ing genius. I saw things which, while they excited my admiration, made me also feel ashamed that we in this country, from one circumstance or another, are so greatly behind our German brethren. The researches to which I desire specially to refer are still in progress, and fresh facts are accumulating day by day. As they have not yet been published, I am not at liberty to mention details, but there can be no harm in my saying thus much, that I saw, in the case of two of the most virulent infective diseases to which man is liable, the course of the otherwise deadly disease cut short in the animals on which the experiments were performed, by the injection of a small quantity of a material perfectly constant in character, an inorganic chemical substance as easily obtained as any article in the materia medica. And not only so, but by means of the same substance these animals were rendered incapable of taking the disease under the most potent inoculations; perfect immunity was conferred upon them. I suspect that before many weeks have passed the world will be startled by the disclosure of these facts. If they can be applied to man—though our experience of the different behaviour of Koch's fluid in guinea-pigs and in the human subject makes this a matter of uncertainty until tested by experiment—but if they can be applied to man, the world will be astonished, and the beneficence of these researches will be recognised on every hand. At the present time Koch is engaged in the earnest endeavour to produce his remedy for tubercle by some process which could be divulged without the risk of the public being supplied either with material useless from its inertness, or, on the other hand, with deadly poisons. Koch, I believe, would not have published his method at all, had it not been for great pressure brought to bear upon him, until he could have produced it in a form capable of being revealed in every detail. It is nothing but the fear that, by publishing now the precise mode of preparing this material, he might do immense harm instead of good that prevents him from making it known; and I must say that the carping against Koch on account of what is spoken of as a "secret remedy" can only proceed from absolute ignorance of the beautiful character of the man. But if it should so happen that, as with the other diseases to which I have referred, so with tubercle, complete immunity should be obtained by means of some inorganic chemical substance which anyone can prepare, then would be achieved the complete triumph of the treatment of tuberculosis. And, for my part, I rejoice that we are permitted to look forward with hope to that glorious consummation.

SOME ASPECTS OF PROFESSOR KOCH'S TREATMENT OF TUBERCULOSIS.

BEING AN ADDRESS DELIVERED IN THE WARNEFORD HOSPITAL,
LEAMINGTON, ON DECEMBER 6TH,

By I. BURNEY YEO, M.D., F.R.C.P.,

Professor of Clinical Therapeutics in King's College, London; and Physician
to King's College Hospital.

[DR. BURNEY YEO, after some introductory remarks, expressed his thanks to Professors Ewald and Fraenkel, and to Professor von Bergmann's accomplished assistants, Drs. Nasse and Roth, and added that he had had the advantage of the companionship and co-operation of Dr. Bowles, of Folkestone, during his recent visit to Berlin.]

Our first visit, he continued, was to the clinic of Professor Ewald at the Augusta Hospital, and it was here—thanks to that eminent physician's characteristic courtesy and kindness, as well as to his thorough and painstaking methods—that we were able to make ourselves familiar with the effects of the injection of Koch's fluid in many cases of phthisis, as well as in other diseases. Here, however, as well as elsewhere, it was scarcely possible, so short a time had the patients been under treatment, to observe that any actual curative changes had taken place.....But it was exceedingly interesting and important to note the action of Koch's injections in cases in different stages of this disease.

Advanced Cases of Phthisis.—First, with regard to its action in advanced cases. In some of these cases the reaction to this agent is very severe; a high degree of fever is excited, and occasionally very serious symptoms are observed. In one case I had the opportunity of seeing, after an injection of 2 milligrammes, total collapse occur, associated with violent diarrhoea; and camphor and ether had to be injected to rally the patient. After a second

injection no collapse occurred, and she bore a third injection of 4 milligrammes with only the usual reaction, namely, rise of temperature and pulse (to 140) and much flushing of the face.....This case, I have recently heard, is doing well, notwithstanding the serious symptoms attending the first injection.

In another case of advanced phthisis in this clinic, a woman with a cavity in the upper part of the right lung, and with a very cachectic aspect, much cerebral excitement followed the second injection of 2 milligrammes. She became delirious during the strong reaction that followed, when the temperature rose to between 104° and 105° F.

Early Cases of Phthisis.—In a case of phthisis in the early stage, with strong reaction, hæmoptysis occurred six hours after the injection, though no hæmorrhage from the lung had occurred before.

The Dose necessary to Produce Reaction.—As illustrative of the dose necessary to insure reaction in cases of pulmonary consumption, we observed a case in which no reaction occurred after the three first injections of 2, 3, and 4 milligrammes respectively; but, when 5 milligrammes were injected, the characteristic reaction appeared. We also saw a case of chronic phthisis that had been in Davos for two years, and failed to react to doses of 3, 5, and 8 milligrammes respectively; and there were one or two more cases of undoubted chronic phthisis with bacilli in the sputum that had not reacted to the injections that had been made up to the time of my last visit. Another case in Professor Ewald's clinic that yielded no marked reaction after injection of ordinary doses was that of a highly neurotic young man, with tubercle bacilli in the expectoration, but no well-marked pulmonary physical signs. This was also the case with a gentleman who was in a private sanatorium in Berlin, and whom I had seen in London so long ago as September, 1887. In this case there were evidences of a good deal of pleural thickening, and probably extensive fibroid changes in the left lung. He may, however, have reacted by this time to larger injections.

Another case that reacted very slightly to the injections was that of a medical man I saw in a private clinic with Professor Fraenkel. He had been attacked with tuberculous disease of the right lung twelve years ago; the disease was arrested at Meran, and he remained well for ten years. Two years ago he had a slight return of the former symptoms, with some catarrhal signs over the right apex, but his general health remained good. In this case, also, the very slight reaction might be due to the fact that fibroid changes had occurred in the neighbourhood of the old disease, and that there was very little tuberculous tissue accessible to the circulatory current. Koch has pointed out that his fluid has no effect on necrotic cheesy masses.

There is a case in King's College Hospital now, under my colleague Dr. Beale, with a cavity in one lung, who did not react to the first two injections of 2 and 4 milligrammes respectively, but he has reacted to one of 8 milligrammes.

Laryngeal Tuberculosis.—In Ewald's clinic, as well as in von Bergmann's and in the private clinic of Professor Fraenkel, we saw several cases of laryngeal tuberculosis under treatment. It had been feared that, owing to the swelling and redness observed in cases of lupus, this treatment would be attended with much inconvenience, if not serious risk, in cases of tubercle of the larynx; but, somewhat strange to say, this does not appear to be the case. In the case of laryngeal tubercle we saw in Professor Ewald's clinic there were also physical signs of deposit in the apex of the left lung. The injection produced no oedema of the larynx, and only slight dyspnoea occurred during the reaction. The voice was improved. In von Bergmann's clinic we saw a man with laryngeal tubercle, who had much dyspnoea during the reaction, and being seized with a severe fit of coughing he coughed up a bit of necrotic tissue, in which giant cells were found on microscopic examination. In this case also the voice was much improved. We were also shown a man in this clinic with tubercular deposits and ulcerations of the mucous membrane covering the hard palate; and it was most remarkable to see how, under the influence of the remedy, the deposits could be seen melting away and leaving clean excavations behind. Professor Fraenkel showed us a male patient in whom he had, as he thought, completely removed by the curette a tubercular deposit on the posterior wall of the larynx, but he still reacted to the injection, and it was observed that the excavated part had become swollen, and still, doubtless, contained tubercle. He also showed us a case in which the tubercular deposits in the larynx were disappearing under this treatment.

The Reaction in Various other Cases and its Diagnostic Value.

—In this and some of the other clinics the patients protested that they did not feel ill during the reaction and were able to eat well even with a temperature of 104° . To return to Professor Ewald's clinic, we saw other cases of interest there. There was a case of pleural effusion with enlarged cervical glands, in which the injection was first undertaken for diagnostic purposes to ascertain if the pleurisy was metastatic, and it was concluded to be so from the reaction obtained. In a case of chronic phthisis of ten years' duration, with empyema and pneumothorax, five injections had been given with the usual reaction, no other result was noted than that the patient, who had previously been sleepless, slept better. Another interesting case was one of cystitis, of doubtful etiology, in a young medical student. There was no physical signs in the lungs and no history of gonorrhœa. He reacted strongly to a second injection of 2 milligrammes, and it was therefore concluded that the cystitis was of tuberculous origin. It was interesting also to see here a test injection applied to a case of former excision of the elbow-joint by von Bergmann. A strong reaction ensued together with pain and tenderness in the joint; and in another neurasthenic case with chronic dyspepsia and old

lasted twenty-four hours. The temperature fell to 100° , and again rose the next day to the same point as before, then fell to normal, but rose the following day to 102.6° , and it was not until the third day after the injection that the reaction came to an end. He was then given a second injection of 10 milligrammes, and his temperature again rose rapidly to 105.6° , and fell also rapidly to below normal; this rise of temperature being accompanied by somnolence for about twelve hours. The reaction after this second injection was of much shorter duration, and was quite over the next day, and he was then given a third injection of the same strength. After this injection the temperature did not rise above 104.8° , and he was again somnolent, and it was in this state that I saw him.

Rash: Diarrhœa.—Several instances of the occurrence of cutaneous eruptions were to be seen in these surgical clinics. One was very like the rash of scarlet fever, and was followed by desquamation; another was rough, raised, and patchy. The occurrence of diarrhœa, frequently severe, during the reaction was often observed in the case of children; vomiting was not infrequent.

Technique.—Dr. Yeo then described the technique of the method.

Some Important Questions.—The question we are asking ourselves, and that everyone is asking us, is, What are to be the results of this method of treatment? It is not easy—perhaps it is not wise to attempt—to answer this question at present. Of one thing there can be no doubt; we have in this fluid of Koch's an agent which exerts a specific action on tuberculous processes. A minute quantity, such as from 1 to 10 milligrammes, which produces no effect on non-tuberculous persons, gives rise to the remarkable effects with which we are now familiar in persons affected with tuberculosis.....

Have we here a cure for tuberculosis? and a cure for pulmonary consumption? I put the two questions separately because I do not consider them identical.....In advanced pulmonary consumption we have morbid changes to deal with other than those originally started by the tubercle bacillus, and even if we could destroy every bacillus in the lung as well as the products of their agency, we should in many instances still have to deal with a hopelessly damaged organ. And, even although Koch's treatment may be essential to the arrest of the disease in less advanced cases, hygienic and medicinal measures will be as needful as ever to guide the patient to a permanent cure.....I am disposed, from what I have already seen, to conclude that Koch has not been deceived in the observations on the human subject which he has already made, and that his published conclusions will, in the main, be found just and accurate.

Are there any special dangers in the application of this method? Is the rapid solution of tubercle and the great local reaction which follows the introduction of this fluid into the body always free from danger, in whatever part of the body the tubercle may be deposited? We have seen intense diarrhœa and collapse occur in advanced phthisis after the injection of a small dose of this agent. Is this not due to the local reaction of tuberculous deposit in the intestinal canal, and is there not a risk of perforation of the intestine in such cases from the rapid solvent action of this agent on tubercle? What might we calculate its effects would be in meningeal tubercle and in tubercle of the kidney? Are there no risks of serious hæmorrhage from the lungs by the rapid destruction of tuberculous tissue in these organs? We cannot avoid asking ourselves these questions, and desiring to obtain answers to them. Caution and care in handling the remedy may doubtless minimise these dangers, supposing they really exist.....

That some fatal results should have occurred in advanced cases of phthisis was only what every one must have anticipated. These poor patients are always the first to present themselves as candidates for any new treatment of consumption. I have myself injected this fluid in a small dose—1 milligramme—in a case of advanced pulmonary tuberculosis—a case of extensive diffused infiltration, with scattered pneumonic foci, and with very shallow, rapid breathing, respirations being 42 in the minute, and the temperature ranging about 102° . The case was one of hæmorrhagic phthisis, starting with two large hæmorrhages last July. I did so with much hesitation, fearing the local reaction in the lungs might intensify the distress of breathing; but, instead of this, after the reaction, which was quite characteristic, though mild, the patient's condition seemed improved, and he expressed himself as feeling decidedly better. The only changes in the local physical signs were that the area over which moist crepitations

had been heard was somewhat increased, and the crepitant *rales* had become much louder, coarser and moister.

In another case in which I injected 2 milligrammes, the patient had only just had a severe attack of hæmoptysis, and it was thought by some that the injection might provoke further hæmorrhage; but, on the contrary, the expectoration became freer and more mucous, and without any appearance of fresh bleeding.

Nothing to me is more remarkable in connection with this treatment than the feeling of subjective amelioration which so constantly follows these strong reactions in cases of advanced disease.....

Relapses.—Finally, there is the question of relapses. I suppose there is no doubt that cases of lupus have already relapsed, but this, it seems to me, was to be anticipated. It is too much to expect that with one course of treatment extending over a few weeks only, a disease like tubercle is to be wholly eradicated from the body. Koch himself appears to have expected that relapses would occur, and that a reapplication of the treatment would be in many cases needed.

PERSONAL IMPRESSIONS OF KOCH'S TREATMENT AT BERLIN, WITH EARLY NOTES OF CASES TREATED IN THE ROYAL INFIRMARY OF EDINBURGH.

Read before the Medico-Chirurgical Society of Edinburgh, December 3rd, 1890,

By R. W. PHILIP, M.A., M.D., F.R.C.P.E.,
Physician to the Victoria Consumption Dispensary, and Assistant Physician,
Royal Infirmary, Edinburgh.

I HAD proposed to-night making a communication regarding an extended research into the local therapeutics of the respiratory apparatus. But the publication by Dr. Koch on the 14th November of "A Further Communication on a Remedy for Tuberculosis," and the opportunities afforded by a visit of ten days to Berlin for studying the results obtained, have led me to delay the other in favour of a summary of the impressions produced by this visit. If these should appear imperfect or disjointed, I beg you will allow the short time which has elapsed, and the press of work during the few days since my return, to be the excuse.

I have had an opportunity of observing, more or less fully, some 200 cases in different hospitals, and what I have to say is based entirely upon my personal notes. I take this opportunity of testifying to the courtesy and kindness displayed by the physicians and surgeons in charge.

The fluid—of which, through the personal kindness of Dr. Koch, I have been able to bring home a small quantity, and of which I show you a few drops, is transparent and of brownish colour, resembling an East India sherry. Of its chemical constitution little can be said definitely. But from statements made by Dr. Koch to his Excellency Herr von Gossler, the Minister of Education, and other incidental references, it is probable that it contains one or more of the chemical resultants from the growth in given media of the tubercle bacillus. From what I learned at the Hygienic Institute, it is clear that the process of elaboration and separation is difficult. Koch has stated that it would take months for a good worker to become thoroughly familiar with the method of preparation. This, along with the necessity for uniformity of strength, explains the apparent delay in the distribution of the fluid. There seems every likelihood that, meanwhile, the German Government will keep the preparation and distribution in its own hands.

In its undiluted state, the fluid may be kept indefinitely without change. But when diluted for injection—as it is, usually, with distilled water—it is liable to decomposition, the fluid becoming turbid. This difficulty may be overcome by diluting with a half per cent. solution of carbolic acid. Boiling causes no precipitation, but the addition of alcohol does.

For injection it is generally used in solutions of 1 to 10, or 1 to 100, or 1 to 1,000. The proportion of the solution is, of course, of less importance than the actual dosage. For most internal conditions, such as phthisis, empyema, etc., the treatment is commenced with 0.001 gramme (in delicate patients and children, it may be, with 0.0005 gramme). Comparatively early a relative tolerance is established, and the dosage is increased gradually up

to 0.01 gramme or more. For more superficial conditions, such as lupus, tubercular adenitis, articular tuberculosis, etc., the dose begins usually at 0.01 gramme for the adult, and this is gradually increased up to, say, 0.1 gramme. The rate of increase I found to vary considerably in the hands of different operators and with different patients.

The fluid is introduced subcutaneously. It has apparently no action by way of the stomach. Fräntzel and others have tried its introduction by way of the respiratory passages; but while it was found to be operative, greater difficulty was experienced in regulating the dosage. The seat of injection is quite independent of the seat of lesion. That selected by Koch (at first for convenience, and that the patient might not know what was going on), in the loose fold between the shoulder blades or in the lumbar region, is usually adhered to, though I have frequently seen the injection made into the leg and arm, apparently with equally good result. The instrument in general use is Koch's bacteriological syringe. It has been sufficiently described in the medical papers, so that I need not enter into details regarding it. For rapid clinical work it has disadvantages, which can, in my judgment, be avoided by the use of one of the recently perfected hypodermic syringes, without any risk of harm to the patient, if cleanliness be properly attended to. Already in some of the clinics other syringes are in use. Meanwhile, in the Royal Infirmary, I have preferred to continue Koch's syringe and rigidly to follow all his instructions till the method be fully tested. The injection is practically painless. I have never seen local disturbance occur at the seat of injection, saving slight pain when the patient happens to be percussed over the point of entrance of the needle, it may be on the succeeding day.

Effects of Injection.—On a healthy subject, that is, a non-tubercular subject, injection of so comparatively large a dose as 0.01 gramme produces practically no result. There may be passing, hardly appreciable, *malaise*, with, perhaps, rise of temperature to 100° F. To produce serious symptoms on such a subject, so large a dose as 0.25 gramme is required, as tested by Koch in his own person, when three to four hours after injection there supervened pain in the limbs, fatigue, inclination to cough, and difficulty in breathing, which speedily increased. In the fifth hour a prolonged rigor ensued, and, about the same time, sickness, vomiting, and rise of temperature to 103.8° F. After twelve hours these symptoms abated. The temperature fell till next day, when it was normal. A feeling of fatigue and pain in the limbs continued for a few days, and the site of injection remained similarly slightly painful and red.

In most of the cases of lupus which I saw treated the dose was commenced with 0.01 gramme, except in case of children, or when, in addition to the lupus, there was evidence of other tubercular processes. If internal processes, pulmonary or otherwise, complicated the case, the dose was that given for internal cases. With such a dose, 0.01 gramme, in practically every case results of a most striking character ensued, conveniently divided into general and local.

General Reaction.—This begins to be manifest from four to six hours after injection. It consists in the onset of fever—the temperature rising, often rapidly, to from 102° F. to 105° F., or even higher. Associated with this there is an increase in the pulse rate and in that of the respiration, the latter, as a rule, relatively greater than the former. In one case, where, however, there was undoubted lung complication, and the patient had a correspondingly smaller dose, the respiration became 60 per minute at the height of the reaction. (I have also seen this rate attained in a case under treatment in the Royal Infirmary of Edinburgh.) The patient lay panting for breath, but was not so livid or otherwise disturbed as when a corresponding rate occurs, say, in croupous pneumonia. The pulse, while rapid, was fairly full and perfectly regular. Associated with the increase in respiration, and sometimes apart from it, there is coughing, often troublesome, accompanied, in many instances, by expectoration, even when there has been none previously. Sickness, vomiting, and general *malaise*, of varying degree, occur. In some instances diarrhoea was noted. In some dozen cases I saw a distinct exanthem—something between a roseola syphilitica and measles, but in others more papular. (I have seen this occur twice in the cases I have since injected at Edinburgh.) In a fair proportion of cases an icteric tinge of the skin was distinctly evident. A few appeared to be unusually pale.

More serious manifestations consist in loss of consciousness and delirium (which I have seen at least a dozen times in young children at Berlin and once in Edinburgh), followed by a condition of som-