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

REMARKS

ON

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

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

By PROFESSOR RUDOLF VIRCHOW,
Berlin.

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

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

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

Of the 21 cases which we had up to the end of December, 16 were phthisical in the narrow sense in which the word is usually employed as denoting disease in which the essential element is that the lungs are affected. As regards the

other 5 cases, there were among them an exquisite case of severe bone and joint tuberculosis; a case presenting the peculiar complication of carcinoma of the pancreas, with some small smooth-walled cavities with surrounding induration in the apices; a case of empyema in a lying-in woman, who would probably have died even without the injection; a case of pernicious anæmia with very slight old-standing changes in the lungs and tuberculous pleurisy; lastly, a case of tuberculous arachnitis. The other 16 cases were, as I have already said, cases of pulmonary phthisis, in all of which ulcerative processes of greater or less extent were present; most of them were examples of true consumption.

I cannot now enter into the details of these cases; perhaps I may have an opportunity of doing so at some future time. I may, however, be allowed to make some general remarks on them to the following effect: Just as the activity of Koch's remedy, as seen externally, manifests itself principally in the setting up of very acute irritation in the affected parts, with intense redness and great swelling, so does it also in the internal organs. We have seen very marked instances of this. I have here a preparation which may well be taken as a typical specimen. It comes from the clinic of my colleague, Professor Henoch, and belongs to the case of tuberculous arachnitis already referred to. I may observe that there were also changes in the lungs, consisting in some rather old-standing patches of caseous pneumonia, which might be looked upon as the source of metastatic arachnitis, and a number of recent inflammatory changes. After four injections, in all amounting to 2 milligrammes, the last of which was given sixteen hours before death, the patient (a boy, aged 2½ years) died, and colossal hyperæmia of the pia mater as well as of the brain substance, the like of which I never remember to have seen before, was found. The preparation before you was at first preserved simply in glycerine; it has kept fairly well also in the dry state. It shows on the surface extreme engorgement of the vessels of the pia mater, whilst internally the brain substance is dusky red in appearance. I take this opportunity of mentioning that in this case—the only one, it may be added, of tuberculous arachnitis which has yet come before us for examination—I personally examined the tubercles; I cannot, however, say that I saw any evidence in them of retrogressive changes. The tubercles were very well formed, and presented the usual appearances of meningeal tubercles.

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

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

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

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

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

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

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

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

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

A second change is likewise found in the lungs, which must also be described as inflammatory. It is, in my opinion at least, even more different from what we usually find, although I must here also say that I cannot lay down any universally valid pathognomonic criterion. The pneumonias which develop in the course of phthisis can, as is known, be divided into three different classes. They are either caseous or of the ordinary fibrinous type—these also occur—or catarrhal, the so-called smooth pneumonias in which the essential feature is that accumulations of cells are present in the alveoli. All this is occasionally seen in phthisical patients. I may also remark that pure fibrinous pneumonia, in the ordinary sense of the word, has been present in none of the injected cases.* The caseous form I have already mentioned. Any other variety will approximate in type to one of the

forms which, according to the ordinary ritual, are classified under the head of catarrhal pneumonia. Injection pneumonia has, in fact, points of similarity to the catarrhal variety, but I must say it has also certain differences. The ordinary catarrhal pneumonia, as we find it in phthisical patients, shows accumulations in the alveoli, which can easily be squeezed out, and are relatively fluid in character. Sometimes they are so thin as to resemble jelly, and it was on the observation of this fact that Laennec based his old doctrine that tuberculous infiltration, as he expressed it, begins with a gelatinous infiltration. Here, however, the product is not gelatinous; on the contrary, it is very watery and turbid, and it might be called a turbid infiltration. It reminds one of a phlegmonous condition. In some places it is somewhat thicker; occasionally it has, to a certain extent, the external aspect of caseous infiltration, without, however, attaining the decidedly dry character of the latter, so that if the two are situated side by side there is no difficulty in distinguishing the one from the other. The catarrhal-phlegmonous product is softer, moister, and looser than the other. Among the specimens here exhibited there is a perfectly fresh one, which, besides a colossal ulcerated cavity at the apex, shows caseous, and—if I may use the expression—catarrhal infiltration side by side in the lower lobe. In two other specimens also caseous and catarrhal hepatisation may be seen side by side. Among the 16 cases of last year, there are 7 which show this more diffuse soft hepatisation.

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

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

* Only partial fibrinous hepatisation was sometimes found in conjunction with other changes.

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

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

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

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

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

Even large tubercles show themselves very refractory. We have lately had a very remarkable case, in which tuberculosis of the vertebral column and long bones was present in a boy aged 3 years; large tubercles were also found in the brain. The injections in all amounted to 0.012 g. It was a case from the surgical department in which there was vertebral caries with gravitation abscesses, and many points of disease were present in the joints and long bones of the lower limb. At the necropsy it was found that the boy had an unusual abundance of the so-called solitary tubercles in his brain and cerebellum. As is well known, these tubercles owe their name to the fact

that there is usually only one which may be of the size of a walnut; in this case, however, there was a whole heap, I think seven; they were therefore properly not solitary, but they belonged to that category. They were like large lumps of cheesy matter. Neither in them nor in their vicinity were any considerable changes to be seen. I noticed in their interior some soft places, but these occasionally occur in other cases without anything particular having taken place. At all events, the nodules showed no marked breaking down.

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

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

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

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

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

HOSPITAL FOR DISEASES OF THE CHEST, VICTORIA PARK.

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

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

no reaction whatever. The patient says that he is much better with only a slight occasional cough, no sweats, the shortness of breath has almost disappeared. He has gained three pounds in weight. There are still tubercle bacilli in his sputum. Physical signs: The dulness of the left side has not altered. *Râles* can be heard all over the left front. They are, however, not so numerous nor so liquid as they were at first. On the right side no adventitious sounds could be heard on January 13th, nor were any to be heard over either back.

CASE II. *Phthisis*.—A. D., aged 40, has had thirty-six injections, of which the last twelve have been of a decigramme each. This patient also had a severe reaction on December 27th, with temperature seven hours after injection of 103.8° F., accompanied by thirst, rigor, headache, and *malaise*. He had a second reaction on January 11th, with temperature of 103.8° F. in twelve hours, with rigor, increased cough, headache, and pains in the joints. No reaction since January 13th. Dulness unaltered. An occasional *râle* can be heard on coughing, under the right clavicle and in the right supraspinous fossa, but nowhere else. Tubercle bacilli are still present in the sputum. The quantity of daily expectoration has diminished from 3ij to 3i. He has gained ten pounds in weight since the commencement of the treatment.

CASE VII. *Phthisis*.—H. B., aged 28, has been injected thirty-eight times, the last eleven being of a decigramme each. The patient has gained four pounds and a half in weight. Physical signs, January 13th: Right front, slight dulness, with bronchial breathing above the right clavicle. No adventitious sounds. An occasional creak can be heard in the right supraspinous fossa. Left side: An occasional crepitant sound below the left clavicle. No dulness. In left supraspinous fossa breath sounds harsh, with crepitation after coughing. This case was the first injected for phthisis in this country.

The above cases are those that are about to go away to a convalescent home.

CASE III. *Phthisis*.—B. W., aged 22, has only had twenty-seven injections, of which the last ten have each been of a decigramme. He has only had one reaction, on December 27th. It is remarkable that this case, for the first time on that day, as well as Cases I and II, which had not reacted for a long time previously, should all have shown such considerable reactions. Although a decigramme was injected in each case, yet only in B. W.'s case was it the first time that the injection was of this amount. Owing to increased hoarseness and the presence of an ulcer on the left aryteno-epiglottidean fold, the injections in this patient have been discontinued since January 9th, and potassium iodide in 10-grain doses, with inunction of mercurial ointment, substituted. The patient, however, is not improving, and Dr. Heron proposes shortly to recommence the injections. This patient has been remarkable for the want of reaction to the injections, and Dr. Heron has noticed in two other syphilitic cases that they are very refractory to the fluid. This patient's physical signs are unaltered, and there are still tubercle bacilli in his sputum.

CASE IV. *Lupus*.—L. T., aged 21. Twelfth injection of 12 milligrammes on January 12th followed by a slight local and general reaction. The local condition is much improved and she has gained five pounds in weight.

CASE V. *Lupus*.—E. R., aged 27, has greatly improved.

CASE IX. *Lupus*.—E. F., aged 57. Tenth injection of 12 milligrammes on January 10th, the condition of her face is much improved, and the small patch on the back of the right wrist has entirely disappeared, it being now difficult even to discover the scar. On January 5th a centigramme produced a violent reaction in this patient.

CASE VI. *Phthisis*.—H. D., aged 14, had an attack of pleurisy with effusion on the left side which commenced on December 17th, 1890, during which she lost two and a half pounds in weight. Injections were recommenced on December 30th, and she has had altogether twenty-six injections, the last being 3 centigrammes. There has been no reaction, and the patient's general condition is improving. She has regained the two and a-half pounds weight lost during the pleurisy and added two pounds more.

CASE VIII. *Anæmia*.—A. B., aged 18, left the hospital for Christmas. She returned to be seen last week and was then perfectly well; the swellings in her knees had disappeared, and no signs could be discovered anywhere.

GLASGOW ROYAL INFIRMARY.

REPORT OF CASES UNDER KOCH'S TREATMENT.

[Third report by JOHN LINDSAY STEVEN, M.D., and CHARLES WORKMAN, M.D., Assistant-Physicians to the Hospital.]

IN this report details are given of three fresh cases of which no notes have previously appeared.

CASE V. *Phthisis Pulmonalis: Bacilli in Sputum: Marked Reactions*.—J. McC., aged 38, clothier, married; admitted December 6th, 1890, under Dr. Wood Smith, complaining of cough and expectoration, with debility, but no severe night sweats, of nine months' duration. Expectoration mucopurulent, and examined on two occasions by Dr. Cameron was found to contain bacilli. Cough not severe: no hæmoptysis. Fistula-in-ano three years ago. Family history not tubercular. Physical Examination:—Anterior aspect: flattening, diminished movement, dulness, and numerous fine crepitant and wheezing *râles* in right infraclavicular region. Posterior Aspect: Slight dulness and fine crepitant *râles* at right shoulder. Vocal fremitus equal at both apices in front and behind. Bronchial wheezing *râles* throughout the chest. Urine non-albuminous. Temperature for two days before treatment commenced normal or subnormal. Treatment: From December 8th, 1890, to January 3rd, 1891, seven injections were administered, the highest dose being 0.008 gramme, this having been given on the last three occasions, and the treatment having been commenced with 1 milligramme. A marked reaction followed each injection, lasting on an average about twenty-four hours. The lowest maximum point of the reactions was 102.8°, the highest 104.2°, the latter having taken place upon January 3rd, after the patient had been absent from hospital for a week. Between the first six injections an interval of one, or at most two, days elapsed between each, the temperature during the intervals falling to normal or subnormal. The phenomena of the reaction were strictly typical; nothing unusual in the state of pulse or respiration, the highest pulse-rate having been 132, and respirations 32, during reactions. Injections produced changes in the sputum, and sensations of dyspnoea, as well as pain in the chest. After the first injection sputum became tinged with blood for first time in the illness. *Râles* at right apex not so abundant, and patient considers his general state improved.

CASE VI. *Phthisis Pulmonalis: Bacilli in Sputum: Marked Reactions*.—J. C., aged 23, single, a clerk; admitted December 11th, 1890, under Dr. Wood Smith, complaining of cough and expectoration of nine months' duration. Pleurisy five years ago, since which winter cough. During the last nine months severe cough, dyspnoea on exertion, night sweats, emaciation, debility, and frequent hæmoptysis. Dr. Cameron found tubercle bacilli in the expectoration. Physical Examination:—Anterior Aspect: Flattening, dulness, tubular respiratory murmur, and crackling *râles* over right apex as low as the third rib. Posterior Aspect: Dulness in both supraspinous regions: sonorous and sibilant rhonchi at both bases. Urine non-albuminous. Temperatures for five days before treatment commenced ranged between 98° and 100°. Treatment: Between December 16th and January 2nd seven injections administered, ranging from 1 to 8 milligrammes. Characteristic reactions after each, with the exception of two given on December 26th and 29th, when the temperatures did not go so high as on the other occasions. The most severe reaction took place after 0.008 gramme, administered on January 2nd, when the temperature reached 104.4°, the pulse 140, and the respirations 29; and when the usual temperature level was not returned to till after a lapse of about thirty hours. Nothing unusual observed in the state of pulse or respiration during reactions. Amount of the sputum slightly increased after the first injections, but diminishing somewhat as treatment is continued. After the last injection sputum rusty and pneumonic in character, and much complaint of dyspnoea, and constriction in the chest. In the intervals of injection the temperature curve presents the same characters as noted before treatment was commenced. No great change in patient's general state, except that crackling *râles* are now quite distinct in the left infraclavicular region.

CASE VII. *Phthisis Pulmonalis: Bacilli in Sputum: Ankylosed Hip-joint: Reactions not Characteristic*.—D. K., aged 27, a clerk, single; admitted December 6th, 1890, under Dr. Wood Smith, complaining of cough and expectoration of six months' dura-

tion; frequent hæmoptysis, night sweats never severe, emaciation and debility slight. Morbus coxæ at 8 years of age, operated on by Dr. Hector C. Cameron, and completely recovered from at the age of 18, since which good health till the present illness. Mother died at 45 years of age of bronchitis. Sputum, examined on two occasions, contains bacilli. Physical signs made out by Drs. Wood Smith, Lindsay, Steven, and Workman. Anterior Aspect: Dulness, tubular respiratory murmur, and abundant coarse crackling *râles* throughout the whole inspiratory murmur in right infra-clavicular region. Posterior Aspect: Dulness, loud tubularity, and crackling *râles* (less numerous than in front) in right supra-spinous region. Rest of chest presents nothing remarkable. All the phenomena indicate a very chronic case, not producing much constitutional deterioration. Urine non-albuminous. Temperature for two days before treatment normal or subnormal. Treatment: Eleven injections have been administered, the first of 1 milligramme on December 8th, the last of 0.015 gramme on January 2nd, 1891. On six occasions this patient has received a centigramme or more of the fluid, and the peculiarity of the case consists in the comparatively slight reactions which resulted from these tolerably large doses. On three occasions, however, a distinct rise is recorded, when the temperature curve was elevated to 100.8°, 100.4°, and 100.6° respectively, after doses of 1 centigramme. During these reactions there was nothing noteworthy in the state of the pulse or respiration. After each injection, however, he suffered from sickness and *malaise*; and the last of 0.015 gramme, although not elevating the temperature above 100°, produced a slight hæmoptysis accompanied by considerable uneasiness in the chest. Between the injections the temperature has been mainly normal or subnormal. The patient has not lost in weight, and the condition of his chest is, if anything, improved.

HARVEIAN SOCIETY OF LONDON.

At a meeting of the Harveian Society on January 8th, Dr. J. EDWARD SQUIRE read a paper entitled "Remarks on Some Cases of Phthisis treated on Dr. Koch's Method." He said no doubt a notable epoch in therapeutics was attained. Here was a fluid with a selective affinity for the pathological products of a specific inflammation, itself a product, as was stated, of the micro-organism associated with this special disease. This possibility had long been recognised. It was five or six years since Dr. Wooldridge, from a pure culture of the bacillus anthracis in a liquid proteid material, separated the bacillus by filtration, and found that inoculation of this fluid in animals was protective against the anthrax virus. Encouraged by this success he had commenced similar researches on the tubercle bacillus which were interrupted by his untimely death. Dr. Squire proposed the following theoretical explanation of the limitation of the action of the lymph to tuberculous tissue. He defined active tuberculous tissue as tissue in a condition of inflammation produced by the specific irritation of the products of the vital activity of a colony of tubercle bacilli. Dr. Koch's lymph was believed to contain as its active principle these products of the bacilli, and though not sufficiently powerful to set up a specific inflammatory action in healthy tissues, it was enough, when added to the actively inflamed (tuberculous) tissues, so to increase the morbid changes that death of the part resulted from the intensity of the inflammation (that is, by sloughing). Some details as to dosage were then given. Dr. Squire's remarks were illustrated by eight cases under treatment all of which had been so far benefited. Seven were of phthisis, one a child under Dr. Barlow's care with lupus in the Hospital for Sick Children. The dose must be proportioned to the amount of active tubercle diagnosed rather than to the age of the patient. Children were given a smaller dose to begin with than young adults with limited or recent tuberculous deposit, as they were more easily depressed, and in some children a weak and very frequent pulse followed; in others the reaction was not such as to interfere with their sleep at night. Dr. Squire went on to describe the reaction which followed the administration of the remedy. As bearing out the contention that only tuberculous material was affected thereby, he mentioned two cases where the inflamed area produced by blisters showed no change after injection, whilst a lupus patch in close proximity became red and swollen. In con-

clusion, he emphasised the necessity for a careful selection of cases, and competent supervision of patients throughout the treatment, and especially during reaction.—Mr. D'ARCY POWER said that he had seen one of the lupus cases mentioned by Dr. Squire. A third injection of 6 milligrammes had been given ten hours previously. He was quite appalled by the severity of the reaction, and by the amount of collapse which was produced. He thought that if this case was to be in any way taken as a type of what usually occurred, the very greatest care should be exercised in the selection of suitable patients, and injections should only be given when very skilled nursing could be obtained.—Mr. NOBLE SMITH had watched Mr. Watson Cheyne's cases with great interest, and thought that he had witnessed a marked improvement after injections in cases of tuberculous disease of the hip and elbow. He advocated treatment by rest as well as by injection in patients suffering from joint disease.—Dr. WATERHOUSE narrated the case of a lady with advanced phthisis whose life he thought had been undoubtedly prolonged by Koch's treatment as it was carried out by Mr. Watson Cheyne. After the injections the temperature decreased; there were no night sweats or diarrhoea, and the bacilli disappeared from the sputa, though she still coughed up much lung tissue. A herpetic eruption appeared over one trochanter, however, apparently as a result of the treatment, for it was not a bed sore.—Dr. O'CONNOR, in watching cases which had been injected was struck by the effect which appeared to be produced upon the mucous membranes of the body. He asked Dr. Squire whether in his patients the treatment had produced any symptoms of pneumonia. He also inquired whether any perfectly healthy persons had been inoculated.—Mr. EDMUND OWEN was present at the meetings solely that he might express his thanks to Dr. Edward Squire for the kindness, care and discretion with which he had carried out the injection treatment upon the patients at the Children's Hospital. On the inauguration of the treatment, Mr. Owen had stated that his mind was quite open upon the subject of Koch's remedy. It was still open—wide open. He would briefly say that, as regards the children who were injected, their tuberculous joints had undergone no more improvement than might reasonably have been anticipated from treatment in hospital upon the old lines, with rest in bed and fixation of the limb. There was one child with tuberculous ophthalmia, tuberculous dermatitis of the lip, and tuberculous disease of the knee. The eye got worse under the injections, the lip got better, and the knee swelled a little. It was customary, however, for tuberculous dermatitis to improve under ordinary treatment. As regards the knee, when the local excitement subsided, the chronic affection seemed to be unaltered. During the progress of the injections in a case of tuberculous disease of the hip-joint, an anomalous rash appeared upon the child's body. It was shown as a case of "Koch eruption," and as such was regarded with considerable interest. In due course, however, several other children in the ward broke out in unmistakable measles, on which the real nature of the first eruption was manifested. Had they been ignorant of the fact that Koch's treatment was occasionally associated with a morbilliform eruption, the ward would not be—as was now unfortunately the case—in quarantine. Probably that evening's meeting was the first occasion of an able and scientific paper on a medical subject being illustrated by a quotation from a daily newspaper. He did not blame the author of the essay for making the quotation, but he could not refrain from expressing his regret that members of the profession had so widely used the public press for purposes of advertisement. There seemed to be a desire to struggle into the heaven of notoriety by the aid of Professor Koch's coat-tails.—Mr. MORTIMER said that as Registrar to the Hospital for Sick Children in Great Ormond Street he had carefully watched the cases which had been injected by Dr. Squire. He believed that, if the treatment was to be of service, acute and not chronic cases should be selected.—Surgeon WILLIAM A. MORRIS, A.M.S., said that though he had not gone to the Continent expressly to study Koch's method, during a week he had recently spent in Berlin he had endeavoured to see all he possibly could. He saw Professor Ewald's cases as well as those under the care of Professor Bergmann; and though the selective action of the drug was very apparent in lupus, he did not see a single case where

there was a distinctly favourable result. The remedy, which appeared to be chemically allied to the ptomaines, was a virulent poison, comparable to snake poison; and he fully endorsed the lecturer's opinion that the greatest care should be taken in selecting cases for injection. The results hitherto obtained were those of physiological research rather than practical medicine.—Dr. SQUIRE briefly replied.

ROYAL ACADEMY OF MEDICINE IN IRELAND.

THE meeting of the Surgical Section of the Royal Academy of Medicine in Ireland on January 23rd, is set apart for the discussion of Koch's treatment of surgical tuberculosis. Any Fellows having experience of the treatment, and who wish to make communications not exceeding 10 minutes in length, are requested to communicate at once with Mr. Thornley Stoker, the Secretary to the Section, at 8, Ely Place, Dublin.

GENERAL HOSPITAL, NOTTINGHAM.

SINCE December 13th last, Professor Koch's treatment has been regularly carried out in the General Hospital, Nottingham. About sixteen cases in all have been injected, and some have received as many as fifteen doses. The largest single dose reached has been 4 centigrammes, in a case of tuberculous empyema, which has certainly improved, but is still under treatment. Cases of pleurisy, with and without effusion; early phthisis, with laryngeal affection and without; lupus; tuberculous glands; tuberculous testes; and tuberculous joint affections have been treated. The reactions have displayed all the variations described, including a variety of rashes. No untoward or alarming symptoms have arisen, and the cases are progressing favourably.

THE Staff of the Dorset County Hospital have obtained a supply of Koch's fluid for use in suitable cases.

NOTES FROM BERLIN.

[FROM OUR SPECIAL CORRESPONDENT.]

THE address delivered at the last meeting of the Berliner Mediz. Gesellschaft, on treatment by Koch's lymph, made a great impression on the meeting, and medical circles are keenly excited by Virchow's results, which seem to some to be almost a death-knell to the lymph. Others, again, continue as hopeful as before, and point to cases, in which a continuous improvement can be observed, as the best refutation of all pessimistic views. Burgmaster Ninter of Danzig is one of these steadily improving cases, though the newspapers some time ago reported him much worse, half blind, etc. The fact is, that the treatment is agreeing with him wonderfully well, and that his tuberculous symptoms are improving steadily.

It seems that Minister von Gossler's scheme for the State manufacture and sale of the lymph is not destined to run smoothly. We hear on good authority that differences have arisen in the Cabinet, not only on the "secret remedy" question, but also with regard to the principle involved in a profit to be made out of the remedy by the State.

About a year ago a committee was formed for the erection of a consumption hospital for the poor. In view of Koch's discovery the committee suspended work last autumn; but as Koch himself is the strongest advocate of hospital treatment, the meetings of the committee have been resumed, delegates from the different medical societies of Berlin have been chosen, and it is hoped that, with Dr. Leyden as President, the work will be pushed on successfully.

So many consumptive patients have been and are still travelling to and from Berlin, that there is quite an alarm just now about the danger of infection in railway carriages. The railway companies have issued special instructions as to the cleaning and airing of sleeping cars; and besides this, the Reichsgesundheitsamt (Board of Health) has ordered a scientific examination of the cushions, woodwork, etc., of some of the railway carriages on the most frequented lines, hoping thus to clear up the question a little. If danger should really be found to exist, special precautions will be made obligatory.

ITALY.

THE first case of death among patients undergoing Koch's treatment in Italy occurred at Naples on December 28th. A lad of 18 had been admitted into the Gesù e Maria Hospital, under Professor De Renzi, suffering from very advanced phthisis with large cavities, and so weak that he could not stand on his feet. At his own urgent request he received an injection of half a milligramme on December 23rd, and as there was no reaction a dose of 1 milligramme was administered on the following day; this was followed by slight reaction. On the 26th 2 milligrammes were injected, and more marked reaction ensued. During the night there was abundant expectoration of blood-streaked sputum, with hacking cough. On the 27th the patient was in a very prostrate condition, and, although he rallied somewhat on the morning of the 28th, he died at 9 p.m. from suffocation during a violent fit of coughing.

In answer to inquiries whether the restrictions imposed by the Italian Minister of the Interior on practitioners wishing to use Koch's remedy applied to foreign doctors, the Sub-Prefect of San Remo has stated that they can employ the method among their own countrymen, subject only to such regulations as have been enacted by their respective Governments.

DOSAGE.

DR. CHARLES WORKMAN (Glasgow) writes: In reading the Clinical Notes on a Case of Lupus, by Drs. Morris and Pringle, in the BRITISH MEDICAL JOURNAL of January 10th, I note that they write that: "On November 16th, at 8.45 A.M., he received his first inoculation of 0.01 g., of the ordinary 1 per cent. solution." This would mean that he received one-hundredth of a cubic centimetre of a 1 per cent. solution of the original fluid; that is the ten-thousandth of a gramme. What I think the authors mean (on reading the description) is that the patient was given one cubic centimetre of a 1 per cent. solution, which would be one centigramme of the original fluid.

The same mistake has been made in the tabulated statement, by putting at the heading "Quantity of a one per cent. solution," instead of "Quantity of the fluid (administered in a one per cent. solution)."

HARVEIAN SOCIETY OF LONDON.—The following is a list of the names of gentlemen proposed by the Council as officers of the Society for the year 1891:—*President*: *Mr. H. Cripps Lawrence. *Vice-Presidents*: *M. Handfield-Jones, M.D.; Mr. J. E. Lane; *Mr. C. B. Lockwood; Stephen Mackenzie, M.D. *Treasurer*: *Mr. Malcolm Morris. *Hon. Secretaries*: Mr. D'Arcy Power; *G. William Hill, M.D. *Council*: *Mr. T. Bryant, F.R.C.S.; *Mr. W. W. Cheyne; *Mr. G. P. Field; *J. F. Goodhart, M.D.; *Mr. C. D. Bowditch Hale; *Wm. Winslow Hall, M.B.; W. H. A. Jacobson, M.Ch.(Oxon.); *R. Maguire, M.D.; H. W. Page, M.C.(Cantab.); S. Phillips, M.D.; *M. Prickett, M.D.; *C. T. Williams, M.D. An asterisk is prefixed to the names of those gentlemen who did not hold the same office the preceding year.

LUPUS AND TUBERCULOSIS.—On Tuesday last Mr. Jonathan Hutchinson, F.R.S., delivered the first of a series of three lectures on lupus. The lecture, dealing more especially with its relation to tuberculosis, formed a part of the second course of the London Post-Graduate Lectures, and was held in the theatre of the new Examination Hall on the Embankment. The audience, which numbered about one hundred, included Sir Andrew Clark, Bart., Sir Joseph Lister, Bart., Dr. Henry Monro, Dr. Pye-Smith, Mr. Marcus Beck, Dr. Allchin, and Dr. Abercrombie. At the commencement of the lecture Mr. Hutchinson demonstrated a very interesting case of lupus, one of those borderland cases which seem to serve as connecting links between lupus vulgaris and lupus erythematosus. The lecture was throughout profusely illustrated with drawings from Mr. Hutchinson's boundless store.

BABY FARMING.—A woman named Mitchell, living in Vauxhall, was tried on January 14th at the Surrey County Sessions for gross neglect of two children who had been entrusted to her care, and for whom she had received considerable payments. She was found guilty and sentenced to twelve months' imprisonment. At an inquest held before Dr. Danford Thomas on the body of an infant aged one year and six months, one of the eight children found at 18, Eastlake Road, Loughborough Park, a verdict of manslaughter was returned against a Mrs. Reeves.