On the contrary, it was clear that subsequent experiments would be all the more unprejudiced the less was known of the remedy itself, but now that such experiments in sufficient number have been made and have proved the importance of the remedy, the remaining task is to study the remedy beyond the application it has hitherto found, and if possible to apply the principles which lie at the foundation of its discovery to other diseases. This task, of course, demands a full knowledge of the remedy.

The Steps by which the Discovery was made.

I therefore think the right moment has come to make the necessary statements which follow, before I discuss the remedy itself. I think it imperative for the better understanding of its action to trace shortly the steps that led me to its discovery. If a healthy guinea-pig be inoculated with a pure cultivation of tubercle bacilli, the inoculation wound generally becomes sealed, and seems to heal up during the next few days. It is only in the course of from ten to fourteen days that a hard nodule is formed, which soon opens, forming an ulcerating spot which persists until the death of the animal; but the case is very different if an already tuberculous animal be inoculated. The most suitable animals for this experiment are those that have already been successfully inoculated four to six weeks previously. In the case of such an animal also the small inoculation wound becomes sealed at first, but no nodule is formed, a peculiar change taking place at the point of inoculation. Already, on the first or second day, the spot becomes hard and dark-coloured; and this is not confined to the point of inoculation, but spreads around to a diameter of 0.5 to 1 centimètre. During the next few days it becomes more and more clear that the epidermis thus changed is necrotic. Finally it is thrown off, and a flat ulcerated surface remains, which generally heals quickly and completely, without carrying infection to the neighbouring lymphatic glands. Thus the inoculated tubercle bacilli act quite differently on the skin of a healthy guinea-pig and on that of a tuberculous one. But this remarkable action does not belong exclusively to living tubercle bacilli, but also in the same degree to dead ones, whether killed by low temperatures of long duration, which I at first tried, or by boiling heat, or by certain chemicals.

This peculiar fact having been ascertained, I followed it up in all directions, and it was then further found that pure cultivations of tubercle bacilli thus killed, after they have been ground down and suspended in water, can be injected under the skin of healthy guinea-pigs in large quantities without producing anything but local suppuration.[2] Tuberculous guinea-pigs, on the other hand, can be killed by an injection of very small quantities of such suspended cultures, the time being from six to forty-eight hours, according to the dose; a dose which is just insufficient to kill the animal is sufficient to produce a widespread necrosis of the skin in the region of the point of inoculation. If the suspended matter be still more diluted, so that it is scarcely turbid to the eye, the animals remain alive; and if the injections be continued at intervals of one or two days, a noticeable improvement in their condition soon sets in; the ulcer at the point of inoculation becomes smaller, and finally cicatrises. This is never the case without such

[1] As regards the duration of cure, I should like to state here that of the cases which I had provisionally marked cured two have been again received into the Moabit Hospital for further observation, and that for three months no bacilli have been present in their sputum; the physical signs, too, have gradually quite disappeared.

[2] Injections of this nature are among the simplest and most certain methods of producing suppuration free from living bacteria.

treatment. The swollen lymphatic glands become smaller, the condition as regards nutrition improves, and the progress of the disease is arrested, if it is not already so far advanced that the animal dies of debility.

Difficulties in the Way of the Therapeutic Application.

These facts formed the foundation of a therapeutic method against tuberculosis. But an obstacle to the practical employment of such suspensions of killed tubercle bacilli was found in the phenomenon that the tubercle bacilli are by no means reabsorbed, nor do they disappear in any way, but for a long time remain unchanged in their position, producing smaller or larger suppurating centres. Thus it was clear that in this method the curative effect on the tuberculous process is obtained by a soluble substance, diffused, so to speak, into the fluids that surround the tubercle bacilli, and transferred without delay to the circulating fluids of the body, whereas that which has the pus-forming quality seems to remain behind in the tubercle bacilli, or at any rate to be only very slowly dissolved. Thus the only important thing to be done was to carry out the process, which takes place within the body—*outside* of it also—and if possible to extract and isolate the curative substance from the tubercle bacilli. This problem required much work and time before at last I succeeded, by the help of a 40 to 50 per cent. solution of glycerine, in extracting the active principle from the tubercle bacilli. My further experiments on animals, and finally on human beings, were made with liquid thus obtained; and in this way also the liquid which I let other physicians have in order to repeat the experiments was obtained. *The remedy with which the new therapeutic treatment of tuberculosis is carried out is, therefore, a glycerine extract of pure cultivations of tubercle bacilli.*

The Composition of the Remedy.

Besides the active principle there pass from the tubercle bacilli into the simple extract all other substances soluble in 50 per cent. glycerine, and therefore there is found in it a certain quantity of mineral salts, pigment, and other unknown extractive substances. Some of these substances can be removed from it without difficulty, for the active principle is insoluble in absolute alcohol, and can be precipitated by it—not pure, it is true, but in combination with other extractive substances likewise insoluble in alcohol. The colouring matter, too, can be separated out, so that it is possible to obtain a colourless dry substance from the extract which contains the active principle in a much more concentrated form than the original glycerine solution. But this purifying of the glycerine extract has no advantages as regards practical application, as the substances thus removed have no action on the human organism, and the process of purifying would, therefore, only cause unnecessary expense. The constitution of the active principle can as yet be only a matter of conjecture. It seems to me to be a derivative of albuminous bodies, and to be in close relation to them, but it does not belong to the group of so-called toxalbumins, as it can withstand high temperatures, and in the dialysator passes quickly and easily through the membrane. The quantity of active principle present in the extract is, in all probability, very small; I estimate it at fractions of 1 per cent. Thus, if my assumption be correct, we have to deal with a substance the action of which on the tuberculous organism far surpasses that of the strongest drugs known.

Probable Mode of Action of the Remedy.

Various hypotheses may, of course, be formed as regards the specific mode of action of the remedy on tuberculous tissue. Without in any way affirming that my view is the best possible explanation, I imagine the process to be as follows:—The tubercle bacilli in their growth produce in the living tissues—just as in the artificial cultivations—certain substances which have various but always deleterious influences on the living elements of their surroundings—the cells. Amongst these substances is one which, in a certain concentration, destroys living protoplasm and causes it to undergo a transformation into the condition called "coagulation-necrosis," by Weigert. The tissue having become necrotic, this condition is so unfavourable to the nutrition of the bacillus, that it is unable to develop further, and finally in some cases it dies off. In this way I explain the remarkable phenomenon that in organs freshly attacked by tuberculous disease—for instance, in a guinea-pig's spleen or liver filled with grey nodules—numerous bacilli are found, whilst bacilli are rare or entirely absent when the enormously enlarged spleen consists almost entirely of whitish substance in a condition of coagulation-necrosis, such as is often found in guinea-pigs which die of tuberculosis. A solitary bacillus, however, cannot produce necrosis at a great distance, for as soon as the necrosis has reached a certain extent the growth of the bacillus, and, in consequence, the production of the necrosis-producing substance, diminishes, and thus a sort of mutual compensation sets in, and to this it is due that the growth of isolated bacilli is so remarkably restricted, as, for example, in lupus, in scrofulous glands, etc. In such cases the necrosis only extends over a part of the cell, which then, in its further growth, assumes the peculiar form of a giant cell; I thus follow in this statement of my views the explanation of the growth of giant cells first given by Weigert. Now, if the necrosis-producing substance were artificially added to that contained in the tissue surrounding the bacillus, then the necrosis would extend further, and thus the conditions of nutrition of the bacillus would be much more unfavourable than is usually the case. Then, not only would the more completely necrosed tissues disintegrate, slough, and—where this is possible—take with them the enclosed bacilli, carrying them outward; but the baccilli would also be disturbed in their growth to such an extent that they

would die off much sooner than is the case under ordinary conditions. It is in calling forth such changes that, to my mind, the action of the remedy seems to consist. It contains a certain amount of the necrosis-producing substance, of which a correspondingly large dose has a deleterious influence—even in healthy persons—on certain elements of the tissues, probably on the white blood corpuscles or cells closely related to them, thus giving rise to the fever and the whole peculiar complex symptoms. In tuberculous persons a much smaller quantity suffices to cause, at certain spots—that is, wherever tubercle bacilli vegetate and have already impregnated their surroundings with the necrosis-producing substance—a more or less extended necrosis of cells with the accompanying symptoms affecting the entire organism. In this way it is possible to explain—at least for the present—in a provisional way the specific influence which the remedy in certain well recognised doses exercises on tuberculous tissue, as well as the possibility of increasing the doses in so remarkable a fashion, and, finally, to explain the curative effect which the remedy undoubtedly possesses where the circumstances are at all favourable.

REMARKS
ON
THE EFFECT OF KOCH'S REMEDY ON THE INTERNAL ORGANS OF TUBERCULOUS PATIENTS.

Delivered in the Discussion on Professor B. Fraenkel's Paper at the Berlin Medical Society, on January 7th, 1891.

By Professor RUDOLF VIRCHOW,
Berlin.

[Translated from the *Berliner klinische Wochenschrift*, January 12th, 1891.]

With reference to a rather large number of preparations which I have brought here, I beg to be allowed to make a few introductory remarks. In the first place, I wish to say that I do not, as will readily be understood, propose to speak here of my own casual observations on patients, but only of what we have been able to establish by way of anatomo-pathological research. From the beginning of the injection period up to the end of the year that has just passed away the total number of deaths of patients treated by injections of Koch's fluid that have come before us has been 21. Besides these we have already had in the course of the present year, I believe, 6 or 7 other cases; even this very day we have had an opportunity of submitting some new specimens to examination.[1]

It is obvious that this anatomo-pathological material must differ considerably from the clinical, in which processes visible to the eye stand in the foreground of observation and of interest, while we are, of course, much more concerned with the internal parts, most of which are inaccessible from the outside, and the diseases of which can in many cases be only very superficially discovered, even by the most accurate examination. Perhaps, however, you will be interested in having the opportunity, even once, of seeing such results, and comparing them with those obtained by the direct examination of parts within reach.

Of the 21 cases which we had up to the end of December, 16 were phthisical in the narrow sense in which the word is usually employed as denoting disease in which the essential element is that the lungs are affected. As regards the other 5 cases, there were among them an exquisite case of severe bone and joint tuberculosis; a case presenting the peculiar complication of carcinoma of the pancreas, with some small smooth-walled cavities with surrounding induration in the apices; a case of empyema in a lying-in woman, who would probably have died even without the injection; a case of pernicious anæmia with very slight old-standing changes in the lungs and tuberculous pleurisy; lastly, a case of tuberculous arachnitis. The other 16 cases were, as I have already said, cases of pulmonary phthisis, in all of which ulcerative processes of greater or less extent were present; most of them were examples of true consumption.

I cannot now enter into the details of these cases; perhaps I may have an opportunity of doing so at some future time. I may, however, be allowed to make some general remarks on them to the following effect: Just as the activity of Koch's remedy, as seen externally, manifests itself principally in the setting up of very acute irritation in the affected parts, with intense redness and great swelling, so does it also in the internal organs. We have seen very marked instances of this. I have here a preparation which may well be taken as a typical specimen. It comes from the clinic of my colleague, Professor Henoch, and belongs to the case of tuberculous arachnitis already referred to. I may observe that there were also changes in the lungs, consisting in some rather old-standing patches of caseous pneumonia, which might be looked upon as the source of metastatic arachnitis, and a number of recent inflammatory changes. After four injections, in all amounting to 2 milligrammes, the last of which was given sixteen hours before death, the patient (a boy, aged 2¾ years) died, and colossal hyperæmia of the pia mater as well as of the brain substance, the like of which I never remember to have seen before, was found. The preparation before you was at first preserved simply in glycerine: it has kept fairly well also in the dry state. It shows on the surface extreme engorgement of the vessels of the pia mater, whilst internally the brain substance is dusky red in appearance. I take this opportunity of mentioning that in this case—the only one, it may be added, of tuberculous arachnitis which has yet come before us for examination—I personally examined the tubercles; I cannot, however, say that I saw any evidence in them of retrogressive changes. The tubercles were very well formed, and presented the usual appearances of meningeal tubercles.

Similar acute hyperæmias and swellings are also seen in other internal parts. In particular it was repeatedly noted by us that even the surface of old pulmonary cavities showed unusually intense redness of the granulation layers; moreover, hæmorrhagic infiltrations of the walls were not seldom present, and even recent hæmorrhages were observed in the cavities. Thus in a man, aged 30, with an old rectal fistula and numerous tuberculous ulcers of the colon, death was the result of hæmoptysis from an old ulcerated cavity; he had received seven injections, the last thirteen days before his death, on which occasion the first bleeding occurred.

The processes observed, however, are not merely transient congestive swellings as to which it may be assumed that they will, perhaps, disappear in a very short time, but there can be no doubt that in the internal parts actual inflammatory processes, and especially active proliferations, occur to an intense degree. This holds good chiefly with regard to two places in which such appearances are very conspicuous; these are, first, the edges of existing ulcers; and next, the neighbouring lymphatic glands, especially the bronchial and mesenteric. The lymphatic glands present a quite unusual degree of enlargement, and notably that form of medullary swelling characteristic of acute irritations, which is caused by rapid proliferation of the cells in the interior of the glands. It is in harmony with these large acute swellings that frequently also an increase in the colourless elements of the blood can be detected—a condition of leucocytosis to which may, perhaps, be attributable the relative frequency with which various infiltrations of white blood corpuscles in the neighbourhood of the affected parts, especially around the tubercles themselves, can be observed.

These swellings occasionally assume a very dangerous character. I will only refer to the phenomena which are seen in the larynx, where, even in cases in which the ulcerated surfaces themselves become clean, the adjoining parts swell to

[1] In addition to this, my assistants have made necropsies in a large number of similar cases in other hospitals and in private, and I have seen the most important results of these examinations.

an enormous extent, and cause constrictions of a very critical nature. Together with these changes, there occasionally occur other more violent forms, which take on a phlegmonous character, and remind one of œdema glottidis erysipelatodes and retropharyngeal abscess. Here is a fresh specimen of the condition from a case which occurred in January, and which will be particularly interesting to you.

As regards these inflammations, you will understand that it would be difficult to say of every inflammation occurring in such a patient whether or not it had been caused by the injection. We have at present no criterion of an objective kind which could enable us to make such a distinction. I am not in a position, although I have seen rather a large number of such cases, to say precisely how such a kind of inflammation is to be recognised and distinguished from other inflammations which occur in the course of phthisis independently of these injections. Yet there is one thing which is somewhat remarkable; and I will for the present, on account of the lateness of the hour, confine myself to an accurate statement of what we found in the lungs.

It was noticed that among the fatal cases of ulcerative phthisis the large majority exhibited recent changes of great extent, more particularly in the lungs, but also pleurisy—and for the most part very severe pleurisy—simple and tuberculous, frequently hæmorrhagic and not infrequently bilateral.

The changes in the lungs themselves may be divided into two fairly distinct categories. One of these corresponds approximately to that condition which we are accustomed to call caseous pneumonia, or, anatomically, by the name of caseous hepatisation. With respect to this, it should be understood that it is very doubtful whether caseous hepatisation stands in any direct relation to the injection. I should perhaps, for my own part, be inclined to deny any such connection were it not that some of these cases are of quite special significance. From the most characteristic one of these comes this piece of lung, which shows such extensive caseous hepatisation that I do not remember to have seen anything like it for years. The lower lobes of both lungs, especially the right, were as large as in ordinary hepatisation, but the individual foci were packed so close together that there was hardly any normal lung tissue between them. The lung, when fresh, looked like a piece of blood pudding thickly studded with pieces of lard. The parts not occupied by caseous hepatisation had a blackish-red appearance, and contrasted sharply with the caseous portions. This patient (an architect, aged 33) had received six injections, the last one four weeks before his death; the treatment was then discontinued, according to the statement of the doctor, because there was persistent fever, and infiltration of the lower lobe came on. In this case, therefore, the infiltration first began after the injections, whereas previously there had only been induration at one apex; and, as to this, it was afterwards proved that for the most part it presented an older and more indurative character.

Here the acute occurrence of the change after the injections is established beyond doubt. But in other cases also the whole condition of the lungs was in no slight degree different from what we are accustomed to see in cases of consumption. I may also point out that among the 16 cases of phthisis which we had in December there were 5 which showed recent caseous hepatisation in greater or less degree, but none approaching in extent the one just mentioned.

A second change is likewise found in the lungs, which must also be described as inflammatory. It is, in my opinion at least, even more different from what we usually find, although I must here also say that I cannot lay down any universally valid pathognomonic criterion. The pneumonias which develop in the course of phthisis can, as is known, be divided into three different classes. They are either caseous or of the ordinary fibrinous type—these also occur—or catarrhal, the so-called smooth pneumonias in which the essential feature is that accumulations of cells are present in the alveoli. All this is occasionally seen in phthisical patients. I may also remark that pure fibrinous pneumonia, in the ordinary sense of the word, has been present in none of the injected cases.[2] The caseous form I have already mentioned. Any other variety will approximate in type to one of the forms which, according to the ordinary ritual, are classified under the head of catarrhal pneumonia. Injection pneumonia has, in fact, points of similarity to the catarrhal variety, but I must say it has also certain differences. The ordinary catarrhal pneumonia, as we find it in phthisical patients, shows accumulations in the alveoli, which can easily be squeezed out, and are relatively fluid in character. Sometimes they are so thin as to resemble jelly, and it was on the observation of this fact that Laennec based his old doctrine that tuberculous infiltration, as he expressed it, begins with a gelatinous infiltration. Here, however, the product is not gelatinous; on the contrary, it is very watery and turbid, and it might be called a turbid infiltration. It reminds one of a phlegmonous condition. In some places it is somewhat thicker; occasionally it has, to a certain extent, the external aspect of caseous infiltration, without, however, attaining the decidedly dry character of the latter, so that if the two are situated side by side there is no difficulty in distinguishing the one from the other. The catarrhal-phlegmonous product is softer, moister, and looser than the other. Among the specimens here exhibited there is a perfectly fresh one, which, besides a colossal ulcerated cavity at the apex, shows caseous, and—if I may use the expression—catarrhal infiltration side by side in the lower lobe. In two other specimens also caseous and catarrhal hepatisation may be seen side by side. Among the 16 cases of last year, there are 7 which show this more diffuse soft hepatisation.

This form has also something whereby it is clearly distinguished from the ordinary catarrhal hepatisation. It happens that in the midst of these patches foci of softening become developed, which quickly lead to breaking down of the parenchyma and to a kind of excavation—for instance, in the lower lobe—such as hardly occur except in gangrenous bronchopneumonia. This, indeed, was not very frequent. Such a result appears to me to indicate that in these cases a more potent injurious influence has been at work than that which we in other cases recognise as the cause of catarrhal pneumonia. In fact, I am under the impression that—I will not say all these cases—but a certain number of them, exhibit inflammatory processes analogous to those which we see develop on the external parts after injection, and which present a higher or lower degree of intensity, according to the nature of the individual and the special features of the case.

As regards the other results of our examinations, one thing was noted, the signifiance of which will have to be tested by careful clinical observations on the course of a number of cases: that is the development of fresh tubercles in these patients. It must be understood that I speak on this point with great reserve, as we possess no certain basis of fact which would enable us to pronounce with any certainty as to the duration of small tubercles—I speak here of the submiliary forms—and the age of the submiliary tubercles. On the whole, however, we are disposed to look upon such tubercles as fresh formations. A few observations on the eruption of such tubercles subsequent to injection have already been made clinically in the case of the laryngeal mucous membrane. With reference to this, I may point out that under the eyes of the observer small tubercles, speedily giving rise to new ulcers, have suddenly appeared in places which till then seemed perfectly free. People have comforted themselves with the assumption—at least, so I gather from published records—that these tubercles were present before the injection, but had escaped detection; and it is taken for granted that they will be attacked and destroyed by the remedy and transformed into ulcers. As to the correctness of this opinion in the cases cited I can, of course, say nothing; but I can say that we, examining the internal organs after injection—and especially those which I have always considered the most reliable for the observation of these fresh forms, namely, the serous membranes—have seen the eruption of entirely new submiliary tubercles under circumstances which made it scarcely probable that the tubercles were of older date. This holds good particularly of the pleura, the pericardium, and the peritoneum. The supposition that the tubercles would be powerfully influenced by the action of the remedy, and that their substance would thereby become necrosed, was never realised. All the submiliary tubercles, of which I am here speaking, were perfectly intact, even when

[2] Only partial fibrinous hepatisation was sometimes found in conjunction with other changes.

the injections had been made weeks before. All the more am I convinced that the eruption first appeared *ex post*.

As to the lungs themselves, you know well how difficult it is to recognise these very fine tubercles in their interior with certainty. I will therefore not speak of that, and will confine my remarks to parts in which either (as in the mucous membrane of the larynx) miliary tubercles first appeared after the injection, or after a long course of injection entirely fresh and uninjured tubercles have been found on the serous membranes. Here is an intestine from one of the January cases, in which entirely fresh submiliary eruptions are seen in the vicinity of old intestinal ulcers; the same man (aged 41) had also fresh tubercles in his pericardium.

How these new eruptions are to be explained must be left for further consideration. Nevertheless, I venture to point out that if we assume that all tubercles are produced by bacilli, such out of the way parts as the pericardium deserve special attention. In one other case the so-called epicardium presented in one place not in contact with an affected part of the lung, a small focus where four submiliary tubercles were situated close to each other in the middle of an area of intense hyperæmia. Here there was no alternative but to suppose that the germs had reached that place by way of metastasis. How could we help thinking of metastatic processes here, and conjecturing whether, in fact, the bacilli had not been mobilised, and whether they had not been diffused through the body by a process of infection? Since, as you know, Dr. Koch himself considers the bacilli to be sufficiently refractory to the action of his remedy—and we have not found that they are destroyed—the possibility must not be overlooked that if in any one place a process of softening whereby the products of disintegration are rendered more fluid, or at least more mobile, is set up by the action of the remedy, these products will also be displaced, and may give rise to new foci in other places. Such a consideration is not far-fetched; and with it is connected another. If we see that during the treatment a whole lower lobe becomes filled with foci of caseous hepatisation, it is an easy step to the conclusion that material which is set free in the upper lobe by breaking up, and which is not coughed up, will perhaps be drawn in by inspiration, with the result that pneumonia such as is caused by foreign bodies—and in this case of caseous character—is set up.

I consider myself bound at least to give expression to this view, and to add a warning to practitioners to operate with greater caution in cases where it is not certain that patients have the strength completely to expectorate the broken down tissue, and the habit of doing so, and where there is, therefore, a possibility that transference of material to other parts of the lung may take place with the result of creating new foci of disease.

Permit me now to mention a little point: that is, the breaking down itself, to which my colleague Dr. Koch attaches particular importance as being the principal result effected by his remedy. I admit that all which we have seen indicates that such an effect is produced in many places. It is not yet clear to me, however, how it is that this necrotic effect does not occur universally—that, for instance, as I have already said, the submiliary tubercles resist the remedy in many places. I acknowledge that, as has been stated by some earlier observers, for instance, in tuberculous pleurisy, individual tubercles, especially if they are at all of large size, assume an unusual turbid yellowish appearance, and, in fact, can be seen with the microscope to undergo a process of disintegration. But in other cases, even after injections continued up to the day of the patient's death, nothing of the kind occurred.

Even large tubercles show themselves very refractory. We have lately had a very remarkable case, in which tuberculosis of the vertebral column and long bones was present in a boy aged 3 years; large tubercles were also found in the brain. The injections in all amounted to 0.012 g. It was a case from the surgical department in which there was vertebral caries with gravitation abscesses, and many points of disease were present in the joints and long bones of the lower limb. At the necropsy it was found that the boy had an unusual abundance of the so-called solitary tubercles in his brain and cerebellum. As is well known, these tubercles owe their name to the fact that there is usually only one which may be of the size of a walnut; in this case, however, there was a whole heap, I think seven; they were therefore properly not solitary, but they belonged to that category. They were like large lumps of cheesy matter. Neither in them nor in their vicinity were any considerable changes to be seen. I noticed in their interior some soft places, but these occasionally occur in other cases without anything particular having taken place. At all events, the nodules showed no marked breaking down.

In conclusion, I wish to call attention to two points of prime importance which are rightly taken into account in every case of phthisis, namely, ulcers of the intestine, and ulcers in the respiratory organs, particularly the lungs.

As regards the intestine, there can be no doubt that necrotic processes similar to those observed on the external parts of the body in lupus, etc., take place in intestinal ulcers. In old-standing ulcers with extensive surface and thick edges, particularly in which new submiliary eruptions have occurred, we see such necrosis to an excessive degree. An example of this is afforded by the intestine here shown which comes from one of the January cases, namely, the man with the fresh pericardial tubercles. The necrotic process there reaches right through to the serous coat. If the man had lived a couple of days longer perforation would undoubtedly have taken place, as in another case recently mentioned, I believe, by Dr. B. Fraenkel, in which the patient died in consequence of such a perforation. Although perforation and necrosis occur also in other cases of tuberculous ulcer of the intestine, I feel myself obliged to point out that here we have two very severe cases, in which the necrotic process must have taken place very rapidly, occurring in the short space of two months.

The same holds good with regard to ulcers in the respiratory organs in which very rapid disintegration takes place, and the size of the loosened masses is sometimes altogether out of proportion to the ability of the individual to expel them from his body. In this way all kinds of complications from retention and aspiration will be caused.

Among the other specimens I may mention one case of tuberculosis of the larynx of altogether unusual severity, in which twenty injections were given, the last on the day before the patient's death. This was the same man who has already been mentioned as the subject of pericardial tubercles and gangrenous ulcers of the intestine. As regards the point under consideration, a fresh eruption of tubercles of extreme intensity can be seen extending over the whole of the larynx and trachea.

Another specimen shows fresh caseous hepatisation; it comes from a case in which six injections were made—the last four days before the patient's death. We have also one such case in which three injections were given, the last a week and a half before the patient's death, and in which caseous foci and diffuse inflammatory processes are found side by side. Lastly, I exhibit a specimen which was obtained only this morning; it shows the formation of abscesses, starting from bronchiectases of the lower lobe, in progress in the lungs.

HOSPITAL FOR DISEASES OF THE CHEST, VICTORIA PARK.

Since our last report (in the British Medical Journal, December 20th, 1890) there have been marked changes in several of these cases, and as announced in last week's Journal, three cases (those numbered I, II, VII) are about to be sent to a convalescent home. Through the kindness of Dr. Heron we have been able to make a careful comparison of the condition of these patients at the present time with what it was at the commencement of the treatment. Dr. Heron has unreservedly allowed us to examine the notes of the cases as well as the patients. To his fellow-workers, Drs. Wethered, Adamson and Scott, we are indebted for considerable assistance.

Case I. *Phthisis.*—G. M., aged 23, has been injected altogether 38 times—of which the last 14 have been of the maximum dose of one decigramme. The only time that any reaction has occurred with this dose was on December 27th, after the second injection, when the reaction was severe. However, since that date, during the last 12 injections there has been