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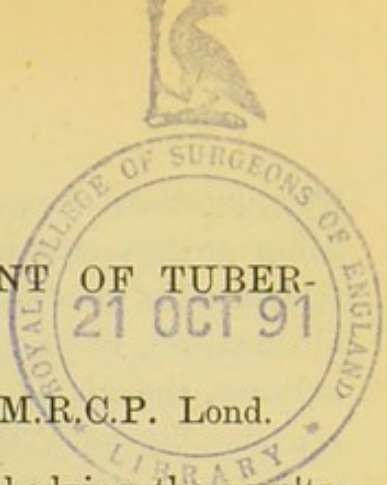

A REPORT ON KOCH'S TREATMENT OF TUBERCULAR DISEASE.

By J. W. Springthorpe, M.A., M.D., M.R.C.P. Lond.

I am hopeful that the following report, embodying the results of a month's study of the effects of Koch's remedy in tubercular disease at the head-quarters of treatment in Berlin and London, will prove of assistance to the profession in Victoria, in arriving at a just estimate of the therapeutic value of this newest and most potent of drugs. When we consider the gravity of the issues involved, and the claims of the speaker, there is little wonder that the civilised world has been in spirit, if not in body, to Berlin to hear Koch. For tubercular disease follows man and beast almost everywhere. In the old world it continues to slay its millions, and in this Australia of ours, "though the rural parts enjoy a comparative immunity, consumption figures in most of our returns as the greatest single cause of death, whilst our principal towns show a proportion of phthisical deaths nearly equal to that of many European cities" (McLaurin). Hence, when Koch, the distinguished discoverer of the cause of the disease, the man most competent to speak, and, as shown by previous experience, most cautious in utterance, announced the discovery of a remedy potent to cure, it was only to be expected that the hopes of all would be raised indeed. And though the time has not yet come when anything like finality has been reached, it seems to me no exaggeration to say that in the past four months, we have learnt more of the effects of this new treatment than could have been gained from four years of ordinary observation, and of more or less isolated experiments. For no drug has ever before met with anything like such a reception, has been anything like so widely tested, so accurately reported upon, or subjected to such a furnace of criticism. It is time, indeed, to report progress, and to discuss some, at least, of the indications for and against its therapeutic use.

The Nature of the Remedy.—After the little delay necessitated by the compulsory disclosure of his experiments, Koch himself has told us that his remedy consists of salts, pigment, and unknown extractives obtained from pure cultivations of the tubercle bacillus, by the help of forty to fifty per cent. glycerine, the salt and pigment being unimportant ingredients, retained only

from questions of expense, and the extractives, the active principle, being present only in a fraction of ·1 per cent. But we are not told in what media the bacilli have been cultivated, whether in blood-serum, human or otherwise, or different glycerine peptone cultures, though, as we know, the results of growth may vary considerably with the difference of the media. It may be, it probably is, the case, that Koch's cultures are from the most suitable media, but of this, we have as yet no satisfactory guarantee. Indeed, the best mode of preparation may yet have to be discovered. And though the genius of Koch as an experimentalist, shines out through every step of the long journey through which he has travelled before he has reached his present goal, yet it seems probable that he owes the germinant idea to France, and the successful method to England. For it was in the laboratory of the immortal Pasteur that it was first discovered how the weakened cultivations of anthrax bacilli rendered the animal into which they were injected immune against anthrax; and how attenuated emulsions of the spinal cords of rabid rabbits, when progressively injected, conferred immunity from the ultimate effects of hydrophobia. The indebtedness of Koch to Pasteur is generally recognised. But his probable indebtedness to Hankin, of Cambridge, for his final success, is not yet so generally understood. I say probable indebtedness, because the matter will remain unsettled until Koch fully discloses his method. As this is so little known, I take the liberty of dwelling somewhat upon it. It had been known as far back as 1887 at least, that immunity against various diseases could be produced by the injection of the soluble products of the life of microbes. But until Hankin's time, all isolating experiments were conducted with the ptomaines made by the microbes. And though many such were isolated, no cases were ever recorded in which immunity had been produced thereby. It was in October 1889, that the observer mentioned, isolated from anthrax cultures, an albumose—a poisonous proteid of a totally different nature to the ptomaines—and by means of this albumose, produced immunity against anthrax. This discovery completely altered the methods of experimentation. Shortly afterwards, Brieger and Fränkel, working in the same laboratory, and abandoning old methods in favour of others practically of the same nature as Hankin's, isolated similar bodies from cultures of tetanus, cholera, and typhoid, though apparently without then succeeding in the production of immunity thereby. In May 1890,

Dr. Sydney Martin reported the separation of two poisonous albumoses, and one poisonous alkaloid from anthrax cultures; whilst prior to July 1890, Professor Bebes had discovered albumoses in glanders, in rabies, and in pigeon diphtheria. It seems probable, therefore, that Koch himself had his attention turned from ptomaines to albumoses by these and similar discoveries, and following these newer methods, came upon the great discovery with which the world has been ringing. Everything, indeed, points in this direction. Like Brieger and Fränkel's, his extract is first called a "tox-albumen;" it is denied that it is a ptomaine, whilst his description of its properties suggests strongly the albumose reactions. It will be interesting, indeed, to know the truth upon this point.

One other point of interest follows from this knowledge of the mode of preparation of the remedy. It is that the strength of the lymph, as at present produced, can scarcely be a constant quantity. Koch himself takes the responsibility that all lymph bearing his name, is both reliable and efficient; but its relative efficiency certainly varies. This variability accounts, in my opinion, for numerous clinical discrepancies, as well as many personal disappointments, and imposes upon all the necessity of carefully testing the strength of one sample, prior to drawing conclusions. With us, indeed, another factor may come into play in the influence of continued heat upon the undiluted as well as the diluted lymph. This may be nil, or may be very great; Dr. Libbertz thinking the former, and Professor Fränkel inclining to the latter. As some precaution, I have divided my seven bottles into two divisions—one I have kept at the temperature of the surrounding air all through the tropics; the other, at a standard temperature, a little below 70°.

The Effects of the Remedy.—Upon this point, a very large quantity of valuable evidence has been already collected—sufficient, indeed, to warrant some very definite conclusions.

(1) Clinically, the effects of the drug in cases of tuberculous disease, have been exhaustively collated, almost all nationalities and shades of thought being well represented. There can be little need, however, for me to do more than touch suggestively upon what Koch and subsequent observers have made known to all. The *general reaction*, which is almost invariably present, is well exemplified in its different degrees in the charts which are arranged round the room, and which represent cases under

treatment in the Friedrichshain, Urban, Charité, and University Clinics. I propose leaving them on view during the week, so that any member interested can at his leisure study the changes produced in temperature, pulse, respiration, &c. I am indebted to Dr. Mullen for the translation of the brief epitome, which gives the clinical facts present during the course of treatment. Undoubtedly variations occur in the reports published by different observers. Some of these discrepancies are probably due to variations in the strength of the lymph. Such for example seem the negative results, obtained by Schroetter, Billroth, Kaposi, and others, in Vienna, during November and December. Errors in administration and variations in the clinical features of the case may, and probably do, account for other differences, whilst others remain due, perhaps, as Güttmann suggests, to idiosyncrasy. In not a few, from some unexplained cause, the reaction "hangs fire" for some twenty-four hours, and to want of allowance for this peculiarity may be fairly attributed some serious effects where the injection was repeated before the latent period had elapsed. Equally well known to you is the *local reaction*, so noticeable and so well illustrated chromo-lithographically in the picture of lupus which I show, taken from the *British Medical Journal*, of January 3, 1891. It is scarcely necessary to remind you that this local reaction is similarly present in whatever locality the tuberculous tissue may be found, whether lung, bone, joint, gland, larynx, meninges, intestines, kidneys, or what not; with the production, of course, of symptoms varying with the organ, its function, and the severity of the reaction. This *local reaction* indeed is the direct result of the action of the remedy upon peri-tubercular tissues; whilst the *general reaction* seems due partly to these local changes, and partly to its effect upon vital protoplasm in general, and the white blood cells in particular. To complete the clinical picture, however, we must remember the marked feeling of *bien être*, which generally follows injection, the splenic swelling, the sickness and vomiting so frequently noted, the occasional presence of icterus, the eruption rubeoloid scarlatiniform and herpetic; the temporary albuminuria, hæmaturia, hæmoptysis, diarrhœa, the changes in the number and structure of the bacilli discharged from the system, and the changes which Henocque describes as found in the hæmoglobin. Nor must we forget the unexpected presence of local reactions in unsuspected positions, suggesting in most instances early and unrecognised

tubercular lesions but in a limited number, suggestive of fresh infection, due possibly to the effects of injection.

(2) Almost as noteworthy, though of course much less limited in scope, is the pathological picture as drawn by Jürgens, Henoch, Koranyi, Jürisch, Chiari, but above all by the master hand of the veteran Virchow. With their discoveries you are probably only too familiar, and for the details it will suffice to refer you to the summary of evidence collated in Appendix A. In the limited time at my disposal I can deal only with commentary. Virchow's paper contains the pathological results which have exercised the most determining influence upon the trend of public, and even professional, opinion, and from their intrinsic importance, no less than their ulterior effects, they merit the most careful investigation. Indeed, it is not too much to say, that for want of such scrutiny they have swung the pendulum of opinion as much to the one side of truth as the unreasoning excitement of the first few weeks had swung it to the other. Looked at calmly, what do Virchow's post-mortem examinations show us? It is true they place beyond all doubt what may be the local results of the drug, (and such evidence is invaluable), but this is only in certain cases, and when the drug is administered therein in a certain manner. What then are those cases, and what the dosage? The answer will startle those who have judged without correction. The cases were:— (1) Boy, $2\frac{3}{4}$ years old, with tubercular arachnitis and old lung mischief, where colossal and unprecedented hyperæmia was found to be present. In all, four doses had been given, amounting to ·002. Such cases then are evidently contra-indicated, at any rate when the remedy is given in anything like such doses as ·0005. (2) Case of severe bone and joint tuberculosis, case of "cavity" with carcinoma of the pancreas, and a case of pernicious anæmia with pleurisy and slight lung mischief. None of these cases can be said to be particularly fitted for any line of treatment—even Koch's lymph,—and until the dosage is known, it would be useless to attempt to draw any conclusions. (3) The sixteen cases of phthisis, therefore, furnish the gravamen of the charge of danger which Virchow has practically brought against Koch's remedy. More than ever is it valuable then to ask, what were these cases, and what the dosage? As to the cases, all Virchow himself tells us is that, with one exception of apical induration with persistent fever (?), they were all cases in which ulcerative processes of a greater or less extent were present. Three only have I been able

to trace further :—one was a case of advanced phthisis and amyloid disease ; one of extensive phthisis, with severe pleurisy ; one of advanced phthisis, with dropsy and albuminuria. If then these are any fair samples, the cases were practically cases of advanced pulmonary mischief—doubtful cases for treatment, even according to Koch's first paper ; cases in which, according to his subsequent paper, treatment may be dangerous and even harmful. And what of the doses administered? My daily comparison of the line of treatment adopted at the different Berlin hospitals, had already prepared me to believe that the dosage at La Charité (of which Virchow is pathologist) was somewhat heroic, and I feel convinced that, when contrasted, for example, with the Moabit and the Friedrichshain Hospitals, it will be found to be excessive in amount, and more frequently administered ; and to some extent, the charts exhibited to-night bear out this contention. And when we turn to the three fatal cases under Professor Leyden, of which I have already gathered the clinical details, we find that in the first ·1 had been administered in seven injections, in twelve days ; in the second ·006 in two injections ; and in the third up to ·04 in eight doses. We have ground, therefore, for stating that Virchow's results are largely, if not entirely, the results of excessive doses, given in advanced cases. Criticism again is possible with reference to his interpretation of some of the lesions which he so well describes. We may admit, without reserve, the local congestions, hæmorrhages, actual inflammatory processes, even extensive caseous hepatisations, and peculiar turbid infiltrations, with tendency to excavation, to which he calls attention, as more or less likely to occur whenever the remedy is administered in such doses in such cases. But whilst admitting the possibility, even the probability, of some local metastasis of the bacilli under similar circumstances, we must not forget that septic organisms also are present ; and some competent judges ascribe the pyrexia and secondary results rather to septicæmia than to tubercular infection, remembering that the bacilli die in blood and lymph for want of pabulum, a fate sooner experienced in all probability, whilst the injections are being continued. Lastly, as to the want of effect of the lymph in certain places, such as submiliary and solitary tubercles, it is open to question whether the first may not have been in reality septic, whilst the latter are distinctly stated to have been "like large lumps of cheesy matter," and Koch has distinctly declared in his first paper, that his lymph

"had no effect upon dead tissue, as for example necrotic cheesy masses." I have dwelt at this length upon Virchow's already classical paper, because of the vast effect which it has exercised upon opinion, and I leave the thoughts here suggested to your consideration without further comment. I cannot leave this point, however, without reminding you of the conclusions which Virchow himself drew from his investigations, viz., a warning to physicians to operate with greater caution in cases where patients had not the strength completely to expectorate the broken-down tissue, and the habit of doing so; and in clinical support of the position which I have here taken up, I would ask you to read carefully, the results recorded by Fürbringer and Güttman, at Friedrichshain and Moabit respectively; the latter of whom, indeed, goes so far as to add that, "when other hospitals make similar selection of cases, they will attain similar (favourable) results."

(3) I must dismiss briefly the effect of the remedy upon non-tuberculous cases. That a sufficient dose will seriously affect the healthy individual, is proved from Koch's experiment upon himself of ·25 cc.; the lowest limit of noticeable effect being found also from numerous experiments to be ·01 cc., when slight pains and transient fatigue were the only symptoms produced. The fact of such results following injection in the healthy individual, shows that in a variable, though excessive dosage, the remedy meets with something in the healthy body upon which it can react. It also prepares us to expect similar reactions in other diseased states, even with much lesser doses, especially in diseases allied to tubercle, and certainly, of course, in the large class of cases of unrecognised tubercle. It is not surprising, therefore, that re-actions have been stated to be present in two cases of actinomycosis, in syphilis, carcinoma, leprosy, and many doubtful lung cases. But after making all allowance for these, at present, unexplained irregularities, the fact remains, that as a reliable and delicate diagnostic agent for the recognition of tubercle in any form or situation, Koch's lymph is at present considered to stand without a rival.

The Effect of the Remedy upon Tubercular Disease.—For the purpose of this paper, tubercular disease is taken to be the expression of the lodgment of the tubercle bacillus in a suitable soil, and its growth therein at the expense of the organism. The bacillus we know, thanks to Koch himself. The modes

of entry we suspect, thanks to Koch, Cornil, Bang, Mosler, McFadyean, and others. But what of the soil? That there must be some susceptibility of the system is certain, otherwise many of us must have ere now fallen victims. That the lodgment in any force is a question of time, and the local fight, not always decided in favour of the invader, is equally sure. What then is this constitutional or local weakness of which the tubercle bacillus takes such dire advantage? Evidently, it is a matter of the most delicate bacteriological chemistry, and without claiming entire certainty or complete accuracy upon such an unsettled point, it may be taken that it is a weakness as deep down as the vitality of the vital protoplasm, and especially of the white blood cells, rendering them more or less impotent to engage the bacillus in pitched battle. Later on again, the tubercle bacillus becomes reinforced by other invaders, such as the streptococcus, aureus and albus, the pus streptococcus, the microbe of pneumonia, and the like. Tubercle then, as we find it, in general and special hospitals, in man and beast, in surgery and medicine, in each and every part of the system, is the theatre of operations between these germs and their surroundings. Now, what effect has Koch's lymph upon the different parties to the fight? (1) Upon the Constitutional Status.—In animals, immunity from fresh attack has actually been produced, whilst in man it remains to be seen whether an equally good effect will be attained. Koch thinks it probable. Lister suggests that it may be a matter of dosage. Everything points in favour of hoping the best from continued trials. Apart from permanent immunity, however, it seems probable that temporary assistance is borne to the weakened system by the administration of the lymph. (2) Upon the Bacillus.—Koch expressly stated in his first paper that his remedy did not kill the bacillus, and subsequent observations have corroborated his view. But, undoubtedly, the wise use of it helps to starve the bacillus out of existence, and finally to procure its disappearance. Equally, undoubtedly, its reckless or unskilful use may lay fresh parts of the system open to invasion by the tubercle and other germs, and their lodgment therein becomes a question of conditions being favourable. In what manner the remedy may give this assistance we have been told by Koch, in his explanatory paper of January 15th, which I leave you to re-read at your leisure in the *British Medical Journal*. It is only necessary now to add that clinical and pathological observations in the main support his view, and to

remind you that in it we have a good working hypothesis, as good indeed, and apparently as reliable as many others in ordinary therapeutic use.

The Clinical Record of its use up to January.—To bring the whole matter of the use of Koch's lymph succinctly before you, I have prepared a summary in Appendix A, which contains an abstract of the experience and opinions of some 90 observers, all of whom have had more or less to do with its administration in different forms of tuberculous disease. The abstract embraces the name of the observer, the date of his communication, his experience with the remedy, his results, and remarks. It is as complete as I could make it with the materials at my hand, and, in my opinion, may be taken as a fair epitome of the scientific world's experience and opinion up to date, and as such it is brought under the notice of those who wish rapidly to review the situation.

Personal Experience.—As regards my own experience with the remedy, you are, no doubt, all aware, that like many thousands of others, I have visited Berlin to ascertain for myself the exact state of matters with reference to its therapeutic value. I remained in Berlin for over three weeks, and then proceeded to London for a week longer. At Berlin I visited the Charité, Urban, Friedrichshain, Moabit, Augusta, University, and other Hospitals, and saw numerous cases, of all kinds, under treatment by Bergmann, Hahn, Senator, Fränkel, Fürbringer, Sonnenberg, Ewald, Leyden, Gerhardt, &c., with their accomplished assistants, Schimmelbusch, Klemperer, Roth, Gumprecht, &c. To all these gentlemen I would take this opportunity of returning my sincere thanks for much courteous assistance; the more appreciated since their patience must have been sorely tried by the previous unparalleled strain upon their good nature. By the kindness of the British Ambassador, Sir Edward Malet, and the English Consul-General, Baron Bleichröder, neither of whom I can thank too warmly, I received official permission to inspect all hospitals, and an early supply of the lymph. Indeed I had my lymph before I was a week in Berlin. But, though I was the first Australian to receive a supply, and not only anxious, but under agreement, to return at the earliest moment, I saw that it would be the height of folly to return until I had something more definite to go upon, especially as too sanguine hopes had at first been freely entertained, and the tide of opinion was as foolishly rushing towards the other extreme. Indeed, I thought it

wise to still further widen the base of my observations, and feeling fairly acquainted with the Berlin aspect of the case, to go on to London and Paris. In London, I visited King's College Hospital with Watson Cheyne, the Victoria Park Hospital, the London and the Brompton Hospitals. I found that with the exception of the first two, where Cheyne and Heron were operating at Koch's special request, little had been done, though much was in the air. This delay was mainly owing to the secrecy maintained by Koch as to the nature of his lymph, and the unwillingness of the College of Physicians, and many leading members of the profession, to depart from their traditions, and experiment with a drug of unknown composition. Before I left, however, St. Mary's, and the other large hospitals, were moving in the matter, and numerous reports had been received from all the large centres in the kingdom. Thence to Paris, where I must confess that the opportunity of visiting Pasteur's laboratory, under the wing of Dr. Adami, drove the tubercle question quite out of my head for the only day at my disposal, until it was too late. It was an inspiration to enter the rooms in which Metchnikoff, Roux, and others had made their discoveries; to watch Roux at work injecting some 60 patients for hydrophobia; to see the marvellous completeness of the whole observatory, and to listen to the voice of the immortal Pasteur.

As to the actual results which I observed myself, I have thought it wiser to collate a few of the more interesting in Appendix B, rather than to incorporate them with the portion of my report which I have rapidly to read over. They will be found, in the main, to support the favourable view which I have taken of the remedy within the limits already defined.

The present position of the Drug as a Remedial Agent.—This is the practical question to which all the foregoing has been a necessary, if lengthy, introduction. What is the truth about Koch's lymph? Let us take a survey of the situation. Here was a disease, of many forms, of universal prevalence, practically the despair of the physician, and the dread of a large section of the civilised world. Somewhat unexpectedly, after years of searching and experimentation, the man most competent to speak, announces the discovery of a remedy of a potency hitherto without parallel. A miracle was, not unnaturally, expected, and the pendulum of opinion swung irresistibly from nothing to the zenith. But the days of miracles are apparently passed, and the unbounded hopes

of the previously hopeless were gradually—for the remedy had that potency—disappointed. Criticism appeared, and it is as difficult for scientific as for all other criticisms to be just, especially when it is one rival individual and school reviewing another, and one nation summing up the good works of its foe. The miracle was, of course, impossible; but, as might have been expected, and as was predicted, the pendulum swung as determinedly in the direction of the other extreme, and those who had not secured a good personal footing were in great danger of being swept away by the returning tide. What, then, is the truth about Koch's lymph? I can, of course, give you only my own opinion, and it is as follows:—I believe it to be a remedy with a practically specific action upon tuberculous tissue, and that within the limits already laid down, there is nothing which we at present know to compare with it. From its potency, it requires most careful handling, but we have already sufficient data to render a wise use of it both possible and advisable. The question narrows itself down largely into one of selection of cases, and cautious administration. It would indeed be folly to assume that we have attained anything like the best results—but the same may be said of almost all therapeutic means—whilst it would be still greater folly to decline the task of following on until greater perfection is attained. Apart from its intrinsic value, it opens the gateway to an almost unbounded field of fresh possibilities of treatment. Already, Behring and Kitisato declare that they have produced immunity against tetanus and diphtheria, and the long inevitable thraldom of the infectious diseases generally seems now to be within a measurable distance of overthrowal.

Coming now to particular instances, in uncomplicated cases of *lupus*, administration is generally both easy, harmless, and exceedingly effective, even in the doses mentioned by Koch. The tendency, however, is towards a more cautious dosage, at more lengthened intervals, and repeated for a longer period. Many relapses have been noted where injections have been abandoned after a week or so. Surely nothing else could have been anticipated. It is wise also to remember the possible presence of other and even unrecognised foci; in complicated cases, the dosage is of course proportionately diminished. As to the actual changes produced, Schimmelbusch (Bergmann's assistant) had, when I left Berlin, numerous specimens taken from infected cases for purposes of microscopic examination (*vide* also Kromeyer's paper). As

regards *laryngeal cases*, the services of a specialist are of course indispensable; and in selected cases, as will be seen from my summary, the balance of evidence is strongly in favour of marked improvement, without serious risk. In *bone and joint cases*, I was more favourably impressed than in any other part of the treatment, and for the sake of suffering children alone, cannot but regard Koch's lymph as of inestimable value. It may be the age of the patients, or the peculiarities of bone and joint, or the facility of operative assistance, or all combined; but whatever be the cause, certain it is that almost all observers are unanimous as to the great good derived from Koch's injections in this variety of cases. Hahn and Watson Cheyne's cases are particularly instructive in this connection. In *tubercular affection of glands* again, the evidence, though much less extensive, points generally in the same direction. In developed *tubercular meningitis*, as already stated, the remedy is probably too risky for use, though the earlier diagnosis of tubercular mischief, which is given by the lymph, may be used to prevent its onset. In *tubercular disease of the eye*, exceedingly good results have been reported, but further evidence is necessary before reliable indications can be laid down. In *tubercular disease of the uterus and appendages*, Bossi, of Genoa, considers it most useful. In cases complicated with *tubercular or amyloid disease*, of *intestinal*, or *genito-urinary tract*, the use of the remedy is no doubt almost always contra-indicated, or hedged round with such individual restrictions that no general conclusions are possible.

More or less agreement exists in reference to most of the foregoing. The discrepancies begin to get more serious, however, when we come to deal with pulmonary phthisis. The extra difficulties of the problem in the case of the lungs, will suggest themselves naturally to all. The main observers whose papers seem especially noteworthy in this category are Koch, Güttman, Fürbringer, Gerhardt, Senator, Leyden, Virchow, Theodore Williams, Wollf, and Cornil of Paris. Extracts from these I venture to read by way of illustration of my contention that the successful application of Koch's remedy in lung cases is a question mainly of selection of cases and careful administration. From this summary, supplemented by somewhat similar statements by other observers, I think certain practical conclusions can be drawn. (1) That cases of early phthisis where the mischief is slight, and the strength good, and pyrexia absent, will in all probability derive

considerable benefit from the injections. (2) That in somewhat more advanced cases it is a matter for some hesitation, having regard to the power of the patient to expectorate, his habit of doing so, the general health, the question of pyrexia, and rendering the dosage both less in amount and less in frequency. So far indeed from aiming at the production of reaction, by gradually increasing the dose, I am inclined in many cases to suggest the retention of a minimum dose, and its exhibition twice a week over a lengthened period. (3) That more advanced cases, and cases with complications, should be injected, if at all, only after most careful consideration, and only, if at all, as a last resort, and with special precautions. And, speaking of the treatment of lung cases generally, I believe that it is probable that it will be found to be more beneficial to give minimum than increasing doses, and once certain of the diagnosis not to aim at the attainment of other than a continued slight reaction, having the patients under observation for some months. By this means perhaps immunity may be gained. As regards operative interference, it is certain that there is a great future in cases of bone, joint, gland, and the like. Diagnosis can be made earlier and with great certainty, and when operations are undertaken, the results are often astonishingly good. The time to operate, whether before or after injection, the local assistance of iodoform, &c., to kill the bacilli, are questions which are ripe for settlement. In pulmonary cases also, operative interference becomes distinctly more hopeful. Before I left, Sonnenberg and Hahn had recorded some half dozen of such, but the results were too recent to warrant any exact conclusions. I am of opinion, however, that in a certain limited number of cases, such as at present tend almost invariably to get worse, operative measures, combined with injection, promise at least considerable temporary improvement.

After all, however, the future treatment of phthisis will not in my opinion be able to neglect the general treatment, so essential in the past. We shall still need preventative measures against infection by dried sputum, tuberculous milk, and meat; we shall need to build up the corporate vitality by all the aids in our power, and shall value as much as ever the beneficial influence of fresh air, sunlight, mountain climate, and diet. But with Koch's lymph, or its perfected substitute, it becomes possible that we shall be able to confer immunity in cases favourably situated, and to avert infection when otherwise it would occur. The future alone can tell

how near or how far we are from this splendid achievement. Even at the present time, however, in my opinion, we can diagnose tubercular disease at an earlier period, and influence it for good more by the right use of Koch's lymph, than by all the rest of the whole army of drugs.

Its Mode of Administration.—Dr. Henry has kindly translated for me in Appendix C, Koch's own directions as to administration, forwarded with each bottle of lymph. The dilutions, the dosage, the precautions against contamination are there so explicitly laid down, that all can understand.

Such then, gentlemen, is the report which I have the honour to lay before the Victorian Branch of the British Medical Association. The unparalleled enterprise of our Journal has already furnished you with exhaustive accounts of almost all phases of the question, and I am in hopes that this paper may be found a useful commentary thereto.

It might be regarded, however, as a matter of discourtesy and even misrepresentation, were I to conclude without paying some attention to an official report upon this same question, published over the signature of a Government Commissioner. It cannot have escaped notice that there is a difference of opinion between us, as to the value of this new method of treatment. It may be that this difference is due to the fact that the time at the disposal of the writer of the report to which I refer, was unfortunately too short, in my opinion, to have given him opportunity to disembarrass his mind of the conflicting reports which were necessarily rife at that early stage. In this respect, I certainly had the advantage, as my stay in Berlin was prolonged to three weeks, and embraced a later period, during which I was visiting all the principal institutions at which this treatment was being carried out. And in further justification of the position which I have taken up, I would point out the fact that the author of the official report seems to have missed the more recent literature, which has had such an influence in crystallising our ideas upon the question. I feel sure that had the same opportunities of information which fell to my lot been enjoyed by our Government Commissioner, he would have considerably modified the conclusions at which he arrived. Thus, we now know a great deal about the composition of the remedy. We have a good and fairly satisfactory working hypothesis as to its mode of action; whilst the dangers on which he dwells so heavily, turn out to be

dangers of misuse, which are present in a small percentage of cases only. And when he recommends "that for the present, in accordance with Professor Koch's desire, it should be employed in hospital practice only," he quotes—somewhat inaccurately it must be added—from Koch's early paper. In his later paper, Koch makes no such restriction, leaving the matter now to the common sense of the physicians who had learned how to use the remedy. For practical example, before I left Berlin and London, within my own knowledge, Professors Leyden, Fränkel, Senator, and Watson Cheyne, to say nothing of many others, were all treating private patients as seemed to them best, and without any arbitrary restrictions.

Appendix A.

Observer.	Date.	Experience.	Results.	Remarks.
Koch, of Berlin Hygienic Institute.	Nov. 15, 1890.	Patients from Brieger's Poliklinic, Levy's private Surgical Clinic, Fraentzel and Köhler at the Charité, and Bergmann's University Surgical Clinic.	General reaction, embracing attack of fever, with rigors, pain, coughing, fatigue, often vomiting, ss. icterus and skin eruption; beginning in 4 to 6 hours, and lasting 12 to 15. Local reaction, embracing swelling, increased sensibility, redness, and necrosis of tuberculous tissue. In lupus—complete cicatrisation, or marked improvement. In bone and joint—speedy cure in recent and slight; slow improvement in severe. In lungs—free from symptoms, and "cured" in 4 weeks if in first stage. Where early cavities, highly improved, and almost cured; where many large cavities, no objective improvement, though subjectively better. In larynx and brain, insufficient evidence.	As a rule, in lupus, began with ·01; when reaction ended, repeated the injection, and continued until it ceased. In bone and joint cases, large doses at long intervals. In lung cases, ·001 daily till no reaction, ·002 till no reaction, rising to ·01, in 4 to 6 weeks. From its specific action on tuberculous tissue, will form an indispensable aid to diagnosis. Considers that phthisis in early stage can be cured with certainty. An open question how far relapses may occur, but such may be similarly cured. Early application of the remedy the most important point, combining, where necessary, with operations, proper sanatoria, mountain climates, fresh air, special diet, &c. [So far, the immunity conferred on animals has been permanent.]
Bergmann, University Surgical Clinic.	Nov. 16, 1890.	18 cases of lupus, 18 of bone and joint, 4 of glands, 4 of larynx.	Confirmed local and general reactions above.	Undeniable and immense value as diagnostic. Therapeutically, enthusiastic as to throat and skin cases, and generally, prognosis decidedly favourable. [Later on, relapses found to occur in lupus cases.]
Fraentzel, at La Charité.	Nov. 17, 1890.	Phthisical cases.	Reaction typical. Decided improvement in early cases, none in advanced cases. Sputum easier, and more abundant; bacilli changed, stunted, but not killed.	The treatment must be continued over a considerable time. Warns against large doses early in advanced cases.
Levy, Private Clinic.	Nov. 18, 1890.	Cases of lungs, skin, bone, joint and glands; two months' treatment.	Reaction typical. First case treated (·1 given), unconscious for 36 hours. As a rule, lung cases lost weight.	General improvement in almost all cases. Joint cases discharged as "cured."

Observer.	Date.	Experience.	Results.	Remarks.
erhardt, La Charité.	Nov. 18, 1890.	Throat and lung cases.	Reaction typical.	Thinks recovery very possible, but the treatment will require the most careful discrimination.
	Dec. 13, 1890.	59 patients, with 380 injections.	Usually began with ·002. As many as 13 doses, highest ·1. 14 lost weight, 10 gained weight; general state usually lowered. Respirations frequently hurried. Sweats often ceased. 2 left quite well, 3 died, 11 felt very well, 7 comfortable, 6 wretched.	Diagnostic value beyond doubt; better in larynx than lung cases. Prognosis unfavourable where hectic present. Earnestly repeats Koch's warning as to using it only in early stage.
Köhler, La Charité.	Nov. 24, 1890.	Skin, bone, and joint cases, 6 weeks; began several weeks before Von Bergmann.	Usual reactions, with corneitis (1); has seen recurrence in lupus. Observed keratitis and kerato-conjunctivitis.	Immense value for diagnosis of early joint cases; renders surgical aid easier and more effective. In deep parts, the method must be supplemented by removal of the affected tissues.
Lubinski.	Nov. 21, 1890.	Larynx cases.	Local reactions very marked. No fear of œdema.	Cases improved; ulcers cleaner and less; *débris* expectorated; swelling disappearing.
Krause, Ziegelstrasse.	——	15 cases of larynx.	Usual reactions. Ulcers covered with slough, separating, and leaving healthy granulations	One case much worse; 14 markedly alleviated.
Senator, University Clinic.	Dec. 10, 1890.	53 medical cases; 400 injections during 3 weeks.	Intensity of reaction bears no relation to extent of disease. Reaction lowering, causing loss of weight for some weeks. Bacilli altered in shape, but no diminution.	Indicated in all cases of tubercle where elimination of killed tissues easy, *e.g.*, lupus, larynx, nose, mouth, intestine. In lungs, good only when recent and slight; little scope in closed cavities. Contra-indicated in nephritis, large pleurisy, extensive amyloid disease, and debility generally. Very marked improvement in laryngeal. In phthisis, no case of cure, but marked amelioration.
Fränkel, Urban.	Feb. 11, 1891.	83 cases.—48 treated for 7 weeks, 13 for 4 weeks; 2 deaths; treatment suspended in 7.	Bacilli absent in 3 for seven weeks; no change in 15; 28 cases improved; in 20 no change; 9 got worse.	General improvement very striking; marked improvement in a limited number, especially of slight cases—cannot predict. Improved nutrition in about half. In no small percentage the moderately severe cases grew worse. Would exclude severe cases.

Observer.	Date.	Experience.	Results.	Remarks.
Güttman, of Moabit.	Dec. 15, 1890.	66 medical cases under treatment.	Reaction after ·001 in apyretic early cases; larger dose required in others. "Idiosyncrasy" necessary to explain differences in similar cases	Bacilli found where previously absent. Many gained weight remarkably; two practically cured. Under observation since October. Dose has been increased to ·05; one case with dose ·1.
	Jan. 14, 1891.	170 cases; 120 assigned to Koch.	41 early phthisis; great majority notably improved, 10 lbs. weight gained; physical signs improved; subjectively better. 30 laryngeal cases, all show marked improvement and tendency to cure. No "circulating bacilli" found in any examination (30).	One other lung case "cured." Results of treatment depended largely upon selection of cases; only early lung are suitable; on no account treat very advanced. When other hospitals made similar selection, they would attain similar results.
Sonnenberg, of Moabit.	Dec. 12, 1890. Dec. 17, 1890.	Operations on chest cavities, combined with injections.	In 3 cases, cavity at apex; in one, lower down; in last, pneumo-thorax developed. Operation—Careful dissection to pleura; exploration by syringe; opening enlarged by actual cautery; cavity and wound stuffed with sterilised wool.	—
Fürbringer, of Friedrichshain.	—	63 medical cases	Compares classical reaction to influenza attack, with occasionally eruptions, jaundice, sweating, diarrhœa, and albuminuria. Physical signs modified or disappeared; sputum lessened; bacilli absent; weight increased.	For diagnosis—Useful in many, unreliable in 5. Of 41 phthisical cases, 10 benefited more than any of the thousands of cases similarly situated previously, within 4 weeks. In the others, considerable benefit.
Hahn, of Friedrichshain	Jan. 1, 1891.	59 cases, from November 21 to December 23; 300 injections. Surgical cases—bone, joint, gland, and lupus.	Excluding 27 cases, where treatment too brief. In the other 32, 16 considerably, and 12 appreciably benefited; in 4, no change. In bone and joint—Better results where sinuses present than where no sinus or surgical opening. In one, reaction ceased after resection.	Marked local and general reaction in 1 case of sarcoma of the larynx.

Observer.	Date.	Experience.	Results.	Remarks.
Ewald, of Augusta Hospital.	Jan. 21, 1891.	114 cases.—5 deaths; 36 discharged, 7 before getting the full dose of ·1, 12 because improved.	7 not improved; 7 considerably improved; 5 in moderately good condition; 15 received full dose, 14 continuing well. Subjective symptoms improved, auscultation also; percussion unchanged.	No general rule as regards suitability of case. Patient should be warned of danger, though chances of good result are in his favour, and rapid improvement frequent—more rapid than under any other treatment. In certain number, as good results obtained by other methods of treatment. Worthy of more trial.
Henoch, of La Charité.	Dec. 4, 1890.	In children between 2 and 11 years—6 of phthisis, 1 of lupus and caries, 1 of caries and peritonitis, 1 of T. Meningitis, 1 of scrofulosis, and 1 of spina ventosa.	3-10th milligramme required to produce reaction.	Post-mortem showed colossal, unprecedented hyperæmia of meninges in case of meningitis, without any change in the tubercles; treatment contra-indicated in such; had 4 doses, amounting to ·002.
Rosenbach, of Breslau.	——	56 cases under treatment.	Reaction produced in cases otherwise doubtful.	——
Kromeyer.	——	Microscopic examination of lupus tissue 7½ hours after injection.	Swelling and redness of the tissues; small cell infiltration in border skin and round nodules; nodules also invaded; epidermis and papillary layer breaking down vessels infiltrated.	The appearances suggesting suppuration. Thinks chemical substances produced leading to inflammation and breaking down of tissue. Hence, fears danger in disseminated lung cases, from œdema, or large portion rendered useless for breathing purposes.
Helferich, of Griefswald.	——	Lupus (4), hip (4), bones, and glands.	Usual local and general reactions, the latter frequently higher after a few doses. The interval before it occurs becomes less as injections increase and duration is less. No untoward effects. Eruptions like measles, scarlatina, and herpes.	Compares the specific effect on tubercle to that of Hg. and KI. in syphilis. Such improvement in lupus as under no other treatment. In joints, extension lessened, local pain. Compares the treatment to antisepsis, and speaks very hopefully of it.
Lindner, Augusta Hosp.	Dec. 18, 1890.	In 2 cases—1 disease of elbow, with old fistula; 1 sternal disease, with fistulæ and lung affection.	No reactions, but marked local improvement; ·03 produced no result.	Spoke most strongly of its therapeutic, as well as diagnostic value, especially in joint cases; the tubercular matter could be evacuated with a facility previously unknown.

Observer.	Date.	Experience.	Results.	Remarks.
Jürgens, La Charité.	Dec. 14, 1890.	2 post-mortems under Leyden.	Wide-spread changes; only small parts permeable to air; hæmorrhagic hyperæmia on walls of cavities; recent sero-sanguinolent effusion into the pleura; tuberculous ulcers in intestine and throat transformed into simple ulcers. Similar modification of the tuberculous process in spleen and other glands. In kidney caseous focus, surrounded by zone of intense hyperæmia.	Very advanced cases. In one, up to ·006 in several injections; in other, up to ·04 in 8 doses. First case was extensive phthisis, with severe pleurisy; second, advanced phthisis, with dropsy and albuminuria.
Schmidt, of Stettin.	Jan. 1891.	60 patients in Bethany Hospital.	400 injections in all.	Results so far satisfactory, and justify the best hopes for the future.
Korte, at Urban.	Jan. 14, 1891.	28 surgical cases.	So far no definite improvement. Perhaps time too short.	Diagnostically useful, except in one case of actinomycosis. Two fatal cases, injected without any hope of recovery.
Sir Joseph Lister, King's College.	Dec. 3, 1890.	Visit to Berlin.	Effects simply astounding, the tuberculous tissue is necrosed. Where discharge of necrotic tissue possible, it is expelled; where impossible, absorption occurs occasionally, though tedious where portion extensive. In many cases combination of injection with operation very promising.	Highest diagnostic value, powerful curative effect also. To render the treatment perfect, immunity from fresh infection required; this not yet attained in man, though attained in animals. Perhaps possible, if we could increase the dose. Already increased 500 times in 3 weeks, but guinea-pigs can take 1500 times the dose.
Watson Cheyne, King's College, and Paddington Green Children's Hospital.	Dec. 3, 1890 to Jan. 3, 1891.	Joint, bone, skin, glands, lungs; one case of leprosy.	Effects as described by Koch. Consider that it acts by producing rapid necrosis.	Probably more valuable in surgery; early cases may recover without operation. Generally corroborated German results. Extremely favourably impressed in bone, joint, gland, and skin cases. Practically, no experience in chest cases. Some improvement noted in case of leprosy.

Observer.	Date	Experience.	Results.	Remarks.
Heron, of Victoria Park Chest Hospital.	Dec. 1, 8, 20, 1890 to Jan. 1, 1891.	Mainly phthisis.	Acts upon living tuberculous tissue, not upon caseous, calcareous, or bony matter. Bacilli not killed. [One injected 38 times in 6 weeks (·1 in 12) without reaction; now 3 lbs. heavier, no sweats, no dyspnœa, still bacilli, chest sounds improved. Another, 36 injections (12 of ·1) without reaction; gained 10 lbs., bacilli still present, sputum $\frac{1}{3}$, chest improved. Another, 38 injections (11 of ·1) without reaction; gained $4\frac{1}{2}$ lbs., chest improved.	Only 8 days' treatment at most. Results as in Germany. A week later—generally favourable; the 3 phthisical patients sent to Convalescent Home. In 3 syphilitic cases, noticed reaction slight; 3 lupus cases improved wonderfully; also one case of anæmia.
Eve, of London Hosp.	Nov. 26, 1890.	At Berlin; in Bergmann, Levy, and Köhler's clinics; joint, gland, and skin cases.	Little short of the marvellous. Even advanced cases seem arrested. Diagnostic power wonderful.	In an attitude of "favourable expectancy;" suggests "coagulation necrosis," as the mode of action.
Theodore Williams, of Brompton Chest Hosp.	Dec. 20, 1890.	At Berlin with Ewald; Fränkel, Krause, &c.; some 100 cases of phthisis; also joint and skin, with Bergmann and Levy.	In larynx cases, improvement common, but cure rare. In lung cases, no solid improvement, even loss of weight for first fortnight; but considerable improvement after several months in some 10 cases. Equally good results at Brompton without injection, and incomparably better results at Davos, &c. Effects in bone, joint, and skin seem brilliant.	The treatment opens the door to a brilliant and apparently unlimited series of experiments in the treatment of disease generally. In phthisis, worthy of careful and prolonged trial, not forgetting pure air, good food, careful nursing. Many Berlin hospitals open to improvement from sanitary point of view.
Philip, Victoria Chest Hospital, Edinburgh.	Dec. 3, 1890.	Some 200 cases at Berlin, during a 10 days' visit; also lung, lupus, gland, joint, and kidney cases under treatment.	Good general record of reactions, general and local. Corroborated in his own experience.	Accepts its diagnostic power; sanguine in early cases and local states; has seen lupus practically cured after 10 injections; definite improvement in joints, and great improvement in joints. As for phthisis, defers opinion; in advanced cases, local reactions verified post-mortem. Gives strong warning against false hopes in such; more hopeful in less advanced; has seen very definite amelioration in many.

Observer.	Date.	Experience.	Results.	Remarks.
Morell Mackenzie, London Throat Hospital.	Nov. 20, 1890.	3 laryngeal cases.	Marked local effects, withot danger. Line of demarcation left after necrosis.	Rendered diagnosis certain in suspicious cases. Agent of the highest value in the detection of tubercle; a remedy of great potency for certain of the slighter manifestations; a palliative for some distressing symptoms in severer forms, and a deadly poison in advanced or unsuitable cases.
Burney Yeo.	Dec. 6, 1890.	Cases under Ewald, Fränkel, and Bergmann; larynx, lung, glands, and skin.	Hæmoptysis in early cases, serious symptoms in advanced; nothing more remarkable, however, than subjective amelioration in such. Saw deposits melt away, leaving clean surface behind.	Considers Koch's conclusion just and accurate; must often expect relapses. Fresh tubercle elsewhere. (?)
Hunter, Wm.	Dec. 13, 1890.	50 phthisical cases at the Augusta Hospital; selecting 3 early cases for special report.	—	—
Saundby, Simon, and Barling, Birmingham.	Dec. 1890.	Fortnight at Berlin; laryngeal and pulmonary cases, under Fränkel, Senator, Ewald, and Levy.	Improvement in many lung cases; remarkable improvement in lupus; considerable improvement in gland cases; distinct improvement in joint cases. Unable to affirm curative influence of local reaction.	Impossibility of sometimes removing necrosed tubercle, with its living bacilli, is the weak point of the treatment. Not improbable that continued injections may confer immunity.
Lennox Brown.	Dec. 27, 1890.	Laryngeal cases under Gerhardt and Krause, with illustrations	Results simply astounding; after necrosis, ulcers heal with an unexampled rapidity.	Where no improvement, diagnostic value very great. Recommends to begin all laryngeal cases with the minimum dose ·001, or even less.
Squire, Children's Hospital, London.	Jan. 1891.	8 cases.	All benefited.	—
Grainger Stewart, Royal Infirmary, Edinburgh.	Dec. 10, 1890.	19 cases.	Same results as at Berlin.	Great diagnostic value; great therapeutic value in certain cases; great caution in its use; doubtful if tolerance produced by repeated injections.

Observer.	Date.	Experience.	Results.	Remarks.
McCall-Anderson, Western Infirmary, Glasgow.	Dec. 10, 1890.	Cases of Cheyne and McKenzie; also personal experience.	—	—
Sir W. Stokes, Meath Hospital.	Dec. 8, 1890.	—	—	So far, satisfactory results.
Smith, Steven, and Wakman, Royal Infirmary, Glasgow.	Dec. 10, 1890, & later reports.	Visit to Berlin; also personal experience in 28 cases.	Only indicated in early cases; dangerous where wide-spread; greatest caution in advising patients.	Most favourably impressed; no two opinions as to diagnostic power.
Gumprecht, Manchester Women and Children's Hospital.	—	Visited Berlin; also cases of larynx, lung, joint, and skin.	Produces more promptly than any other known drug, the retrogressive changes necessary for the elimination of tuberculous tissue.	—
Grossman, Liverpool.	Dec. 10, 1890.	Visited Berlin.	The rigors unlike those of acute disease in wanting the sense of serious illness.	Opened a large field for surgery; the necrosed tubercles requiring operative interference for removal.
Crocker, University College.	Nov. 22. 1890.	Visited Berlin; skin and joint cases.	Influence on all forms of local tuberculosis conclusive; much ground for hope in early phthisis also; more good in lupus than anything else.	Established claim to most thorough and careful trial.
Chadwick, of Leeds.	Dec. 5, 1890.	Short visit to Berlin.	Definite improvement observed in cases of joint, lupus, and phthisis.	The danger of sepsis in phthisis largely theoretical.
Malcolm Morris, and Pringle.	Jan. 10, 1891.	Case of lupus, treated in Berlin. Under observation from Nov. 15th to January 3rd.	From Nov. 15 to Dec 3, ·01 to ·1, 14 injections in 18 days, no reaction for the last 7; result far exceeding that produced by any other known treatment in both rapidity and efficacy.	Six years' duration, repeatedly cauterised; no relapse since December 3rd.
Stacey Wilson, Birmingham General Hospital.	Jan. 10, 1891.	Visited Berlin.	Points out that extreme internal reaction may occur without much rise in temperature; notes the disappearance of consolidation in favourable cases, and signs of fresh cavity formation in others.	Raises the question of the dosage in advanced cases, and in hectic, in some cases of purulent pyrexia, larger doses. Notes extensive ulceration of stomach and bowels from sloughing of the tuberculous tissue; hence special care in advanced cases.

Observer.	Date.	Experience.	Results.	Remarks.
Porter and Burgess, Sheffield.	Dec. 11, 1890.	Visited Berlin.	Merely constitutional reaction not conclusive, *per contra*, failure to react even to ·01 did not exclude tubercle.	Possible sources of danger in tubercle of urinary passages and alimentary canal. *Re* curability of phthisis, treatment must be pursued for months, and test injections now and again afterwards. *Re* lupus, the effects must be seen to be believed. *Re* joint cases, too soon to give conclusions; subsequent surgical interference necessary; perhaps tendency to relapses averted.
Markham, Skerritt, and Baron, of Bristol.	Dec. 1890.	9 days at Berlin.	Noted variations in reactions; for diagnosis may require more than one injection; in lungs and larynx, dose ·001, with "fever free" days.	Nothing to equal the treatment in bone and joint cases, undoubted benefit also in skin, glands and throat; in phthisis good reason to hope, but not sufficient time to form an accurate estimate.
Weichelbaum, of Vienna.	——	Visited Berlin.	Owing to frequent abnormal results, needs constant supervision.	Important aid to diagnosis. Healing process at least started.
Schnitzler, of Vienna.	——	Visited Berlin; also cases of lungs, joint, gland, and skin in Poliklinic.	——	Symptoms ameliorated.
Drasche, of Vienna.	Dec. 13, 1890.	Austrian delegate to Berlin; also 8 cases of phthisis.	Reactions corroborated; blood changes noted as in severe blood or hepatic disease.	——
Schroetter, of Vienna.	Dec. 13, 1890.	20 cases of larynx and internal disease.	Local reactions almost nil; case of larynx and lung, no reaction after ·025.	No curative effect observed; patients lost weight considerably after prolonged treatment.
Billroth, of Vienna.	Dec. 13, 1890.	Surgical tuberculosis.	Showed cases not reacting.	Well-marked reaction in case of actino-mycosis.
Kaposi, of Vienna.	Dec. 13, 1890.	Lupus.	Similar variations in reactions.	——
Maydl, of Vienna.	Dec. 20, 1890.	Personal experience.	Of 6 perfectly healthy people, 3 reacted; 2 with carcinoma reacted; in 5 of undoubted tubercle, all reacted, but 1 only after 4 injections.	Faith in diagnostic value "seriously shaken."

Observer.	Date.	Experience.	Results.	Remarks.
Rydygier, of Cracow.	Dec. 17, 1890.	Personal experience.	Typical reactions; in almost all, spleen enlarged; frequently slight albuminuria.	Therapeutic effect, especially in bone and joint disease, with open fistulæ; remarkable improvement in larynx cases; diagnostic value corroborated.
Koranyi, Buda-Pesth University Clinic.	Dec. 10, 1890.	10 cases of phthisis and 2 of lupus.	In 1 advanced case, complicated with diabetes. Post-mortem—noticed in lungs extensive œdema; sanguineo muco-purulent mass in large cavity, with hæmorrhagia on walls, and succulent granulations around; similar in other cavities, also numerous caseous nodules surrounded by zone of congestion.	Showing that changes occur in lungs similar to those in lupus. Only minimum doses given. As in case of Fränkel, the diabetes disappeared.
Jürisch, of Innsbruck.	Dec. 17, 1890.	1 fatal case of lupus after ·002.	Striking evidence of the activity of the remedy on all tuberculous foci, *e.g.*, glands in neck and lungs, ulcerated areas throughout intestines, numerous infiltrations in lungs, œdema of brain and chest, acute swelling of spleen, slight swelling of kidneys.	Also hæmorrhage in pleura, pericardium, thymus, cord and brain membranes.
Bottinger, of Munich.	Jan. 13, 1891.	3 tuberculous cows.	Typical reactions absent in 2 healthy bulls, ·1, ·2, and ·3 injected.	Valuable aid to diagnosis in cattle suspected of tubercle.
Chiari, of Prague.	Dec. 23, 1890.	3 post-mortems.	Great accumulations of leucocytes in all foci, with considerable fibrinous exudation round them; marked hyperæmia & ss. hæmorrhage; large masses of bacilli in bronchi, and on bases of intestinal ulcers.	Similar changes to those in skin, as shown by Cornil, though to less degree, showing abnormal exudative inflammation around foci, and tendency to expulsion of bacilli through lungs and intestine. Further extensive observations necessary, before exact conclusions can be drawn.
Wollf, of Görtersdorf Phthisis Sanatorium.	Dec. 27, 1890.	68 cases; 300 injections.	Reaction varied; small doses only needed in acute stage, and seriously ill; only very slight in patients for some time in the open air.	Important to increase the dose gradually; thinks treatment inadvisable in patients feeling well, as it may quicken old capsuled tubercles into fresh activity, and cause development of pneumonia.

Observer.	Date.	Experience.	Results.	Remarks.
Cornil, of Paris Lænnec Hospital.	Nov. 29, 1890 and Dec. 7, 1890.	30 patients.	Reaction corroborated; temporary albuminuria and hæmaturia noticed; changes also in hæmoglobin; seems to act by producing severe peri-tubercular inflammation.	Noticed considerable amelioration, even cicatrisation in lupus; good grounds for hope of equal success in early phthisis. Diagnosis certain, revealing latent tubercle; suggests the local injection of iodoform to kill the bacilli.
	Dec. 10, 1890.	Studying effects on lupus patches.	The injection produces the peri-tubercular congestion seen at the beginning of healing, *e.g.*, enormous quantity of lymphates with abundant serosity.	Remains to be seen if cicatrisation will follow; by injecting iodoform before Koch's fluid, it may reach the bacilli during congestive stage of reaction; otherwise never reaches, owing to fibrinous coagula so common in the vessels.
	Dec. 14, 1890.	—	From 3 cases of lupus, showed that effect on temperature varied in duration, as well as intensity, hence allow sufficient interval to avoid cumulative action.	Referred to Henocque's spectroscopic analyses, and expressed the opinion that where the amount of oxyhæmoglobin is diminished, patient becomes worse and injections are doing harm; thinks that with proper care, little risk of doing any harm; further trial justifiable.
	Dec. 21, 1890.	Summarised results.	In skin, abundant serous exudation on surface of lesion: solidifies and forms crusts, under which is layer of w.b.c., with numerous bacilli. In articular tuberculosis without fistula, there is swelling, tension and pain; where there are fistulæ, serosity may escape. In larynx, extreme caution lest local œdema endangers life; surgical means may here facilitate. In lung cases, indications are extremely limited, in the majority it may be very dangerous. In case of tubercle of epididymis, disease appeared on other side.	Thinks that the congestion produced drives the bacilli outside along with the discharge; improvement, therefore, only in proportion to the ease of elimination. Symptoms here aggravated and results "more than problematical." Results may be better. "Beneficial results may perhaps be obtained." No one should be treated without legal consent. Not to be thought of in acute phthisis. Positively injurious in large cavities; doubtful of benefit in incipient phthisis; fresh consolidations may occur. Hæmoptysis and pleurisy have been produced; not unlikely in quiescent cases to return to activity; may do good in limited number of cures, where cavities communicating freely with bronchi; little fever and not much impairment of general health, if avoid too violent a reaction. Thus must, in lung cases, abandon the greater part of the hopes at first entertained.

Observer.	Date.	Experience.	Results.	Remarks.
Pean, of St. Louis, Paris.	Dec. 6, 1890.	Surgical and skin.	Records an all round amelioration; fistulæ heal up; suppurations diminish; ulcerations granulate.	So far, well satisfied; opinion reserved as to permanency of results.
	Dec. 13, 1890.	Fatal case of T. ischium.	So low that no conclusions drawn.	—
Vidal, of St. Louis, Paris.	Jan. 14, 1891.	32 skin cases.	Reactions far from regular; fluid sets up violent congestion and inflammation in all parts; difficult to forsee.	Organs previously diseased liable to attack; myo-carditis, endo-carditis, bronchial and basal congestions found; advise lessening the dose and increasing the interval.
Henocque, Paris.	Dec. 17, 1890.	Spectroscopic examination of blood in 22 patients.	Oxyhæmoglobin increased in 13, increased in 3, diminished, then increased in 3, unchanged in 3; in proportion to the number rather than the strength of the injections.	Increase seems accompanied by improvement.
Thibierge, of Paris.	Dec. 5, 1890.	Visited Berlin. Lupus.	In all cases, some two months under treatment, was able to discover typical tubercles; saw no case of cure.	Considers that in assuming that absence of reaction meant cure, the Germans have shown more enthusiasm than sagacity; still acknowledges that the injections have a marvellous rapidity of action, and a cicatrising influence upon extensive and rebellious lupus ulcerations.
Cuffer, of Paris.	Dec. 10, 1890.	Visited Berlin.	Saw congestions and symptoms of acute phthisis supervene.	Thinks the effect of the remedy is to produce congestion of the affected parts; this may of course be the starting-point of favourable changes, but no proof thereof up to the present; *contra*, unfavourable changes and accidents cannot be denied.
Rémond, of Paris.	Dec. 10, 1890.	Visited Berlin.	Case of leprosy treated by Joseph, of Berlin; local reaction as in lupus.	Diagnosis had been previously confirmed by microscopic examination.
Ferraud, of Paris.	Dec. 10, 1890.	Examined general effects of the remedy.	Likens results to muscular poison; in phthisis, contra-indicated in extensive disease, adynamia, hæmoptysis, and pyrexial cases.	None of effects justify the belief that it has a curative effect.

Observer.	Date.	Experience.	Results.	Remarks.
De Rechter, of Brussels.	Dec. 7, 1890.	Visited Berlin.	Corroborates general and local reactions; insisting on great caution in internal cases.	Diagnostic value absolutely demonstrated; no question produced remarkable changes in lupus, and favourably influenced joint diseases; but difficult to say how much benefit it did in phthisis.
Crocq.	Dec. 14, 1890.	—	No evidence that it is other than a pyrotogenous agent, producing local reaction, by specially acting on the point of least resistance.	Phthisis and lupus not comparable. In phthisis, very real danger of setting up acute inflammation.
Masius, of Liege.	Dec. 1890.	3 weeks; 10 lung, 1 gland, 3 lupus.	Reaction not proportionate to extent of lesions. Hæmaturia, hæmoptysis, albuminuria, abortion, changes in bacilli, scarlatinaform eruption, all noticed.	Amelioration in 5; aggravation of symptoms in 2; no notable change in 7; time too short for opinion. Abortion after ·1 to ·09.
Casse, Brussels.	Dec. 27, 1890.	4 lupus, 12 hip, 7 Potts, 8 joint, 1 gland, 2 scrofula.	Dose ·001 to ·005, usual reactions; half large abscesses, discharge serous on ceasing in fistulæ; skin wounds healing.	Definite improvement in 3 Potts, 6 hip, 9 previously resected, all improved; 3 cured "for the time;" gland swelling gone; 4 joint improved; 1 lupus "cured;" 2 greatly improved. Of 2 scrofula, corneal ulcers, kerato-conjunctivitis, photophobia, &c., all gone; treatment of incontestable utility in the treatment of tuberculosis.
Eichorst, of Zurich.	Nov. 24, 1890.	Phthisis, lupus, bone.	—	—
Gelbke, of Dresden.	—	—	—	—
Immerman, of Basle.	Dec. 1890.	Phthisis, bone and joint, lupus.	Reactions as usual.	Most wonderful results in lupus. In laryngeal, results justified the best anticipations. Scarcely less astonishing in bone and joint. Least positive, still favourable, in phthisis.

Observer.	Date.	Experience.	Results.	Remarks.
Socin, of Basle.	Jan. 1891.	20 cases, surgical.	Doubts its position as a remedy. Desires accurate reports of effects on animals.	Physiological action wonderfully precise. Knife still the necessary resort, but the new method enables to operate more certainly and more satisfactorily.
Bacelli, of Rome.	Dec. 20, 1890.	27 with phthisis. 3 lupus.	Injected 5 intra-venously; action more rapid, and when hypodermic, failed.	Variable, but encouraging, in phthisis; progressively favourable in lupus.
Cantani, of Naples.	Jan. 1891.	20 with phthisis, 1 gland, 1 joint, 1 lupus.	No "circulating" bacilli found in 20 reactions examined. Virchow's effects rare, occurring in non-injected cases, and easily avoided. Small doses the rule, and no bad effects noticed.	Astonishing improvement in lupus, in phthisis most hopeful. Believes that, by adapting treatment to case, and aiming at local reactions, with minimum general reaction, and combining with open air, diet, &c., real cures will be obtained more easily than hitherto. Possible that it will cure tuberculosis.
Bossi, of Genoa.	Dec. 23, 1890.	Uterine diseases.	Sacro-lumbar pains, with bacilli in discharge; ulcers healed; swellings disappeared.	Most useful in gynæcology for diagnosing tubercle of uterus. Good therapeutic results, without interfering with pregnancy and fœtus.
Bozzolo, of Turin.	Dec. 19, 1890.	7 cases of lung, skin, joint, pleura, and tuberculosis.	Reaction may "hang fire" for 24 hours. Perhaps this explains serious effects when injection repeated. Noticed swelling of spleen, loss of weight, scarlatinaform eruption, acetinuria, epistaxis, albuminuria, pains in chest.	Defers opinion.
Forlanini, of Turin.	Dec. 19, 1890.	7 phthisis cases.	In old case, no reaction after 5 injections up to ·005. In one early case, enormous local reaction, followed by improvement.	In case of tubercle of testicle, so much fluid secreted that operation was necessary.
Salomonsen, of Copenhagen.	Nov. 23, 1890.	Sent to Berlin by Danish Government.	Laid some stress on the pain produced.	Admi s the diagnostic value; not commit himself to therapeutic value; believes that sooner or later the lymph will gain the mastery over the tuberculous process.

Observer.	Date.	Experience.	Results.	Remarks.
Haslund, of Copenhagen.	Dec. 17, 1890.	Visited Berlin. Saw 40 to 50 cases of lupus.	Not seen one completely cured case. Denies that the fluid acts on the deeper nodules. Apparent cures frequently mistaken for real.	Thinks the treatment an auxiliary remedy of the highest value, to be supplemented by surgical treatment.
Uckermann.	Dec. 1890.	At Berlin with Bergmann, Levy, and Krause.	Has caused more deaths from hæmoptysis than any other treatment. Two deaths also in laryngeal cases.	So far, only proven to be apparently reliable diagnostic re-agent. So far, dangerous in larynx cases; fatal in miliary and meningitis; injurious, even dangerous, in phthisis; and without effect in bone cases.
San Martin, ville	Dec. 28, 1890.	Lung, hip, and kidney.	Had to intermit in kidney case from local and general reaction. Astounding local exacerbation in bone and lung case, after 6 injections to ·005.	In 2 other cases, wonderful improvement; also in hip case.
Kinnicutt, St. Luke's, New York.	—	Over 100 cases.	—	—
Jacobi, Mt. Sinai Hospital, New York.	—	Selected cases.	—	—
Virchow, of La Charité, Berlin.	Jan. 12, 1891.	Careful post-mortems on 21 cases—16 phthisis, 1 bone and joint, 1 lung and cancer, 1 empyema, 1 anæmia (pernicious), with old lung and pleurisy, and 1 of tubercular arachnitis.	As in external, so intense redness and great swelling in internal parts; redness of cavity walls, hæmorrhage into cavities and walls. Actual inflammatory processes also, and active proliferations to intense degree, well seen at edges of ulcers, and in near lymphatic glands; also condition of leucocytosis; further, pleurisy, frequently severe, bilateral, and hæmorrhage; in arachnitis case of Henoch (q.v.), colossal and unprecedented hyperæmia of pia mater and brain substance.	The swellings occasionally dangerous, *e.g.*, in larynx. In the lungs—Extensive caseous hepatisation, or peculiar diffuse turbid infiltration, with tendency to excavation. Even fresh tubercle formations, or entirely fresh and uninjured tubercles, present after long course of injections. Lastly—Appearance as if by metastasis of the bacilli. Admits necrotic effect of the lymph in many places, but not universally, *e.g.*, absent in sub-miliary and large tubercles. This increase may be dangerous in ulcers of intestine and of lung. Warns physicians to operate with greater caution in cases where patients have not the strength completely to expectorate the broken down tissue, and the habit of doing so.

Observer.	Date.	Experience.	Results.	Remarks.
Koch, of Berlin. Explanatory paper.	Jan. 13, 1891.	Further experience in 150 cases of various forms of tuberculosis. Publications and private letters.	*Nature of Remedy.*—Pure cultivation of tubercle bacilli produces a pus-forming compound, non-diffusible, and one affecting tuberculous tissue, causing death or necrosis, according to dose. By repeated diluted doses, noticeable improvement attained and disease arrested. This latter he succeeded in obtaining by help of 40 to 50 per cent. solution of glycerine. It contains salts, pigment and ·1 per cent. of unknown extractives, the active principle. Dose found experimentally.	Agreed on all sides that remedy is a very delicate and certain re-agent in searching out hidden, and diagnosing doubtful tuberculous processes. Therapeutically, despite short time, most agree that many patients show improvement, and some are cured; though in too advanced cases it may be dangerous and harmful. *Probable mode of Action.*—The extract in certain concentration produces "coagulation necroses" in living tuberculous protoplasm. By adding certain doses, we can increase this effect where the tubercle bacilli, having already impregnated their surrounding necrosis, extend further. Completely necrosed tissues disintegrate, slough, and where possible, take with them the enclosed bacilli, carrying them outwards. Further, the bacilli are so disturbed in their growth that they die off much sooner than under ordinary conditions. A correspondingly large dose has a deleterious influence even on healthy persons, possibly on the W.B.C., hence the fever and other phenomena.

FIRST OFFICIAL STATISTICS.

The Official Reports demanded by Dr. von Gossler, Minister of Education, from all the Prussian University Clinics and Pathological Institutes, on the efficacy of Dr. Koch's tuberculine, have just been published by Professor Guttstadt. They are 55 in number, including the report of the Municipal Hospital in Moabit, one of the departments of which is under Dr. Koch himself. The reports extend only to the end of 1890, comprise about eight weeks, and contain no final results; but their contents are, nevertheless, of great importance.

During the time in question, about 17,500 injections were made on 2172 patients. The greatest number of injections received by one person was 54, the largest dose 3·826 grammes. Most of the reports contain exact histories of cases. Opinions differ considerably as to the value of the fluid as a diagnostic aid in discovering tuberculosis of the internal organs. Of 1061 patients suffering from internal tuberculosis, 13 were cured, 171 were considerably improved, 194 improved, 586 not improved, and 46 died. Of 708 patients with external tuberculosis, 15 were cured, 148 considerably improved, 237 improved, 298 not improved, and 9 died.

End of the First Summary.

Appendix B.

I have here collated some of the more interesting notes of cases, the course of which I followed from day to day, supplementing them with the criticisms of the surgeon or physician in charge, and such explanatory remarks as seem pertinent to the occasion.

I.—*At the Charité Hospital, with Professors Leyden and Gerhardt, and their Assistants, Klemperer and Roth.*

The wards containing these cases were much overcrowded, and far from commendable from a sanitary point of view. The remedy was tried indiscriminately upon all stages of the disease, with German thoroughness, and with a rapidity and size of dosage, which I did not find anywhere else. It was almost entirely from this hospital that Virchow's observations were derived. There were quite a number of cases in which consolidations broke down (the same was observed in other hospitals, but the moist sounds disappeared under further treatment, and contrary to previous experience and present expectancy, the chest cleared up afterwards). There were also a number of cases with large cavities, in which well marked reactions were obtained, the progress being downwards. It was the course of these cases indeed, which first suggested to me the thought that, in seeking such reactions in such cases, we were following a wrong line of action. Further observations has shown that such is really the case. It is one thing to produce marked effects in lupus and bone and joint disease cases, where free exit is easy, or operative interference intended, and even in early lung cases in otherwise strong subjects, which can stand the reaction, and expectorate the increased amount of sputum; but it is quite a different matter to hamper the action of a vital organ already extensively diseased, by adding to it the congestions, &c., of a strong local reaction. Before I left Berlin, the tendency was rather to deal with such, if at all, upon quite different lines; to shun strong reactions, and to be content with small ones; and for that purpose, once sure your lymph was potent, to give small doses less frequently, and over a longer period, attempting in fact, slowly to vaccinate the part and the system generally, against fresh infection, and slowly to affect the large amount of tuberculous tissue already present. Almost all subsequent experience seems in the same direction.

Thus from my note book, I extract the following cases :—

(*a*) Cavity formed in left axilla since treatment commenced, hectic appeared, injections abandoned, but resumed, up to ·01 cc., temperature still high, lost five pounds in weight.

(*b*) Case of infiltration of the apex, broke down under injections.

(*c*) Two cases of large cavities with strong reactions, getting worse.

(*d*) Case of cavity with *slight* reaction, improved.

(*e*) Case with dulness and moist sounds at right apex, in which the dulness increased after the injections.

Around the room, also, you will find the charts, &c., illustrating the following :—

(1) Æt. 12 ; incipient phthisis, infiltration of both apices, and suffering since July 1890. Treatment started 20th November, 1890, with ·0015, and increased up to ·04 in sixteen doses. Tubercle bacilli numerous throughout ; weight unaltered, 98 lbs. *Case improved*, and note on 19th December, 1890, says, " At bases things are normal ; in other parts, much improvement

(2) Infiltration both apices ; tubercle bacilli absent. On 22nd November, 1890, treatment started with ·002, ending on the 2nd January, 1891, with ·02. On 25th December, 1890, ·04 given, and temperature went up to 41·7° C. 19th December, *little or no change.*

(3) Incipient phthisis ; infiltration right apex ; ordinary case. Treatment started 24th November, 1890, with ·002, ending 31st December with ·05. On 11th December, injection ·20 caused rise to 40° C. *Results, not marked.* Weight 113, 111, 114 lbs.

(4) Æt. 21 ; infiltration left apex, and retraction with bronchial breathing and pleurisy. Treatment started 23rd November with ·003, seventeen doses, to 27th December ; ·09 given then, and no reaction then. *No alteration* in physical signs.

(5) Æt. 26 (medical student) ; infiltration both apices, more on right side. Treatment started 27th November, 1890, with ·002, fifteen doses up to 27th December, when ·09 is given, and no reaction then. No tubercle bacilli found at all after 28th November, 1890. Weight increased from 116 lbs to 120 lbs (German). *Marked improvement ; almost all sound clearing.*

(6) Advanced phthisis ; infiltration of both apices ; tubercle bacilli sparingly present. Treatment started 21st November with

·001, sixteen doses to 31st December, when ·09 was given, with slight reaction. Weight increased from 114 lbs to 117 lbs. *Results, not much.*

(7) Infiltration both apices; bronchitis; copious expectoration; 350 c.c. at start, decreasing slightly. Treated with ·002 on the 24th November, up to ·03 on the 27th December, in thirteen injections; last reaction 38·1° C. *No history of progress given.* Weight increased from 122 lbs through 120 lbs to 123 lbs.

(8) Æt. 21 (smith); dulness, clavicular over and under; early apical phthisis. *History incomplete.* Weight increased 1lb (111 to 112); numerous tubercle bacilli. Treated 27th November, ·002 up to 30th December, ·05 in fifteen doses.

(9) Æt. 36 (doorkeeper); trouble started March 1890; tubercle bacilli numerous throughout; râles in apices; crackles in left apex. Treatment started 27th November, ·002 to ·1 (27th December) in fifteen doses. 23rd December, crackles weaker; 29th December, *all signs less marked, but still perceptible.* Weight, 121 to 127 lbs—gain of 6 lbs.

II.—*At the University Surgical Clinic, under Professor Bergmann, and his assistants, Schimmelbusch and Roth.*

It will be remembered, that Bergmann began by being very enthusiastic in favour of Koch's method. He seems, indeed, to to have expected too much, and perhaps, as a consequence, left off treatment too soon. Hence, in many cases, relapses occurred, which necessitated another course of treatment. Still, his results were such as no previous treatment could approach. Some thirty cases of lupus were under experiment, besides numerous cases of bone and joint disease, &c. Here, also, they were using very large doses, up to ·4; ending, however, by giving less. Most of the cases had been long under treatment, and were well-known as inveterate, and otherwise incurable. The following extracts of cases may be of interest:—

(*a*) *Tuberculous Glands of the Neck.*—Not much altered after five weeks' treatment.

(*b*) *Lupus.*—After seven weeks, immensely improved; local and general reactions good. Simply a reddened glazed skin left after the exudation and scab came off. The affected parts now altogether paler, with superficial scar tissue, and a few nodules left behind the right ear.

(*c*) *Lupus.*—After seven weeks, also immensely improved; redness and swelling gone, but some suspicious brownish elevated spots, which Schimmelbusch thinks may be lupus recedivus.

(*d*) Case of *Lupus* from England.—Colossal reactions; up to 40°-41° C.; dosage being ·008 up to ·4. An old coxitis became painful after the first injection. Now all the crusts have fallen off; the skin, though red, is even and desquamating; altogether wonderful improvement. The chart illustrating these reactions is amongst those open to your inspection.

(*e*) *Lupus* of Nose and Face.—Nodules disappeared after three injections.

(*f*) Case of *Hip-disease.*—During treatment, a lupus patch appeared on the cheek.

(*g*) *Lupus.*—Injected on November 16th; looking splendid.

(*h*) Case of re-appearance after suspension of treatment. Fresh nodules vanishing when treatment resumed.

(*i*) Case of *Lupus* of twenty-nine years' standing.—Immensely improved; twenty-nine injections in seven weeks; now up to ·15. Confirming the opinion that cases where the local reaction is marked, do well.

(*j*) *Child* five years old, with *Hip-disease.*—Operation; quiescent; tested up to ·04 without reaction.

(*k*) *Disease of Carpus.*—No reaction after ·01, but good general and local reaction a week later, after same dose.

(*l*) Disease of *Knee,* in boy aged three.—Good reactions and improvement; erythema, with injection; went up to ·01.

(*m*) In *Hip-disease,* æt. 11; redness over malar bone after injection.

(*n*) Three cases of *Lupus.*—Improvement, but fresh nodules appeared.

(*o*) Tubercular disease of *Lungs, Neck, Arms, and Ribs,* with fistulæ, in young man æt. 22.—Thirteen injections, from ·001 to ·02, then without reaction; looking well; some of the fistulæ closed.

(*p*) In boy æt. 13, Disease of *Skull, Elbow, Knee, Leg, Fistulæ in Neck.*—Thirteen injections, up to ·005, without effect; strong reactions.

(*q*) *Extreme Case of Lupus,* mouth and nose eaten away.—Scraped 111 times. After eight injections upper part healed, but fresh eruption on cessation.

(*r*) Tubercle of *Larynx*, man æt. 31.—From ·002 to ·08, now without reaction. Voice returned; weight increased; great local improvement.

(*s*) *Lupus Erythematosus.*—Injected, but without effect.

(*t*) *Lupus of Face.*—Spot appeared on leg after injection.

III.—*At the University Policlinic, with Professor Senator.*

Here lupus cases and early phthisis cases were treated, between 9 and 10 a.m., in the out-patient department. Professor Senator's name is sufficient guarantee as to the exercise of proper caution. Cases came up, were examined, and, if severe or complicated, admitted into the hospital. The procedure with those treated in the Policlinic was as follows:—Careful notes were taken, the Professor ordered the dosage, the patient was then and there injected, and sent home. Later on, he was visited by a physician, records taken and written in their note books, and the patient advised as to his next day's procedure. The following day he again appeared in the Policlinic, and was examined prior to further treatment. In no case did I hear of any mishap. Both Professor and patient stated that, in nearly all cases, there was improvement both subjective and objective. One was struck here, as indeed in almost all the wards, with the general appearance of comfort, and absence of coughing. Professor Senator was very well satisfied with his results. The average duration of treatment he gave as eight to ten weeks. At his request, I visited one case of lupus eight hours after his first injection. As illustrating his care in ambulatory practice, I may add, that the dose was ·002. The lupus was of thirteen years' standing, and had been extensively treated. I found the patient with the usual local and general reactions well marked. One other case is worthy of record; it was one of lymphoma of neck and right lung, reacting, and said to be improving.

IV.—*At the Urban Hospital, with Professor Fränkel.*

This, and the Friedrichshain, are the two municipal hospitals recently built, regardless of cost, upon the pavilion plan, and with the most recent improvements. It would be difficult to surpass them in any part of the globe; the plan, structure, and arrangements being perfection itself. At the former, I visited mainly the medical cases under Fränkel's care. Here, as in La Charité, almost all the beds were occupied by phthisical cases, and

professors who, as a rule, had grown so tired of watching phthisis tread its downward course, that they had become accustomed to hand all such cases over to their assistants, were now devoting themselves to the unusual task of attempting to do some real good to these hapless sufferers—a token, truly, of the general hopelessness of the disease, and the importance attached to Koch's manifesto. Professor Fränkel was critical, and scientifically sceptical. His cases bore ample evidence to the potency of the lymph, but were not sufficiently advanced to draw conclusions. His dosage was far more cautious than that adopted at the Charité, and his record of effects the most suggestive and complete. He noticed, with others, the marked improvement in symptoms, upon which many dwelt overmuch, but marked the want of equal improvement in physical signs, dwelling, in my opinion, rather too soon upon this delay, and scarcely allowing sufficiently for the fact that alterations in the physical signs were not essential to arrest of disease, and even immunity against fresh attack. The following were among his more interesting cases :—

(*a*) Case in which tubercle bacilli were noticed in the excreta; absent before the injections.

(*b*) Case of nine months' duration, which gained weight, lost bacilli, and generally improved with injections, gradually up to ·1, combined with creasote in large doses, and cod oil.

(*c*) Case of extensive consolidation; bacilli present; gradually injected up to ·02, and still reacting; the bacilli not found on repeated examination; the Professor admitting that he would think it a great result if his creasote treatment produced such effect.

(*d*) Child; phthisis, with pleurisy; doing splendidly.

(*e*) Child, æt. 13; injected ·001 up to ·01; had to stop the injections, because became worse; improved again on small dose, to his surprise.

(*f*) Cases illustrating the effect of the lymph upon the bacilli; first a few, then plenty of bacilli; then a few, then none.

(*g*) Cases illustrating the change in the character of the sputum —nummular, pneumonic, mucous.

(*h*) Case, four weeks in hospital; bacilli disappeared; weight increased two pounds, and no reaction now to ·1.

(*i*) Case of incipient phthisis, nine months' duration; plenty of bacilli in the sputum, though no reaction to ·1.

(*j*) Case, girl æt. 16, with very slight signs; injection gradually up to ·1 in twenty-seven days, with practically no reaction; then with ·1, rise to 104°, hectic, plenty of sputum, lots of bacilli, and locally, breaking down; now again improving very noticeably; typical of several others.

(*k*) Case of diabetic phthisis; injected one month; sugar vanished, but bacilli still present. (In diabetes without phthisis, no effect after ·008).

(*l*) Phthisis, with tubercular otitis; improved by ·007, but bacilli still in discharge.

(*m*) Case of stationary phthisis; injected ·001 to ·1, without reaction.

(*n*) Case of lupus of palate and larynx, with tubercle of kidney; no reaction even to ·07.

(*o*) Case of hæmoptysis; ·1 in seven days, the hæmoptysis lasting three weeks.

Around the room, you will find charts which illustrate the foregoing.

V.—*At the Friedrichshain Hospital, with Professors Hahn and Fürbringer.*

This hospital and its results pleased me most of all in Berlin. The hospital itself is second to none, and its medical and surgical directors seemed to preserve their equilibrium under circumstances which swept away the common sense of many. Both began by being sceptical of the good promised in Koch's lymph, and both found reason, after trial, to entertain a more favourable opinion.

Taking first *Hahn's Surgical Cases.*—It was the clinical sight of my visit to see the number and variety of tubercular cases, daily visible in the superb operating theatre at Friedrichshain, and to watch their general progress towards improvement. In most cases, Hahn had been driven to inject the cases by the entreaties of their friends, operating after seven or eight injections, and finding the injections had been a wonderful help, so that he was able to see all the diseased tissue, remove it with certainty and ease, and leave apparently healthy tissue behind. Later on, however, he thought it better, in some cases at least, to operate first and inject afterwards—the bacilli, &c., escaping through the vent thus produced. He likened the therapeutic use of the lymph to that of mercury in syphilis, and regard its diagnostic

power as practically certain. Out of many, I select the following examples :—

(*a*) *Syphilis* of Elbow-joint.—No reaction with the lymph; good results from mercury and iodide of potassium.

(*b*) *Inflammation of Knee.*—No history of tubercle; no reaction after ·005, but typical reactions after ·01, and bacilli found in the joint.

(*c*) Local reactions well shown in case of *Phlyctenular Conjunctivitis*, followed by improvement.

(*d*) *Tubercular Disease of Pelvis*, with fistulæ.—Results not so good.

(*e*) *Lupus Hypertrophicus.*—Ten years' standing; slight reaction after ·005, then given ·01.

(*f*) *Hip Disease.*—Great reaction; operation; still great reaction after ·003; weight gained and general health much improved.

(*g*) *Lupus in Child.*—Extensive and spreading; injected ·001 to ·004; still reacting, but healed above and below, with clear skin between.

(*h*) *Hip Disease.*—Frequently operated upon; always recurring. Now, after injections up to ·006 and operation, the state of the parts is better than Hahn has ever seen it before.

(*i*) *Knee*, in child $1\frac{1}{4}$ years old.—Sequestrum removed from patella; injected with ·0015. Now, no reaction; great improvement; increased two pounds and a half in weight.

(*j*) *Spondylitis* of Hip in child, aged four.—Great reactions; walked after the seventh injection, and put on three pounds in weight; no other treatment, not even extension.

(*k*) *Knee.*—Anchylosis, with fistulæ, in boy, aged five; injected ·0005 to ·005; resected; healed unusually quickly.

(*l*) Case in which the third reaction was much the largest; typical of many. Further, upon the walls you will find charts illustrating the following :—

(*m*) *Old Coxitis*, with fistulæ, fifteen years' standing; resection before injections; after eight injections ·005 to ·008, the fistulæ healed; great success; seeming cure; reactions always slight.

(*n*) *Chronic Pyo-nephrosis.*—Operated upon without diagnosis of tubercle. Injected ·002 four times, with immediate great reaction; decrease of suppuration.

(*o*) *Lupus of Nose*, three years' duration; often treated, but always recurring. Ten injections ·002 to ·01; great reactions, local and general; very greatly improved.

(*p*) *Knee* in girl, aged eleven and half years; no success from previous operations; seven injections from ·001 to ·006; violent reactions; re-resection; then almost no reactions with the same injections and striking improvement.

(*q*) Typical reactions in lupus after doses of ·005, disappearing after the fourth dose. For these, and for many similar favours, I am indebted to the courtesy of the Resident Officer, Dr. Gumprecht.

Upon the medical side, Professor Fürbringer's cases were equally noteworthy. Unfortunately, however, for me, the visiting days were restricted during my stay, so that my clinical opportunities were minimised. One could not help noticing, however, the tendency to employ small and not increasing doses not oftener than weekly, or at most, twice a week. There was, also, the great care in the selection of cases, and the promptness to abandon the use of the lymph where the disease was becoming worse. The Professor showed several cases "provisionally cured," and many which had progressed better than any in his previous experience. Upon the whole, his results were most encouraging, and his cautious testing of indications for treatment most suggestive. His future records of cases under treatment will, I feel convinced, be of unusual clinical value.

At this hospital, also, I saw one patient who had been operated upon two days previously for pulmonary cavity, and I was present whilst another was similarly treated. In the former, there had been a cavity at the right apex. After the operation, the temperature scarcely rose, but the pulse was 140 and 128, and the respirations 56 and 40 on the two following days. The wound was dressed with iodized mull; there was no drainage-tube, and as yet, the patient had not been injected. The size of the cavity was tested by warm water introduced through a tube, and also by means of a probe. The cavity held 400 cc., and the Professor drew its outline on a black board. An injection of ·001 was ordered, the Professor remarking that if he could be sure of adhesions behind, he would drain the cavity right through. Upon the same day, another case was operated upon. The man, who was pale and anæmic, had a large cavity at the left apex. Under chloroform, the surface was washed with carbolic solution, and a long incision made, great care being taken, by forceps and ligatures, to prevent any bleeding; the intercostals were separated, and a hollow probe attached to a syringe, passed into the cavity. Once sure of the position, a Pacquelin cautery was passed along

its track, and repassed, as the cavity was deep-seated ; the wound was dressed with iodized mull. It remains for the future to show what results may be expected by such procedure.

VI.—*At the Augusta Hospital, with Professor Ewald.*

This is a good, but small, hospital, and I visited the medical cases rather to extend my basis of observation, than to study them in detail. Practically, the results were, upon the whole, very promising, both subjectively and objectively ; rapid improvement seemed frequent, and great care was taken with the dosage. The main question indeed was, not so much the value of the treatment, as the indications for and against its use. The Professor's own account of his experience, is to be found summarised in Appendix A, and supersedes my notes.

VII.—*At the Moabit Hospital, under Güttman and Sonnenberg.*

Here were the cases assigned to Koch himself, and in reference to them, I cannot do better than refer my readers to Guttman's papers, published in December and January (*vide* Appendix A). Taken with Fürbringer's, &c., they will be found to support Koch's contentions as to the value of his lymph, and to show how dosage and frequency of administration are points of supreme importance. I had the opportunity here also of seeing two of Sonnenberg's cavity-operation cases.

VIII.—*At the Hygienic Institute.*

This celebrated bacteriological laboratory I visited first, in the hope of seeing Professor Koch, only to find that he had left fifteen minutes previously for a holiday in the mountains. Upon subsequent visits, I was shown round by Mr. Hankin, to whose work in reference to anthrax and albumoses, I have already referred. Besides seeing Brieger, Fraenkel, Weyl, Shakspeare, and others at work in their separate researches, I had the—to me—unbounded satisfaction of seeing the animals that Koch had rendered immune against tubercular infection, by means of his lymph. It is scarcely too much to call this performance one of the greatest achievements of the century. Apart from all other evidence, it makes it almost certain that it is only a question of time and testing, to confer similar immunity in the case of man. I also saw the animals that Behring and Kitisato had rendered immune against diphtheria and tetanus. Such far-reaching experiments could not but raise one into a new therapeutic atmosphere, where the doings of science seemed about to rival the marvels of tradition.

IX.—*At the Pasteur Institute, with Pasteur, Roux, &c.*

My visit to the corresponding French home of bacteriological research may be appropriately mentioned here. Armed with an introduction from Mr. Hankin, I was welcomed by Dr. Adami, introduced to M. Pasteur, and shown over this model of all laboratories. It may be questioned whether there is any place of greater scientific interest in the Europe of to-day. To look on it was a privilege and an inspiration. Its Annales are among the glories of our time. The matter of greatest interest during the hours of my visit, was the inoculation of some sixty patients against hydrophobia, by M. Roux. The completeness of the arrangements was beyond all praise. One could not help thinking how much Koch himself owed to Pasteur; how worthy a successor he had proved himself to be, and how the success of the parent institute augured well for the fulfilment of the hopes of its German relative.

X.—*At the Victoria Park Hospital, with Dr. Heron.*

To widen my basis of comparison, I visited London for the purpose of ascertaining how far English experience supported Continental. At the time of my visit, Dr. Heron was the authorised and main exponent of Koch's treatment, as far as pulmonary cases were concerned. As suggestive records of his cases are to be found in Appendix A, I will deal here simply with generalities. Dr. Heron was observant and painstaking to a degree. His experience and results may be classed in the same category as Fürbringer's and Güttman's. He was soon led to select his cases, and to observe caution in his dosage; and, as a result, he stated himself that he was more hopeful in his treatment of cases of pulmonary phthisis, than ever before.

XI.—*At King's College, with Mr. Watson Cheyne.*

Here were collected together most of the surgical cases under treatment in London, Mr. Watson Cheyne having been deputed to deal with such. Upon the whole, they bore out the favourable opinions expressed by Hahn, Bardelebin, and others in Berlin. Some were of extreme interest. I take the following from my notes:—

(*a*) Man, aged 30; *Glands in Neck and Axilla* for five years, steadily increasing; eighteen injections up to ·02; strong reactions; operated, and removed cheesy parts with a scraper; all non-cheesy parts had been destroyed; now doing extremely well.

(*b*) Child with *Dactylitis and Sinus in Buttock* for twelve months; seventeen injections, ·002 to ·012; operation; much improved.

(*c*) Child, aged 10; *Disease of Internal Condyle of Elbow.*—Operated upon several times; nine injections, ·003 to ·01; now no reaction; very much improved; sinus almost healed.

(*d*) Child 5, *Knee affected.*—Only first reaction good; extension continued; very much improved.

(*e*) *Lupus*, fourteen years' duration; great reaction after ·002; scarlatina rash; locally, scabs and redness.

(*f*) *Lupus of Thigh and Axilla* in boy of 15; seventeen injections in six weeks, up to ·1; improved immensely at first, now at standstill; still reacting.

(*g*) *Sinus in Os Calcis.*—Twenty-one injections, to ·15, lessened to ·1, because of cardiac pain; no reaction since the ninth; no previous good from any treatment.

(*h*) *Acute Knee-joint* in boy of 9.—Worse with extension; going rapidly to the bad; six injections, up to ·013; immensely improved.

(*i*) Man, aged 22; *Diseased Elbow.*—Opened, scraped, arthrectomy; still septic sinuses and swellings round the joint; sixteen injections, up to ·08; improving.

(*j*) Disease of knee in man of 32; immensely improved after eighteen injections, ·01 up to ·2.

(*k*) Hip, double excision; ·01 to ·1; ever so much better; one sinus healed; only one open sore left.

(*l*) Woman; swollen knee. After two injections, old scrofulous scars on the right arm reacted.

(*m*) *Hip.*—Three weeks' history; could only be drawn up with difficulty; no treatment except injections; in six weeks eighteen injections, ·003 to ·01; good reactions; now all movements possible.

(*n*) *Old Abscess in Elbow.*—Fifteen injections, ·003 to ·02; operation; much easier, and results better.

(*o*) *Lupus* in girl of 26; scraped thirty times; sixteen injections up to ·12; practically healed; no trace of disease left.

(*p*) Disease of os calcis and astragalus in child of eighteen months; eighteen injections, up to ·008; still reacting.

(*q*) *Diseased Elbow.*—Twelve months' duration; getting worse with rest, splints, &c.; after injections, swelling much less, and movement freer.

(*r*) Two cases with septic sinuses, and temperature raised; injections had to be stopped.

(*s*) *Disease of Spine, with iliac abscess.*—Not healing after operation; sixteen injections, ·006 to ·015. Now, the lumbar wound healed, and cannot pass a probe.

(*t*) Hip Disease, with great shortening.—Fifteen injections, from ·002 to ·02 ; one injection on to the hip, followed by a local abscess.

(*u*) Lupus in man of 60.—Great improvement ; still reacting to ·1. Cheyne advised continuing twice a week after local reaction has ceased, to try to establish immunity ; thinks recurrence probable where the dose is abandoned too soon.

(*v*) *Child*, acute disease of Knee.—Injected up to ·02, with only slight reaction. Now, can draw up the knee.

(*w*) *Leper.*—Twelve years' history ; anæsthesia, with contractions of hands and toes ; also, half-way up the leg. After injection, macular rash, bullæ on the legs, loss of pain, and able to open the hand.

XII.—*At the Brompton Hospital.*

Dr. Kershaw kindly showed me the sixteen cases of phthsis, and two of lupus, under treatment at the time of my visit. The experience was too limited to warrant definite conclusions. They were of opinion, however, that early cases showed improvement ; the doses were small, and the reactions slight.

XIII.—*At the London Hospital.*

Dr. Galloway was good enough to show me round. There were only a few cases of phthisis, the doses were small, the reactions slight, the lymph apparently relatively weak. A few lupus cases were reacting nicely, and showing improvement. Altogether, treatment was only beginning.

Appendix C.

Directions for using Koch's Lymph.

The remedy will keep for a lengthened period. The dilutions on the other hand, which have to be specially prepared for the purpose of treatment, are easily destroyed and become cloudy. Fluids which have become cloudy must not be used.

In order to preserve the dilutions, it is necessary to boil them every time the vessel is opened in which they are contained. This is however rendered unnecessary, when the dilution is made with a half per cent. carbolic acid solution.

The dilutions are made by first manufacturing a solution of 10 per cent., which is done by adding to 1 cc. of the lymph, 9 cc.

of distilled water, or of a half per cent. of carbolic acid solution. In the same way, a 1 per cent. solution is prepared from the 10 per cent. solution. In this manner, the necessary dilutions are obtained for the treatment of adults. For children, it is advisable to make further dilutions, for example, to a half per cent.

As the weaker solutions lose in potency by being kept, it is as well to prepare a fresh quantity whenever it is required. If in making the dilutions distilled water is used, then the same must be sterilised by pouring the liquid into test tubes, plugging the mouth of the tube with cotton wool, and allowing the fluid to boil over a gas jet or spirit of wine flame.

The remedy is introduced into the system by means of subcutaneous injections, and experience has shown that the best spots for hypodermic injections, are between the shoulders and in the lumbar regions. The injections are best carried out by means of a sterilised Koch's syringe of a capacity of 1 cc. and divided into $\frac{1}{10}$ cc.

In order to sterilise the syringe, it suffices to wash out the cylinder and the needle with absolute alcohol. By doing this, abscesses are avoided.

If an ordinary Pravaz syringe is to be used, it must be thoroughly sterilised before using by means of absolute alcohol, but even then abscesses are not altogether avoided.

The course of the temperature must be observed, both before commencing the injections, and afterwards. It is necessary to begin taking the temperature every three hours, at least, one day before the first injection, and to see that this is regularly carried out during the whole period of cure.

The injections are to be made in the morning, in order that the effect it produces, particularly on the body temperature, and which only shows itself after some hours, may be observed on the same day.

In cases of pulmonary consumption, the strength of the first injections to be used, should be 0·001 or 0·002 cc. of the lymph; this quantity is obtained by injecting up to one or two division lines of the syringe, with the 1 per cent. dilution.

During the next days, the dose is cautiously increased. In case the fever reaches above 38·5 (101·3° F.), the dose is repeated, or even left off; or if only slight fever, or none at all shows itself, then the dose is increased by 0·001 to 0·002 cc. If at last a dose of 0·01 cc. has been reached, it may be still further increased, while carefully observing the temperature, by 0·01 or 0·02 cc. If the

daily dose has reached 0·1 cc., then as a rule it does not require to be further increased. In only exceptional cases will it be necessary to go as high as 0·2 cc., or more. The injections are continued with interruptions of one or more days, until the symptoms of disease have disappeared.

If the case is one of not very extensive lupus, the first dose may be begun at once at 0·01 cc., and according to circumstances repeated. This same instruction applies to bone-joint and glandular tuberculosis.

The correct preparations of the lymph can only be guaranteed if it is procured direct from Dr. A. Libbertz, Berlin, N.W., Lüneberger Strasse.

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