

A Thesis.

on

SERUM - THERAPY with SPECIAL REFERENCE to TUBERCULOSIS.

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The method of the treatment of disease by means of Serums or what is now termed Serum - therapy, is of comparatively recent date. In the word treatment one also includes prevention or prophylaxis. Previous to the discovery of the microbic origin of many diseases, no advance could be made in this line of treatment. There is only one exception to this, viz. the production of immunity to variola by means of the production of vaccinia.

The idea presently accepted is that variola and vaccinia are one and the same disease, a modification having occurred in the human form, variola, by passage through an animal, the cow.

The first method practised was the direct inoculation of small-pox, always with the hope that a mild form of the disease would be induced; but this result did not always occur, and besides the induced disease was quite as infectious as the disease, contracted in the usual way. The first vaccination was performed by Jenner in 1796, and it is rather strange that this, the first conferring of immunity to any disease, has remained the most perfect to this day.

In Variola too, no specific organism as a causative agent, has been as yet discovered.

With the discovery of the first bacterium by Davaine in 1850, that of the anthrax bacillus, a decided advance was made, and it was soon followed by the discovery that the organism could be cultivated outside the body, artificially, and also that the disease could be transmitted to animals by means of such cultures.

Specific bacteria have been discovered in the case of many diseases but there are still many in which the presence of organisms, as the causative agents, is suspected.

These micro-organisms exercise their deleterious influence on the tissues by the production of bodies, to which the name toxins has been given. Regarding the nature and composition of toxins, much doubt still exists. They are supposed to be of the nature of albumoses.

Toxines are obtained artificially by cultivating the micro-organisms in suitable culture-media. Some bacteria produce their toxins quite readily, being found in solution in the culture-medium. Others again do not part so readily with them. This latter class is said to have "intracellular toxins". The two best known examples of bacteria with such toxins are the bacillus tuberculosis and the bacillus typhosus. In the first class, those which part readily with their toxins are, the bacillus diphtheriae and the bacillus tetani. By making a culture of the bacillus of diphtheria, the toxins can be obtained free from the germs themselves by filtering. The toxins in solution pass through the filter but the germs remain in the filter. In the production of antitoxines, the toxins obtained as above are injected into certain animals, usually the horse, and the blood-serum of the animal becomes antitoxic.

Thus it will be seen that in the case of diphtheria and tetanus, antitoxines can be obtained readily, but in the case of tuberculosis and enteric fever no such antitoxines can be obtained.

This characteristic creates a difficulty in the serum treatment of tubercular disease at the very start. When a person is treated with the antitoxins of any disease he becomes insusceptible or immune to that particular disease.

The first attempt to confer immunity was in the case of tetanus by Behring and Kitasato. They published their results in 1890. Their experiments consisted in injecting animals with gradually increasing doses of tetanus toxine, when they found that animals so treated were able to stand poisonous doses of the tetanus poison. They also found that no ill effects followed the injection of the serum with an equivalent amount of the poison in a susceptible animal, and that the immune serum conferred immunity on a non-immune one. Lastly they found that an injection of the immune serum, shortly after inoculation with the tetanus bacillus, prevented the occurrence of the disease; i.e. it acted as a curative agent.

The same discoveries were made regarding diphtheria by the same two observers and also by Wernicke. To a serum so rendered immune, the name "Antitoxine" was given.

All antitoxines which have been prepared are specific, that is to say, they only neutralise their corresponding poison.

In the case of diphtheria and tetanus the toxins are extracellular and soluble; hence the corresponding antitoxines are readily obtained.

Antitoxines have no action on the bacteria themselves in the way of destroying or even inhibiting their action. They act by neutralising, in what way it is as yet unknown, their products, the toxins. In the case of those bacteria which

have no soluble toxins, no anti-toxine can be prepared but a serum is prepared which has a direct action on the bacteria themselves, hence called "antibacterial" or "bactericidal" serum. This is prepared by injecting an animal with increasing doses of the bacteria themselves, attenuated or weakened cultures at first being used, but ultimately large doses of the virulent bacteria. This is what is done in the case of the cholera vibrios. Antibacterial serum thus prepared has no power to counteract the toxins already set free by the growth of the bacteria, but it has a direct action on the bacteria themselves, causing their destruction.

Further, there is a class of substances to which the name "vaccines" is given. By the use of vaccines an active immunity is conferred. Here a person is inoculated with the actual bacteria, as in the case of vaccinia. But unfortunately the results obtained in other cases in which vaccines have been used, are not so good as in small-pox.

There is too much risk in using the pure cultures even in small doses, but to obviate this drawback the cultures are attenuated in various ways, or the route of entrance into the body may differ from that by which the disease usually enters.

Vaccines have been employed in the case of hydrophobia, anthrax, typhoid, cholera, plague, etc.

This method of treatment, as practised by Pasteur, has been beneficial in the case of rabies. In rabies the incubation period is long, hence the vaccine has time to act. In the other cases the inoculation has to be done before the

the infection, as the incubation periods are short. The inoculation, however, even made after infection, may modify the disease as is seen in the case of small-pox.

Lastly Koch has used the toxins of the tubercle bacillus, prepared in a special way, under the name of "tuberculin", in the treatment of tubercular disease. Afterwards he brought out another body "new tuberculin" in which the toxic bodies of the tubercle bacilli were dissolved and injected.

These however, will be mentioned later on.

We thus have in Serum-therapy the following agents :-

1. Antitoxines ; whose action is to neutralize the toxins of the corresponding bacteria.
2. Antibacterial Serums; whose action is to destroy the bacteria themselves
3. Vaccines; whose action is to produce the corresponding diseases, in a modified or mild form.
4. Toxines; whose action resembles that of vaccines, evidenced by fever, etc.

I now wish to mention shortly the results that have been obtained in serum-therapy, before taking up that part which relates to tubercular disease.

In speaking of the results obtained by treatment with serums one must always bear in mind the fact that it is a comparatively common occurrence for improvement to take place, or it may be even cure, in a disease without any special treatment at all having been employed, only ordinary rules of health and diet. These remarks too, usually apply more markedly to

tubercular disease than to any other. Everyone has met with cases of tubercular phthisis, in which the patient seems to have more or less suddenly "turned the corner" and started to improve. Evidences of a similar nature are also met with frequently in the post-mortem room, in the shape of healed cavities and other signs of healing in the lungs. These facts must always be kept before one in dealing with any new form of treatment. However, a person inclines to become too sceptical, and here again more so in the case of tubercular disease than any other.

The best known and undoubtedly the most effective anti-toxine at the present time is that of diphtheria. It is used both as a prophylactic and a curative agent. There can be no doubt that since its introduction and use the mortality due to diphtheria has greatly fallen. But to be effective it must be administered at the very start of the disease. Statistics all go to prove that the earlier the antitoxine is administered the less chance there is of a fatal termination.

The above may be said to apply to all diseases in which serums are employed.

In diphtheria you have a disease which lends itself to this form of treatment, because before the toxic effects have been produced the local condition in the throat is well marked and can be readily diagnosed.

In the case of tetanus, however, in which disease an antitoxine is also employed, you have a disease which cannot be diagnosed till the toxins have produced their general

effects upon the central nervous system, evidenced by twitchings or convulsions; hence the antitoxine has not the power that it has in the case of diphtheria. However, there is no doubt that if it could be administered early enough it would be efficacious. Hence as a prophylactic agent it has proved of value.

In hydrophobia or rabies, Pasteur has introduced a method of vaccination and this has proved beneficial. Here also the treatment must be started as soon as possible after the disease is contracted - that is after the bite. The general symptoms must not have started.

In addition to Pasteur's method of vaccination an anti-rabic serum has been introduced by Tizzoni and Centanni, but whether antitoxic or antibacterial is unknown. It is recommended, when it is too late to employ Pasteur's method. Experimentally in animals it appears to have proved beneficial.

Vaccination against small-pox has, of course, proved so far the most successful in this form of treatment.

Plague is a disease the causal organism of which, the bacillus pestis, is of pretty recent discovery and treatment by vaccine and serum only dates back about ten years. Haffkine has prepared a vaccine which is very valuable as a protective agent, but it is recommended that it should not be given during an epidemic of plague, as it appears at first to increase a person's susceptibility. A serum which is curative in its effects has also been prepared by Yersin but it requires to be given early and in large doses. It is also prophylactic to

some extent. In addition to these two agents, a serum has been used by Lustig and a vaccine by Terni and Bandi, but they have not been so much used as the two former ones.

In enteric fever you have a disease the causal agent of which in some respects resembles that of tubercular disease. Thus in both, as has been said previously, the toxins are obtained with difficulty or not at all - they are intracellular.

Chantemesse, however, by cultivating the bacilli in a special medium containing spleen-pulp and bone marrow, is said to have obtained a toxin of considerable potency and from this he has prepared an antitoxin. Good results have been reported from its use. It is said to be antibacterial as well as antitoxic in its action. An antibacterial serum has also been used, but with uncertain results. Lastly, in enteric fever a process of vaccination has been introduced by Wright, and so far the results go to prove that it is preventive to a certain extent and also, as in vaccination against small-pox, when the disease does occur, it does so in a modified or mild form.

In cholera again, we have a disease due to an organism the vibrio cholerae, with intracellular toxins, so that an antitoxin cannot be obtained. Here also, however, a form of vaccination has been employed, with the result that a certain amount of immunity is conferred.

In anthrax an antibacterial^{serum} is used with beneficial results.

Glanders, a disease occurring usually in animals, resembles tubercular disease in some respects. Thus a serum is prepared

termed mallein, analagous to tuberculin. It is used chiefly as a diagnostic agent in animals. In its action it resembles tuberculin. That is to say, in animals affected with glanders, the use of the mallein causes a reaction, evidenced by fever, etc

In the class of diseases caused by the streptococci, including septicaemia, erysipelas, puerperal fever, ulcerative endocarditis etc. the results of serum treatment have so far been disappointing. Perhaps this is due to the fact that there are so many different varieties of streptococci, but one would imagine that if a serum or a vaccine, got from the variety of coccus causing the disease, could be got, good results would follow its use. With a view to overcome this difficulty a serum, termed a polyvalent one, and obtained from several different strains of cocci, has been used but its use has obvious drawbacks. The following diseases have also been treated with antistreptococcic serum, viz; rheumatism, chorea, scarlatina, and pernicious anaemia, but here also the results obtained have been far from satisfactory.

Related to the above diseases is pneumonia, due to the diplococcus pneumoniae. Generally speaking, the results obtained by serum treatment in pneumonia have been unsatisfactory or inconclusive.

The diseases which have just been mentioned, with the addition of tubercular disease, are those in which serum-therapy has made the greatest progress, but there are very many others in which this method has been employed; viz; whooping cough, leprosy, syphilis, malignant tumours, dysentery,

Yellow fever, leuchaemia, hay fever, Grave's disease etc. In some of these - dysentery, hay fever, and yellow fever the results have been to a certain extent beneficial; in the others the results are doubtful and it is difficult to see how in some of these diseases serum-therapy could be of service.

That brings now to speak of serum-therapy in its application to tubercular disease.

Serum-Therapy with special reference to Tuberculosis.

Very many attempts have been made to prepare a serum or vaccine, curative of tuberculosis, but generally speaking, the results, so far at any rate, have not been altogether satisfactory. There are several reasons to account for this.

In the first place as has been mentioned previously, the tubercle bacillus does not lend itself to the preparation of a serum, an antitoxic one at any rate, at all readily. This is on account of the toxins being with difficulty isolated. Again too, we have to deal with a disease in which you very readily get a mixed infection, more particularly when the disease is at all advanced. The mixed infection is very frequently due to streptococci. Thus you see it in advanced phthisis with cavity formation, and also tuberculous joints with discharging sinuses. All serums have a specific action; hence where you have a mixed infection only partial good could be expected to follow the use of the serum. The employment of two would, theoretically at any rate, appear to be of more service.

The above fact points to the necessity for the early

II.

employment of any curative serum in tubercular disease, as in all others; that is to say before there has been time for any mixed infection, which means destruction of tissue.

B.

The tubercle was discovered by Koch in 1882 and he was also the first, in 1890, to prepare from the bacilli a body, termed "tuberculin", believed to be curative in its action. It is prepared by growing the bacilli in a glycerine veal broth, in flat flasks, for six to twelve weeks, a free supply of oxygen being allowed the whole time. The cultures, bacilli and all, are then passed through a porcelain filter and the solution is then concentrated over a water-bath to 1/10 of its volume. The bodies of the bacilli remain in the filter and the thickish yellow fluid contains the poison or all the toxins obtainable. (Hewlett).

Analysis reveals this to be a very complex body, containing among other things, albumoses, alkaloids and extractives. The albumoses are supposed to be the active agents, while the extractives are believed to be the cause of the fever which follows the use of the tuberculin. (Bosanquet & Brit. Med. Journ.)

In 1897 Koch brought out a modification of his "old tuberculin". It is prepared from virulent cultures and is not boiled. It consists essentially of a solution or emulsion of the tubercle bacilli themselves and is prepared as follows:- The bacilli are grown on glycerine serum and the growths scraped off and dried. The dried masses are then triturated for 5 or 6 days. An emulsion is made by adding distilled water and this solution is centrifugalised. The upper slight-

ly opalescent layer is next drawn off with a pipette and is called "tuberculin O" . The residue of powdered bacilli is again dried, powdered and treated with more water. After being again centrifugalised, the upper layer is drawn off and is termed "tuberculin R". This process is continued till all the residue is used up. The fluids thus obtained are mixed and filtered to get rid of the bacilli, and to it 2 per cent of glycerine is added as a preservative. The tuberculin O resembles the " old tuberculin" in causing a reaction in tubercular subjects, local at the site of injection, or rather in the local lesion, and general as evidenced by rise of temperature.

Lastly a third tuberculin, termed "tuberculin A", got by emulsifying tubercle bacilli in a 10 per cent solution of caustic soda has been used, but its use has been discontinued as it gave rise to local abscesses.

Regarding the results obtained by the use of these agents, naturally there has been much diversity of opinion, but on going over the literature on the subject, on the whole one is inclined to think favourably of the remedies. The old tuberculin and the new differ so much in their actions that they have to be discussed separately.

We will take up the older preparation first then, "T" as it is called. When it was first introduced it caused a great deal of excitement and it was generally thought that at last a "cure for consumption" had been found. At first it appears to have been used recklessly and indiscriminately in all cases of tubercular disease, and instead of being followed by good results

was in many cases followed by bad, and in some even by fatal ones. As a consequence it came into disuse for a number of years, but within the last few years it has come to be used again, more or less extensively, and from a better knowledge of its action, better results are being obtained.

It is a pretty well accepted fact that in very many cases of lupus vulgaris, tuberculin is curative. It sets up a local reaction round the lupus patch and gradually the patch is exfoliated altogether, leaving a more or less healthy skin surface below. In addition to the local reaction, it also gives rise to a general reaction evidenced by a rise of temperature. The rise of temperature, however has been found to occur in 90 per cent at least-only in subjects affected with tubercular disease. Hence tuberculin is also useful as a diagnostic agent. Koch himself puts the per centage at 99, but 90 is certainly on the safe side. No bad results seem to follow its use. It is used in this way both in animals and in human beings, and has undoubtedly proved of value. Old tuberculin, therefore is of service as a diagnostic agent and also in the treatment of lupus.

New tuberculin T.R. is only used as a therapeutic agent and in all forms of tubercular disease. It differs from tuberculin O. in causing no local reaction; therefore it would seem to be better to use it in tuberculous phthisis, where a local reaction might be harmful.

Prof. A. E. Wright describes T.R. as a vaccine containing the protoplasm of the bacilli; it will therefore confer an active

Immunity. He has used it extensively and has adopted a new method of dosage depending on the phagocytic power of the white blood corpuscles of the person being treated. He claims to have proved that there exists in the normal serum, and more particularly in the serum of persons successfully inoculated against any micro-organism, an element which enters into chemical combination with the microbe in question, in such a way as to prepare it for phagocytosis. This element he has named an "opsonin". The extent to which any specific opsonin is present in the blood is susceptible of accurate measurement by observation of the rapidity with which phagocytosis of the corresponding organism takes place. In a capillary tube are mixed one volume of the patient's serum, one volume of suspended tubercle bacilli, and one volume of corpuscles from normal blood, citrated to prevent clotting. This tube is placed in an incubator at body heat for twenty minutes, at the expiry of which interval film preparations are made. After appropriate staining, the first 30 or 40 white blood corpuscles which come into view are examined and the number of ingested bacilli in each corpuscle duly noted. A similar count is then made from the contents of a tube similarly prepared in every particular, except that instead of the patient's serum, there is added one volume of serum from a healthy man. The "phagocyte count" of the normal blood is taken as unity and the ratio in which the phagocyte count of the patient's blood stands to the former is called the "opsonic index".

By repeated tests he found that this index varied during

inoculation with tuberculin, and he has described what he calls a period of negative phase which after a few days becomes a positive phase. The positive phase gradually falls away and it is at this period a fresh inoculation should be made.

Immunity is in this way built up. If inoculation is performed during the negative phase, he says that instead of the immunity being raised, it is lowered.

Acting on this hypothesis, he has treated very many cases of tubercular disease with tuberculin R or tuberculin vaccine. In tubercular ulceration of the subcutaneous tissues, in tubercular invasion of the lymphatic glands, bones and joints, and in tubercular disease of the genito-urinary system, in all these he got good results, if not cures. He recommends it especially in local tuberculosis.

Hurry Fenwick also speaks highly of T.R. in tubercular disease of the urinary tract.

The presence of the period of negative phase would explain why in many cases bad results were obtained in the use of tuberculin. One great drawback to the above method is the complicated character of the process, requiring abundance of time and the use of a laboratory, two things not at every ones command.

Regarding the use of tuberculin in tuberculous phthisis I may quote the following, written by Wilkinson. He says:-

" I have used T.R. chiefly, but I have also used the old tuberculin alone or alternately with T.R. It is impossible to give an impression of the results of treatment by mere groups

and tables. Personal experience has a value of its own that cannot be disregarded, and my personal experience in a large number of cases tells me that tuberculin, properly used, has a very high value in the treatment of pulmonary tuberculosis. I have carefully watched the effects week by week for nearly five years, and I assert that while the degree of improvement varies, and the duration of the improvement varies even more, gradual improvement is the almost invariable rule. I have treated nearly 70 cases and I do not remember a single instance in which there was no improvement, provided of course there was no mixed infection. Such uniform improvement under the tuberculin treatment must be due to the tuberculin, for tuberculin was the only uniform remedy. By improvement I mean the cough grows less and less and ceases, the sputum diminishes in quantity, becomes if yellow at first, opaque, white and then clear and frothy and finally ceases. In all cases in stage I (i.e. commencing consolidation) the tubercle bacilli, if found before treatment began, disappeared from the sputum during treatment and later there was no sputum. In many cases in stage 2 (i.e. consolidation with commencing breaking down) tubercle bacilli disappeared from the sputum for months or years or altogether. I never stopped treatment on account of haemoptysis and although there were many cases of severe haemorrhage at one time or other, haemoptysis was extremely rare after treatment. The effect of tuberculin treatment in cases of haemoptysis is worthy of close attention, because if tuberculin has the effect once attributed to it, of causing rapid and extensive soften-

ing, it would surely increase the tendency to haemorrhage. My experience is that it does quite the reverse and that in a striking manner. The rapid and extensive softening, if it has been observed, has been due to mixed infection, not to tuberculin. Mixed infection may certainly cause haemorrhage. Tuberculin treatment, then, is specially indicated in cases of haemoptysis, checking the haemorrhage and preventing its recurrence. Like many observers I have never seen any evidence in favour of the idea that tuberculin may mobilise a dangerous enemy, peacefully sleeping. In no instance did tuberculous meningitis supervene. If then tuberculin does not favour haemorrhage but rather checks it, if tuberculin checks and may completely arrest cough, if tuberculin does not mobilise tubercle bacilli, if tuberculin diminishes expectoration instead of increasing it and causes tubercle bacilli to disappear from the sputum, indicating most surely that so far from favouring disintegration it favours a healing process; if under or after tuberculin treatment patients invariably gain in weight and strength, beyond a doubt all the dangers that were held to be associated with tuberculin treatment vanish into mist. They were ghosts and shadows, unreal and unsubstantial, which no rational being need fear.

I can vouch for improvement in all cases, provided there is no mixed infection. In many cases other physicians have witnessed the effects of the improvement and admitted the improvement. I have not yet seen a case of pure tuberculosis that did not improve greatly."

The above is perhaps optimistic, but on the whole, other observers give pretty much the same account of their cases.

All however, recommend that other means of treatment, hygienic etc. should not be relaxed, during treatment with tuberculin.

At the present time very many men are employing tuberculin according to Wright's method and their results seem to be in favour of the remedy also.

In addition to the various tuberculins, prepared by Koch, various observers have also introduced agents derived from the tubercle bacilli. I merely wish to mention these bodies. Speaking generally their curative or beneficial effects still require further proof, but evidence regarding them is being collected every day.

In speaking of tuberculin it was said that it gave rise to some bad symptoms, or at any rate what were considered bad effects, in the shape of fever, local reaction etc. To obviate this drawback, Klebs in 1894, brought out what he considered to be a purified tuberculin, under the name of "tuberculocoidin". Later he prepared another body termed "anti-phthisin" which has been largely used in America. They are supposed to contain none of the toxines. In artificial cultures, the preparations destroy the tubercle bacilli, bactericidal, and they have also given good results artificially, in animals. Carl von Ruck claims to have got good results with antiphthisin, but much greater evidence is necessary before a definite opinion could be given.

Beraneck also, in 1904, introduced a form of tuberculin which is said to be less toxic than Koch's preparation. He

used a culture medium of veal broth, rendered slightly alkaline with calcium hydrate, and kept at a temperature of 37 to 38 C for a certain time. The culture was then evaporated to a syrupy consistence, in vacuo, without heating. This gave what he called "basitoxin" B.T.* Another toxine was obtained from the bacilli themselves, after washing and drying, by acting on them with orthophosphoric acid. This, he termed "acidotoxin" A.T. A mixture made up of an equal quantity of the two gave Beraneck's serum. Daily injections are said to increase a person's immunity, but here also, more evidence is required, before anything definite could be said about it.

As recently as 1901 Koch brought out a new preparation, containing the actual bodies of the bacilli. He suspended powdered tubercle bacilli in a 50 per cent solution of glycerine, and after standing for some time the supernatant emulsion was poured off and used. Koch himself has got good results with it.

Many attempts have been made to confer immunity by the use of a tuberculo-vaccine. To prepare a vaccine, an attenuated culture of the give organism is required and this in the case of the tubercle bacilli has proved a difficult matter. However, a good number of observers appear to have ~~to~~ succeeded in making such an attenuated culture, and consequently in preparing a vaccine. So far all the attempts have been directed to the rendering of animals immune, by the use of these vaccines; but one would think that they would apply to human beings, if to animals. Thus Trudeau has succeeded in conferring immunity on guinea pigs, and von Behring, on cattle. Here again, however, the subject requires further elucidation.

Of course, as has been said, the T.R. of Koch is really a vaccine.

Then, lastly, attempts have been made to prepare an antitoxine similar to the diphtheritic antitoxine. The difficulty attending this was pointed out before. However, Maragliano and Marmorek claim to have prepared antitoxic serums. Some observers have got good results with Maragliano's but others again have failed to get such results.

Marmorek only brought out his serum in 1903. and he has got good results with it himself. However, much greater evidence is necessary before one could form a definite opinion of their respective merits.

Depending on the mixed infection in advanced cases of tubercular disease being due to streptococci, injections of anti-streptococcic serum have been used and good results have been got in some cases.

--- Notes on Cases treated by a Tuberculo-vaccine. ---

Having thus discussed the progress serum-therapy has made in the treatment of tuberculosis, I now wish to give the results obtained by a serum in a certain number of cases of tubercular disease.

Regarding the nature of the serum, unfortunately I was unable to find out anything. It was described as a sero-tuberculin, and from its action in the cases it seems to be a vaccine

It is administered hypodermically in 2 c.c. doses of graduated strengths. To begin with, 2 c.c. No.1 is injected every second day till five injections have been given. These are

followed by five of No.II, also every second day. Should any rise in the temperature occur, the intervals must be longer. No.III 2 c.c. is injected every day, always provided there is no reaction, when longer intervals are required. No.III may be continued till twenty injections have been given altogether, and is followed by No.IV, No.V. and No.VI. It is only in extreme cases that Nos.V. and VI. are supposed to be necessary.

From later knowledge, I am afraid that some of my cases are not the best that might have been chosen. Some of them, for instance, were undoubtedly beyond all hope of recovery or even improvement. However, I wish to put forward the unfavourable cases as well as the favourable ones, as various facts are to be learned from them.

The treatment commenced in December, 1904 and continued till January 1906, with some intermissions.

My cases were divided into two groups, as regards time of treatment as follows:-

1st. Group.

1. G.W. Advanced tuberculous phthisis with extensive cavity formation, laryngitis and enteritis.
2. A.S. Chronic tuberculous phthisis, in which haemoptysis was the prominent feature.
3. F.M. Advanced tuberculous phthisis, acute, with cavity formation.
4. F.D. Moderately advanced tuberculous phthisis, complicated by cardiac and kidney disease.

5. A.M. Early tuberculous phthisis and chronic tuberculous elbow joint with extensive sinus formation.
6. J.C. Chronic tuberculous elbow and ankle joints, with extensive sinus formation.

2nd. Group.

7. R.E. Chronic tuberculous phthisis, with gastric complication and slight laryngitis.
8. P.M. Advanced tuberculous phthisis-acute.
9. J.M. Tuberculous phthisis, early.
10. W.M. Chronic tuberculous phthisis with marked anaemia.
11. M.B. Advanced tuberculous phthisis-acute.
12. E.B. Tuberculous cervical glands - haemophilia.

Case 1. G.W. M. Age 22. Occupation a steel-worker.

Family History.

One brother died of phthisis, otherwise his family history is unimportant. He is a native of Philadelphia U.S.A.

Previous History.

With the exception of various "colds", patient seems to have enjoyed good health.

Present Illness. 5.12.04.

Patient has been coughing more or less for the last year. His illness began as a "cold". In May 1904 he apparently became worse, and thought a change might help him, hence his being in this country. At that time his cough became worse, the expectoration more abundant and he had a slight haemoptysis. He also began to sweat and to lose his appetite. He was admit-

ted here on Sept. 18, 1904, and since then his condition has gradually become worse. He has become much thinner, and during last month his throat has become affected. For a week, too he has had persistent diarrhoea. A fortnight ago, he complained of pain over the left lung, in the region of the nipple, and examination revealed pleural friction. That to a great extent has disappeared. He says his weight was 9sts.4lbs., before he turned ill, now it is only 6sts.4lbs., a loss of 3 stones.

Present Condition. 5.12.04.

General. Patient's general condition is very bad. He has been entirely confined to bed since admission. He presents a marked malar flush, and emaciation is very marked. His weakness is extreme, the slightest exertion playing him out. In bed, he can only lie in certain positions, usually on his right side or on his back, on account of pain in his left side.

Respiratory.

Inspection and Palpation. Breathing is very shallow and is hurried. The whole chest is flattened and generally speaking badly formed. There is deficient movement, more particularly over the left apex. Over the left apex there is also an increase in vocal fremitus.

Left Lung-Anterior.

Percussion. The percussion note is tympanitic in character, and is most markedly so below the sternal end of the clavicle. There is no dulness in front.

Auscultation. Auscultation reveals the presence of an extensive cavity. It extends as follows, from the first intercostal space to slightly below the nipple, and from mid-sternum

to the margin of the anterior axillary fold, indeed well into the axillary space. These boundaries enclose a circular area, and the physical signs of cavity are best marked in the centre of that area. It was over this area that pain was complained of. The cavity is apparently quite close to the surface. The rales heard are tinkling in character and in addition, bubbling rales are numerous. There is pronounced pectoriloquy. Cavity is also evidenced by change of position of the patient; in certain positions paroxysms of cough are started and also the expectoration of large quantities of sputum.

Right Lung - Anterior.

Here also there is evidence of disease, but ^{not} nearly so far advanced.

Percussion. The percussion note is slightly dull, and as has been said, there is a deficiency in the movements.

Auscultation. Auscultation reveals a harsh respiratory murmur which extends from the apex (supra-clavicular) down to the level of the second interspace. In that same region there are also some crackling rales, to be heard during inspiration.

Left Lung - Posterior.

There is no dulness, but all over there are rales to be heard, moist in character.

Right Lung - Posterior.

In the mid-axillary line, in a line with the nipple, a pleuritic creak is to be heard. The respiratory murmur is good. At the base are a few moist rales.

Sputum, is globular, purulent and contains tubercle bacilli.

Cardiac. There is no heart lesion, but there is a very marked intensification of the sounds, particularly over the pulmonic area, due to the proximity of the large cavity acting as a resonator.

Larynx. For four weeks patient has been troubled with his throat; he has become very hoarse.

Digestive. There has been persistent anorexia. Diarrhoea has been very troublesome, for some time back, and has resisted all treatment.

Weight. 6.12.04. 6 stones 4 lbs.

Treatment and results.

Previous treatment was having no effect on this patient; indeed he was getting worse every day and as a forlorn hope it was decided to try the effects of serum.

Unfortunately an unforeseen event took place in this case. After the thirteenth injection, patient was up being weighed, when he suddenly took haemoptysis and died. The quantity of blood was very small, about 2 oz. death apparently being due to shock. Speaking to him before this occurred, he said he was coughing less and also that he was spitting less. The diarrhoea had also diminished ⁱⁿ. The question might be asked, if the serum had anything to do with the haemoptysis. Koch's tuberculin, at first, was credited with tending to produce haemoptysis, but the opinion now generally held is that it rather tends to prevent the occurrence of bleeding. In this case there was undoubted mixed infection, with a rapid destruction of tissue; inoculations would tend to hasten this process and would thus

tend to the production of haemorrhage.

No reaction followed the injections, as far as was evidenced by rise in the temperature; the patient seems to have been more comfortable, sleeping better at night and coughing less. However, it is difficult to see how the serum could cause that result in such a short time. One has to consider the moral effects of a new treatment, raising the hopes of recovery in a patient.

A post-mortem examination was obtained, and the following is a summary of what was found:-

On the thorax being opened, the Left Lung was seen and felt to be very adherent and was with great difficulty removed. Some of the pleural adhesions were recent, others were old and required cutting. The pericardium was also adherent to the chest wall and the sac was opened up, when the sternum was removed. Lying in situ the apex was seen to be quite collapsed, for 4 inches down, presenting a sac-like appearance, with very thin walls. Over the lower portion the pleura was thickened. After removal and section, a very large thin wall cavity was exposed, occupying practically the whole of the apex. It was empty and the walls were rough and granular looking. Large bronchi communicated with it and a purulent material could be squeezed out of them. A small clot of blood lay in one of these bronchi. Along the floor of the cavity a large blood vessel was exposed, but it was entire. Communicating with this large cavity, was a smaller one, about the size of a plum. This cavity was more recent looking and it was apparently here, that

the bleeding had occurred, as there was a large blood-clot lying in it. All over the lung were cavities varying in size.

There were also some caseous areas, just on the point of breaking down. There was practically no healthy lung tissue, the whole cut surface presenting a yellow caseous appearance.

The Right Lung also presented many small cavities.

The Larynx. On the epiglottis was a small ulcer, but there was no ulceration of the cords.

The Large Intestine presented evidences of tubercular disease, in the shape of ulceration, more or less extensive.

Case 2. A.S. M. Age 29. Occupation a farm labourer - Canada.

Family History.

One of the patient's sister's died of phthisis, otherwise the family history is good.

Previous History.

His chest has troubled him now for $4\frac{1}{2}$ years, and what drew his attention to his chest, was the occurrence of haemoptysis. Previous to that he enjoyed good health. He is not addicted to the use of alcohol.

Present Illness. 5.12.04.

This present illness began $4\frac{1}{2}$ years ago with bleeding. He has become much thinner. All along, the main feature has been haemoptysis. Thus 4 years ago he felt shivery and with a slight cough, he brought up a small quantity of blood. He then underwent hospital treatment for four months, when he was dismissed feeling quite well. But during his stay in hospital he had several recurrences of the bleeding and also an attack of pleurisy in the right side. He remained well till December

1903, when he had a recurrence of bleeding, with a cough and a spit. He also began to sweat slightly. He was again admitted to hospital and has been under treatment ever since. He was admitted to Stobhill in August 1904, and till December, when the serum was started, all his symptoms have become aggravated; his cough has got worse, has expectorated more, has become short of breath, has lost his appetite, and has also lost much flesh. Shortly after admission he had a very severe haemoptysis, and also an attack of pleurisy, this time in the left side.

It will thus be seen that the serum was commenced when the patient was on the down grade.

Present Condition.

General. Patient is markedly thin and pinched looking, and presents an occasional malar flush. Unlike the last case however, the physical signs in the chest are not at all well marked. His present weight is 6sts.4lbs.

Respiratory.

Inspection and Palpation. Generally speaking the chest movements are good, but over the left side there is a slight deficiency, and also a slight flattening. There is also a hollowing out of the supra-clavicular spaces, more particularly the left one. Over the left apex, there is a slight relative increase in the vocal fremitus.

Left Lung.- Anterior.

Percussion. There is no dulness over either right or left lung.

Auscultation. The respiration is of the cog-wheel type,

there being a decided break in inspiration. There is also a slight increase in vocal resonance. No rales are heard till one almost reaches the axillary space, slightly to the outside of the nipple. There, a few fine crepitant rales can be heard, only during inspiration. These are best heard at a point one inch and a half from the nipple, in the 5th. interspace, and extending into the 6th. space.

Right Lung-Anterior.

Nothing is to be made out here; The respiratory murmur is good, both in upper and middle lobes.

Left Lung-Posterior.

Percussion. A dulness and an increased resistance extends downwards from the apex to the level of the 3rd. dorsal spine.

Auscultation. All over the left lung, rales are to be heard, during the first part of inspiration. They are not crepitant, but seem, in character to lie between the crepitant and the sonorous. Vocal resonance is also slightly increased.

Right Lung-Posterior.

There is no dulness, but at the base a few rales are to be heard, similar to those heard in the left lung.

Sputum. It is muco-purulent in character, fairly abundant, and is very often blood-streaked. Examination for tubercle bacilli is positive.

Cardiac. Apex beat is slightly displaced to the right, being felt at the left margin of the sternum. Palpation reveals a fine systolic thrill, and auscultation, a slightly rough ventriculo-systolic murmur.

Treatment and results.

Previous treatment consisted in dieting and hygienic surroundings as applicable to tubercular phthisis. For his various haemoptyses, he had inhalations of amyl nitrite and opiates. But as has been said the patient did not improve.

He had his first injection on December 6.1904, and altogether he had about eighty, including the second series of injections. Previous to this treatment being commenced, the patient was not having a temperature, or only very occasionally, it might rise to 99F in the evening. The serum did not cause any rise in the temperature, indeed after the treatment had been continued for some time, it became steadier. It was noticed in this case and also in the others, that there were few subjective symptoms, connected with the serum. At first there was a complaint of thirst, and also of slight headache and drowsiness. No reaction occurred round the site of injection, and I may say here, that no reaction was noticed, in the cases of local tuberculoses under treatment, except in the glandular case, which will be mentioned later on.

The first thing that struck one in this case, was the great improvement in the rest at night. He would sleep from 9.P.M. till 6.30.A.M., without any coughing. Previously, his cough troubled him during the night, keeping him from sleeping. The sputum also diminished greatly in quantity, and became much lighter in colour. These changes were noticed, gradually occurring, before he had had twenty injections, and there was a continuation of the improvement.

At the end of December 1904, he had a slight haemoptysis. I examined his chest at that time, and did not find any material difference, in its condition. The breathing was still jerky, over the left apex. Behind, I imagined the rales were not so numerous, as they had been, at the first examination. Only once was there a slight elevation in the temperature, but it very soon came down to normal again.

The first series of injections was stopped in May 1905, and the second started in December 1905. During that interval the patient's condition was maintained. His cough troubled him very little, and there was no haemoptysis. His sputum did not amount to an ounce in the 24 hours, and was all expectorated in the morning. He had also increased slightly in weight, the highest being 6sts. 11 lbs., an increase of 7 lbs. All along he has taken his food well. Examination of the sputum, still revealed the presence*of tubercle bacilli.

The condition of his chest, at the last examination, in June this year, was as follows:-

The left lung still shows evidences of disease, but there can be no doubt of there being an improvement. There is no dulness in front, and no rales, only a slight increase in the vocal resonance is detected. Behind there are only a few moist rales to be heard, at the left base, none at the right. At a point opposite the 4th. dorsal spine, the respiratory murmur is slightly rough. The patient himself says he feels well, and that he has only a very slight cough, in the morning. He takes his food splendidly, and has no temperature.

Case 3. F.M. M. Age 20. Occupation, a hawker.

Family and Social History.

This patient's family history ^{dying} is about as bad as it could be - a large family, the majority ^{was} children; one brother who grew up dying of pneumonia, and his mother, of phthisis at the age of 34. His social surroundings were bad also, and his occupation kept him exposed in all weathers.

Previous History.

As a child he had measles, and as a complication, otitis media, with subsequent deafness, in the right ear. Otherwise he seems to have enjoyed good health, till the present illness overthrew him.

Present Illness. 4.12.04.

The present illness dates back 5 years, and the first thing complained of was sweating. After this had lasted for about 5 months, a cough started, and with it, he had an expectoration, which was clear and frothy. Occasionally too, the sputum was streaked with blood, but there was no decided haemoptysis. At this time he underwent hospital treatment, and improved, so that in a year, he was able to start his work again. However he was not able to continue it very long, as his cough started afresh, with a more abundant expectoration, and purulent instead of serous. Again he had hospital treatment, and again he so far recovered that he was able to go out. However, this time as soon as he went back to his old surroundings, he turned ill, and had to enter hospital once more, where he has remained ever since. Since his admission he has been confined to bed, and all his symptoms have been progressing. His cough is much worse,

and the accompanying expectoration is now copious, and his emaciation is progressive. His temperature is intermittent, rising to 102F in the evening. He has had pleurisy in the left side.

Present Condition. 4.12.04.

General. The patient's general condition is very bad, and every day he seems to be getting worse. He presents marked emaciation, weighing only 6sts. 1 lb.. His chest is badly formed, being long and narrow.

Respiratory.

Inspection. Inspection reveals a badly formed chest, with deficient expansile movements, more marked over the left apex. Flattening is also marked.

Left Lung - Anterior.

Palpation. There is slight increase in the vocal fremitus over this apex.

Percussion. The percussion note is as follows;-
Over clavicle - dull. Below inner end of clavicle - also dull.
Below outer half of clavicle - note is tympanitic.

Auscultation. There is a marked prolongation of expiration, and expiration is also very hollow, and blowing in character. At inner end of clavicle there are a few crepitant rales heard best during inspiration, but also at the end of expiration. Vocal resonance is increased, more particularly above the clavicle. It approaches pectoriloquy in character. These signs more or less reach to the level of the nipple.

Right Lung - Anterior.

Percussion. There is no dulness.

Auscultation. Breathing is not of the same hollow type,

as over left apex. The inspiratory portion of the respiratory murmur is better marked. Above level of clavicle and down to the level of the nipple, crepitant rales are to be heard, only during inspiration. There is no increase in the vocal resonance.

Left Lung - Posterior.

Percussion. The percussion note is clear and almost tympanic, at the apex.

Auscultation. The breath sounds^s resemble those in front. There is also a marked increase in the vocal resonance. The base is comparatively clear. No rales are to be heard.

Right Lung - Posterior.

Percussion. There is no dulness. Crepitant rales are heard at the apex, and there is a slight increase in the vocal resonance, revealed by auscultation. In the axilla a few rales are also to be heard.

Sputum, is abundant, but not nummular. It is muco-purulent, and tubercle bacilli are present.

Cardiac. There is nothing abnormal in the condition of the heart, except what is attributable to his general weakened vitality.

Urine, is also normal.

Digestive. The most marked feature here, is the persistent anorexia. Vomiting after food has also been present, but there has been no diarrhoea.

Weight. 6sts. 11lb. Height 5ft. 6½in.

Treatment and results.

Previous to the serum being started, the treatment was

general, a full and suitable diet, and placing patient in the best hygienic surroundings for his condition. Symptoms were treated as they arose - cough, for instance, by means of glycoheroin, &c. But as has been said, no improvement was taking place.

The injections of serum were started on Dec. 7th. 1904, and in all the patient had about 80. This case differed from the last, in the fact that there was a temperature present, and also cavity formation in the left lung.

In spite of his very advanced condition, he seemed to begin to improve right away, and the improvement was much the same as in the last case. That is to say, he began to take his food much better, to cough less, and to expectorate less. It, the sputum very soon dropped to half the amount, and in addition, it became less purulent, till ultimately it was clear and frothy. I examined his chest at the end of December, but was not able to make out much change in it.

However he continued to hold his ground, during the injections. His temperature came down gradually till there was even no rise at night, and he also put on weight.

The first series of injections was stopped in May 1905, and since that time, till December of the same year, he has been gradually improving and gaining weight. The highest point he reached as regards weight was 7sts, a gain of a stone practically. He was also able to be up and to go about the whole day. He presented quite a difference appearance too, being full in the face, and well coloured, instead of being pinched and anaemic. He took his food well, and he also slept well. His cough very

seldom troubled him, and his expectoration was practically nil. Lastly, the condition of his chest showed a great improvement, but it still presented a few physical signs. The sputum still contained a few bacilli.

On December, 6th. 1906; I gave him an injection of No. III serum, and it was followed by a rise of temperature. This however, soon passed off, and I continued the injections, but very soon had to stop them, on account of the reaction continuing to occur. Further too, the condition of the patient seemed to start and go back again, till he was almost as bad as he had been when the treatment was first started. His cough became troublesome again, and with it there was quite an abundant expectoration, and again it was purulent. He also lost weight, became very weak and had to be confined to bed. He had several slight attacks of haemoptysis.

I am inclined to put this relapse down to the serum for the patient began to improve once more, when it was stopped. He was apparently being inoculated to excess. I saw him last on June 19th. 1906, and the condition of his chest then was as follows:-

The right apex showed a few rales during inspiration, and also an increase in the vocal resonance. In the left apex however, were all the signs of active cavity formation, and even more marked, than they had been in December 1904. The bases however were clear.

He had been improving since the injections were stopped, and was able to get up for a short time, as his temperature had fallen considerably.

Case 4. F.D. M. Age 26. Occupation a packer.

Family and Social History.

Evidences of tubercular disease are present in this patient's family. His social surroundings were poor.

Previous History.

Patient ^a appears to have ~~to~~ enjoyed good health, till the present illness started.

History of Present Illness. I4.I2.04.

In this case a right pleurisy was the beginning of the illness, 18 months ago, i.e. July 1903. With the pleurisy there was a troublesome cough and expectoration. At that time he consulted a doctor who told him he was suffering from "decline". At that time also he had a slight haemoptysis, and occasional sweating, which has continued through the illness. He had to stop work, and came into the hospital 8 months ago (April), and has remained ever since. On the whole his condition has improved since admission, the most marked feature of the improvement being the decline of the temperature. At first it was markedly intermittent, but now it only occasionally rises above normal. The sweating has also stopped, and there has been no haemoptysis for some time. The cough is not so troublesome, and there is a corresponding diminution in the amount of expectoration. Since his admission he has had a recurrence of his pleurisy, and with it there was pleural effusion, but this has completely disappeared. His appetite is very poor. During his residence he has been confined almost entirely to bed. He is subject to fainting turns due to the condition of his heart.

Present Condition.I4.I2.04.

General. His appearance is very bad, his face being pale and pinched. He is extremely emaciated, and is short of breath. His present weight is 5sts.7lbs; formerly it was 7sts.6lbs.

Respiratory.

Inspection. The chest movements are deficient, and this is more marked over the left lung. There is quite apparent flattening over this lung also.

Palpation. Vocal fremitus is relatively increased over the left lung.

Left Lung-Anterior.

Percussion. Over the apex there is dulness, with increased resistance.

Auscultation. The respiratory murmur is harsh and blowing in character, with a prolongation of expiration. On deep inspiration moist rales are heard. The vocal resonance is also increased.

Right Lung-Anterior.

The breathing is harsh and jerky, but there is no accompanying rales. The vocal resonance is not increased. The condition of the middle lobe is the same.

Left Lung-Posterior.

The physical signs are not so well marked here as they are in front. Thus at the apex of the left lung, the breathing is harsh, but has no accompanying rales. Both bases too, are comparatively clear, all pleural friction and fluid having disappeared.

Sputum; muco-purulent, and approaching the nummular character. It contains tubercle bacilli.

Cardiac.

There is an increase in the frequency, and an accentuation of the cardiac sounds. The apex beat is displaced to the left and downwards, and is very markedly heaving in character. At the apex beat the heart sounds are booming. As you approach the lower end of the sternum, on the left side, an alteration in the first sound becomes apparent. It is a murmur of a musical character, like a whistle, and is well localised.

Urinary. The urine is loaded with albumen, due to the kidneys being affected secondarily.

Digestive. There have been occasional attacks of diarrhoea, and also vomiting. He has persistent anorexia.

Treatment and results.

Previous treatment was mainly symptomatic, of course, including suitable dieting, and abundance of fresh air. As was previously mentioned there were evidences of improvement, prior to the serum being started, but even then the patient's condition was ~~was~~ very poor. On account of the cardiac and kidney complications, perhaps the case was not altogether a good one for serum-therapy. The first injection was made on December 12th. 1904. and they were continued till May 1905, and patient would have about 50 injections.

As in the other cases, an improvement in all the symptoms was noticed, and the patient himself testified to feeling very much better, but this was probably a purely moral effect. As regards the

regards the temperature no rise occurred during the whole course of treatment. The cough also became much less frequent, and less troublesome, and with it, there was a marked diminution in the amount of expectoration. During the night he rested very much better, and there was a decided improvement in his appetite, and no vomiting nor diarrhoea. Perhaps the most notable feature, however, was the increase in weight, from 5sts.7lbs. to 6sts.8lbs. in June 1905.

As regards his chest condition, an improvement was also noted. The albuminuria had also greatly improved, as estimated by Esbach's albuminometer. All these things, I say, continued to improve, during the injections and for about a month afterwards, when the patient seemed to start and go down the hill again. But his symptoms were more referable to his heart condition, thus oedema began to develop, and the amount of the albumen to increase in the urine. Along with these he had diarrhoea which would not yield to treatment, and persistent vomiting. These conditions continued, more or less persistently till August, the patient getting gradually weaker, when he died.

In this case the improvement during the injections was very marked, and it was strange, that as soon as the serum was stopped this improvement should have stopped. Of course one has to take into account the presence of the cardiac condition, and I am of opinion from constant observation, till the beginning of August at any rate, that it really was the immediate cause of death. His lung condition alone was not sufficient to cause death.

Unfortunately, I was out of the hospital when he died, so had not a post-mortem examination, to verify the condition as found by physical diagnosis.

Case 5. W.M'C. M. Age 39. Occupation a cabinet-maker.

Family and Social History.

There is a history of tubercular disease, his mother died at the age of 44 from bronchitis; a sister aged 16, of phthisis and another sister aged 21, of some chest trouble. His social surroundings have not been very good, living mostly in a crowded house.

Previous History.

As a child he suffered from measles and scarlet fever. When he was six years of age his cervical glands on the left side broke down, and discharged for five years.

Present Illness. 14.2.05.

His chest complaint dates back about ten years. At that time he caught a cold coming out of a hot concert room on a chilly night. He felt shivery afterwards and generally out of sorts; within a week or two a cough began which has not left him since. At first the cough was hard and dry, and what little spit he had was whitish. Eight years ago he had what he calls pneumonia, and it took him three months to recover from this illness. After this illness his cough became worse, the spit more abundant and from being whitish became yellowish in colour. He has had periodical attacks of sweating, but sweating has not been a marked feature. Loss of weight has been a marked feature

however, his former weight having been 12sts. and his present weight only 7sts. 12lbs. Within the last five years his appetite has failed very much, and he has also had occasional attacks of indigestion.

His elbow has troubled him now over four years, starting with pain and swelling. After two years the swelling and redness became worse, so that he underwent treatment in the Western Infirmary for six weeks. He had iodoform emulsion injected into the joint, but afterwards the skin broke down at the point of puncture, and on account of this he attended the ward for dressing. Apparently no advance has been made, and several incisions have been made round the joint at various times.

Present Condition. 14.2.05.

General. This patient is in a poor physical state; he is thin and pinched, and present a malar flush.

Respiratory.

Inspection and Palpation, reveal a flattening and a diminution in the movements, over the left apex. Vocal fremitus is also increased.

Left Lung-Anterior.

Percussion. Over the apex there is a dulness, in the supra and infra-clavicular spaces.

Auscultation. All over the front of the lung are to be heard numerous coarse rales, both during inspiration and expiration. The respiratory murmur is blowing in character, with a prolongation of the expiratory portion. Below the middle of the clavicle the vocal resonance is increased.

Right Lung-Anterior.

Percussion. There is no dulness to be made out.

Auscultation. The respiratory murmur is also accentuated and is accompanied by coarse rales, but to a less extent than in the left lung. The condition does not extend to the middle lobe.

Left Lung-Posterior.

At the apex behind there is also slight dulness. During inspiration similar coarse rales are to be heard and these extend to the lower angle of the scapula.

Over the right apex also, a few rales are to be heard.

Both bases are quite clear.

Sputum. It approaches the nummular type, is fairly abundant and is in white caseous muco-purulent masses. ~~X~~

Cardiac. Heart is quite normal.

Temperature. Since admission on December 10th. 1904. patient's temperature has been unsteady, with evening rises. A month after admission he had his elbow incised and two days later he had a rigor with a temperature of 103.4F. When the injections were started a month later, it was very much steadier, although there were still occasional evening rises.

Weight. When the injections were started his weight was 7sts. 12lbs. and previous to treatment he had been losing steadily as much as one pound in the week.

Right Elbow. 14.2.06.

It was on account of the condition of the elbow that serum-
of
therapy was tried. It has been long standing, and had apparently not benefited much from any previous treatment. The follow-

ing was the condition previous to treatment.

There was extensive sinus formation - one passed inwards right into the joint; another not so deep was situated on the posterior and internal aspect, and lastly one posterior, extending upwards but only involving the superficial structures. From the whole three was a copious discharge which necessitated frequent dressing. The joint was partially fixed in the extended position.

Treatment and results.

It was on account of the local tubercular condition of the of the elbow, that serum was tried in this case. Like some of my other cases again it was a forlorn hope, previous to amputation. The condition in the lung, although troublesome, was ^{not} the outstanding feature. There was nothing special in the previous treatment; it was purely symptomatic; the elbow was dressed with iodoform gauze after iodoform emulsion had been injected into the sinuses. However the patient was steadily losing ground, and there was no improvement in the condition of the elbow. His temperature was unstable, and he was losing weight steadily. His lung condition was also getting worse; his cough was more troublesome, and he did not take his food well.

The injections were started on February 16 1905, and in all 43 were given. The accompanying chart shows the whole course of treatment graphically, and some of the results that were obtained. The first thing noted was the gradual improvement in the temperature. At times a slight reaction was obtained but towards the end of the treatment the temperature

never rose above the normal line, a condition which has been maintained now for over a year. As regards the elbow it began to improve right away, and by the middle of April 1905, was absolutely whole, and I may say here, that when last seen in July of the present year, it was in the same condition. In the end of March 1905, an abscess which formed was opened and drained, but this also had completely healed by the middle of April. I had seen a very large number of such joints, previous to this one, but I never saw one heal as this one did. The discharge became less and less at every dressing and the sinuses gradually filled up, till no packing was required. This condition has been maintained for over a year, so one would imagine it to be permanent. There was no redness nor tenderness surrounding the joint; the cicatrices were quite healthy looking. Of course the joint was firmly fixed in an extended position.

The improvement in his pulmonary condition was also very marked. His cough has gradually improved till now he has practically none. He has also no expectoration to speak of. His sweating has stopped and his appetite is good.

The following was the condition of his lungs in June of this year:- Over the left apex there is flattening and the percussion note is also dull. The vocal fremitus is slightly increased. Auscultation reveals a slight increase in the respiratory murmur and accompanying it a few crackling rales but only during inspiration. There is also a slight increase in the vocal resonance. These physical signs are only present at the extreme apex, and are better marked behind than they are in

DISEASE.

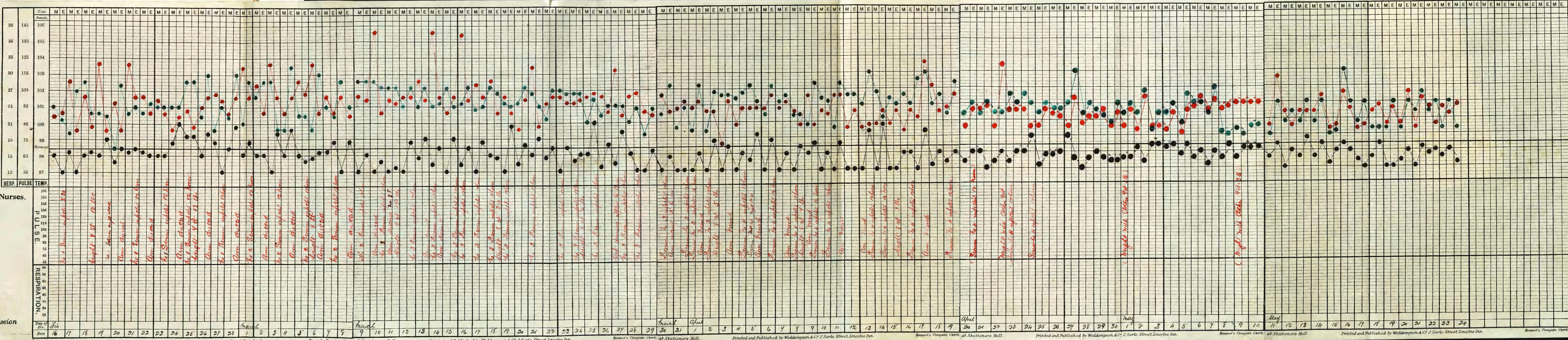
Name
William
McCulloch

Age

Diet

Instructions to Nurses.

Date of Admission



front. Towards the left base a few rales are occasionally to be heard. As regards the right lung there are no physical signs. The only other point to be noted is the weight.

When treatment was started it was 7sts.12lbs., at the end of treatment it was 9sts.11lb., and by the end of July 1905, it had still further increased to 9sts.7lbs.

There is no doubt of the improvement in this case, and I cannot but put it down to the credit of the serum. When it was started things were going from bad to worse, as has been said, and the improvement began as soon as the serum was started.

Case 6. J.C. F. Age 17.

Family and Social History.

In the family history there is nothing of importance. Her social surroundings were poor.

History of Present Illness. 8.12.04.

Patient's first complaint was made three years ago; at that time her right arm, below the elbow, began to trouble her. It was operated on in the Sick Childrens' Hospital, Glasgow, but the nature of the operation could not be discovered. She attended the hospital for two months as an out-patient, when the arm was apparently healed. About six months later, her right foot began to trouble her in the form of swelling. This was operated on in the Western Infirmary, apparently being scraped. There is also a cicatrix over the first interspace, at distal end of metatarsals. She attended the Infirmary as an out-patient for six months, the wound never properly healing. About this time the right elbow started to swell and she was

again admitted to the Western Infirmary in February 1903. After she had been in one week, the right elbow and also the right ankle were again incised, with apparently not much benefit, for during the greater part of 1903, she was in and out of the Infirmary, and had her arm and foot operated on in all four times. Ultimately the right elbow joint was excised, but even after this it did not heal. In November, 1903 the patient fell and hurt her left knee, which thereafter began to swell. It was on account of the condition of her knee that she came into Stobhill Hospital towards the end of 1903. After she had been in a fortnight, an abscess which had formed over the head of the fibula was opened and drained. Sinuses were found leading upwards and downwards, and there was decided evidence to show that the joint was seriously involved. The slightest movement caused very severe pain, and the dressing caused more than the usual amount of suffering. In spite of the draining the disease continued to advance, so the patient was put under chloroform and very free incisions were made, all round the joint. This operation afforded a certain amount of relief, but the joint was hopelessly destroyed, so in July, amputation was performed at the middle of the thigh. At the time of admission, the right elbow was discharging freely and there were sinuses passing inwards to the bone, the joint having been excised. This condition has gradually improved till now there is only a very small surface, the sinuses having almost closed and there being very little discharge. In the right ankle, however, the condition has gradually got worse. At one time it would seem

to improve, but very soon would start to retrograde. There is extensive necrosis of the tarsal bones, mainly the astragalus. At first there was a discharging sinus over the first interspace, but this is now healed. At the time of her first operation the ankle bones were scraped, but this did not seem to do much good.

When the patient was admitted she was in a very poor state of health, but since the amputation of her leg she has improved very much. Her temperature which at first was of a hectic type has now become normal. She has also put on flesh and takes her food well. Still she had the right ankle, in a very bad condition so much so that amputation was spoken of, but it was first decided to try the effects of serum.

Present Condition. 8.12.04.

Her present condition has been given above, the only fact requiring to be added being her weight, which was 5sts.13lbs.

Respiratory and Cardiac.

Both lungs and heart are normal as are the other organs in the body.

Treatment and results.

The previous treatment has been pretty well indicated under "History of Present Illness".

The injections of serum were commenced on December 7th.1904 and altogether patient had about sixty injections. During the course of the treatment, after the 13th. injection she developed a sore throat, with a temperature. In three days, however, she was all right again. With the exception of the above no

reaction local or general followed the injections. Like some of the other cases she complained of thirst but otherwise nothing was noticed.

Regarding the ankle, it gradually improved, the sinuses filling up, and the discharge becoming less, till ultimately the joint was quite whole. The same remarks apply to the elbow. During the injections the same dressing was continued as before treatment, viz. packing with iodoform gauze, and a dry iodoform dressing. Of course, the joint was stiff. The condition had been maintained when the patient was last seen in June of this year.

Along with this local improvement there was also a marked general improvement, best shown by the increase in weight; from 5sts.13lbs. it had increased to 8sts.7lbs. in July, 1905. That weight, too, has been maintained to the present time.

Case 7. R.E. M. Age 44. Occupation a galvanizing worker.

Family History.

This patient's family history is good, both his father and mother living till they were eighty years of age, and the other members of the family being healthy.

Previous History. 30.10.05.

Patient says he has enjoyed good health till four years ago, when he had pneumonia of the right lung. His present illness dates from that time, he never having been well since. The more acute attack lasted seven weeks.

Present Illness. 30.10.05.

As has been said above, his present illness began with

pneumonia, four years ago. Ever since then he has had more or less of a cough, with at times a blood-streaked expectoration, during the first three years. Sweating has also been a prominent feature, and shortness of breath, on the slightest exertion and even when at rest at times. The loss in weight has amounted to about a stone.

For the last six or seven weeks, there has been a complaint of hoarseness, and difficulty in swallowing. He cannot lie with any degree of comfort on his left side. There has been a complaint of gastric disturbance, in the shape of pain and a feeling of uneasiness after taking food.

Present Condition. 30.10.05.

General. Unlike the previous cases, this patient is very well nourished and presents a flushed appearance, probably due to the employment which he followed. His present weight is 8sts.111bs.

Respiratory.

Inspection and Palpation. Generally speaking the respiratory movements are good, and there is no great wasting, except slightly in the supra-clavicular spaces. There is no difference in the vocal fremitus in the two lungs.

Right Lung - Anterior.

Percussion. Over the right apex, there is slight dulness.

Auscultation. Here, also there is a defective respiratory murmur, and on deep respiration, crackling rales can be heard, only during the latter part of inspiration. These extend all over the front of the upper lobe, down to the margin of the middle one. There is no increase in vocal resonance.

Left Lung - Anterior.

Here there is only a slight bronchitis, as evidenced by the presence of rhonchi, all over the front of the left lung.

Right Lung - Posterior.

Percussion. Over the apex there is a relative dulness.

Auscultation. The respiratory murmur is harsh in character but has no accompanying rales.

At the left base the respiratory murmur is harsh in quality, and all over the left lung rhonchi are to be heard.

As has been said there is marked shortness of breath.

Sputum. The sputum is muco-purulent, and as regards amount, averages 9ozs. in the twenty-four hours. Examination for tubercle ^{B.} is negative.

Cardiac. Heart is quite normal.

Digestive. For some time back, there has been a complaint of loss of appetite, and pain and discomfort after food is taken.

For two months back hoarseness has developed, and with it pain in swallowing.

Temperature. All along this has been an afebrile case.

Treatment and results.

In the first place, this case had the physical signs and the symptoms of tuberculous phthisis, but doubt is thrown on it being so, from the fact that tubercle bacilli were not found in the sputum. Examination was made by an independent observer, with negative result.

Previous to serum treatment being started, this patient underwent complete open-air treatment, but did not seem to be improving, so was brought into an ordinary hospital ward.

He then underwent a short course of treatment with horse plasma, in teaspoonful doses, given by the mouth. The horse being an animal, to a great extent immune to tubercular disease, it seems feasible to suppose that this animal's serum contains some body which produces this immunity. Hence by administering this serum to a person who is not immune, that person's immunity might be raised.

The plasma seems to act by improving the general nutrition of the body, improving digestion, and causing a general feeling of well-being. This result was noted in the present case.

Plasma therefore having a general effect on the system, it was thought, that if one could combine with it, a serum with a special action on the tubercular virus - a local action - good results might follow.

The above theory was followed in the present case, but the results were inconclusive.

The hypodermic injections of the sero-tuberculin were commenced on October 31st. 1905, and altogether patient had about 40 injections.

These experiments with the plasma and the serum, were carried out in conjunction with Dr.D.Montgomerie Paton, Melbourne, the result of whose experiments appeared in the Medical Press and Circular, and also in the Glasgow Medical Journal.

The conclusion come to was, in the case of the present tuberculin at any rate, that the two were **antagonistic**.

As the dose of the tuberculin was increased, the effects of the plasma passed off gradually. The plasma was then stopped, and although a much smaller dose of the tuberculin was given,

4 HOUR CHART.

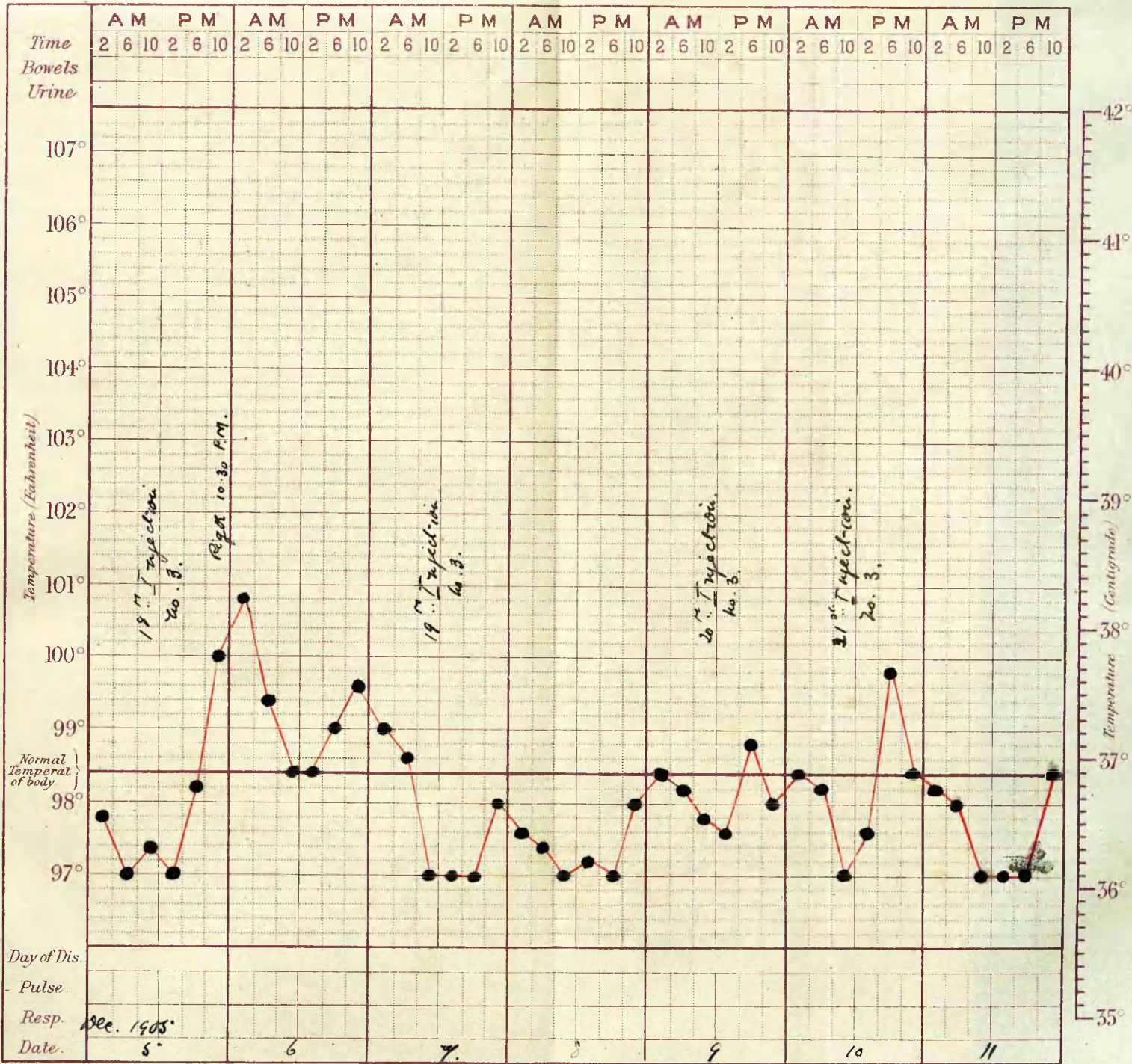
DISEASE.

Name {
 Age
 Diet
 Case Book N^o

Notes of Case

Date of admission

Result



4 HOUR CHART.

DISEASE.

Name {

Age

Diet

Case Book No.

Notes of Case

Date of admission

Day of Dis.

Pulse.

Resp. See. 1905.

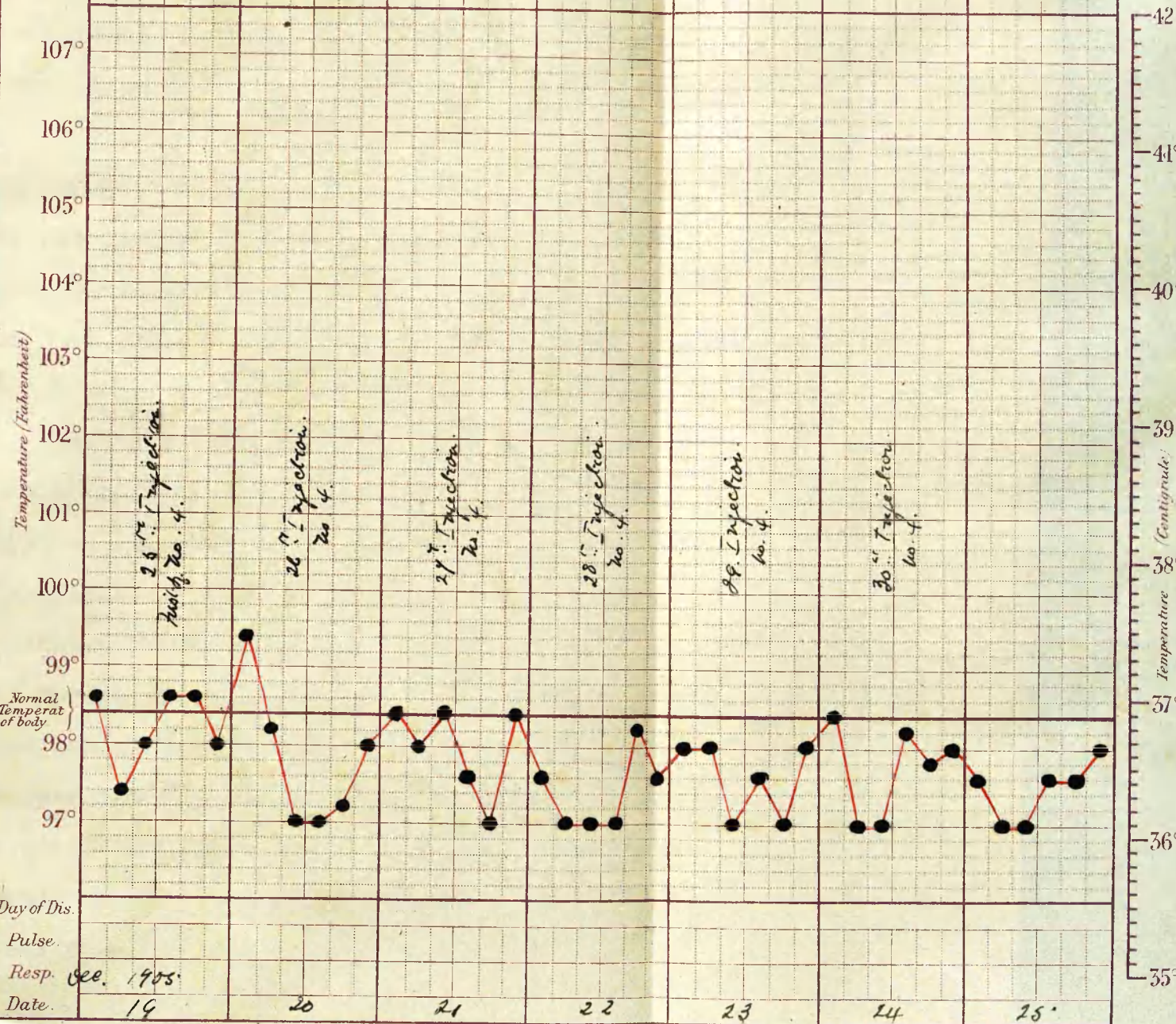
Date.

AM PM AM PM AM PM AM PM AM PM AM PM AM PM AM PM AM PM

Time

Bowels

Urine



it was followed by a marked reaction, some of the temperatures reaching 104 and 105F. Apparently the resistance had been lowered, and the tuberculin, a vaccine, had had full scope to cause reaction. The temperature however very soon came down. Afterwards the serum was continued alone, with no evidence of reaction. The accompanying charts bring out clearly the periods of reaction.

When the treatment was stopped, this case certainly showed improvement, but on the whole it was rather inconclusive.

Evidences of improvement were quite apparent in his chest, but signs of some affection were still present in the right apex. Examination of the sputum in March of this year, ^{for} tubercle bacilli, gave a negative result: As regards the other symptoms, the hoarseness had quite disappeared, the digestion was much improved and with it the appetite. The cough also was much less troublesome, and the expectoration was slightly lessened in amount. The increase in weight, however, was only about 2lbs. During the whole course of the treatment, the temperature remained normal, except at the period of reaction after the plasma had been stopped, when it rose to 101F. Lastly there was a great improvement in the shortness of breath, and patient himself said he felt very well. He left the hospital in May of this year to begin work.

Case 8. P.M'C. M. Age 23. Occupation a labourer.

Family and Social History.

Family history is indefinite, but there appears to have been a high mortality. His father and mother both died when he was a child, so that he was left pretty much to his own resources.

Previous History. 6.10.05.

Up to January, 1905, patient seems to have enjoyed good health, considering the chance he had. At that time he became addicted to alcohol, with its attendant evils. He appears to have led a very irregular life, being very much exposed, living, and sleeping where he could find a place to lay his head. Since June, 1905 he has only wrought about three weeks. The first thing he complained of, was a troublesome cough and spit.

Present Illness.

As has been said above, this illness began in January, 1905. with a troublesome cough. Sweating, also, was a pretty constant feature. This condition continued till June of the same year, when he put up a small quantity of blood. In July he had an attack of pleurisy in the right side. He had no more haemoptysis. This condition of affairs continued to get worse, till October 1905, when he came into hospital. During his illness he has lost 2 stones.

Present Condition. 26.10.05.

General. When patient was admitted here, a fortnight ago, he was acutely ill, with a typical hectic temperature, and since admission he has practically done no good. If anything his temperature has kept going up, and for the last few days, it

has been constant, with very slight remissions. Sweating has also been a prominent feature, necessitating the frequent changing of his clothing. He has an irritating cough which is exacerbated, whenever he attempts to turn on to his right side. This cough gives rise to severe ^{pain} in the right side, towards the base of the lung. His breathing is very distressed, and a full breath sets up the cough, and also "catches" him in the right side. He is very poorly nourished, having lost over 2sts. in weight. His present weight is 7sts.11b. There is marked clubbing of the fingers. His face presents a suffused and earthy colour.

Respiratory.

Inspection reveals a marked wasting, in the clavicular and intercostal spaces. The breathing is shallow and difficult. Over the right apex, there is a very decided flattening, and a corresponding diminution in movement.

Right Lung - Anterior.

Palpation reveals a relative increase in vocal fremitus over the apex.

Percussion. There is dulness in the supra-clavicular space, over the clavicle, and in the infra-clavicular space. It extends downwards almost to the margin of the middle lobe.

Auscultation gives very decided evidence of disease. The whole of the upper lobe in front gives the following signs - a harsh respiratory murmur, with a hollow and prolonged expiratory portion, numerous moist rales both during inspiration and expiration, and an increase in the vocal resonance, broncophony. That is to say the signs are those of breaking down. The middle

lobe, however, shows no evidences of disease.

Left Lung - Anterior.

Here also are evidences of disease, but not so far advanced as in the right lung. There is a slight increase in the vocal fremitus, but no dulness. During inspiration only, a few sub-crepitant rales are to be heard, extending right down the margin of the sternum. The respiratory murmur is harsh in character, with a prolongation of the expiratory portion. Lastly there is an increase in the vocal resonance.

Right Lung - Posterior.

Here also the signs are well marked.

Percussion reveals a dulness at the apex.

Auscultation. There is a deficient respiratory murmur, but no rales are to be heard. However, at the base there is dulness with a harsh respiratory murmur. In the 8th. 9th. and 10th. interspaces, you get a small area, three inches from the spine, where pleural friction is to be heard. Further out too, in the mid-axillary line, friction is also to be heard; it was here the patient complained of pain.

Left Lung-Posterior.

There is no dulness, and generally speaking the respiratory murmur is good.

Sputum is abundant, of a dirty greenish, purulent character, but is not nummular. Examination for tubercle bacilli is positive. As regards amount it averages 12ozs. in the 24 hours.

Cardiac. Heart is normal.

Digestive. Appetite is very poor, and there are periodical attacks of severe diarrhoea.

Temperature. On admission it was a typical hectic temperature, but it very soon became a constant one, with remissions from 102 to 99F. Only very occasionally did it reach normal.

Treatment and results.

I think only one result could be looked for in this case viz., death. The first injection was given on October 31st. 1905, and the patient only had had nine, when he died suddenly, death being due to pneumothorax. It seemed hopeless starting with such a case, but I suppose it was a case of giving the patient a chance of improving, under a new remedy.

Instead of showing any improvement under the serum, he seemed to get worse. None of the symptoms were relieved at all. The cough still continued with an accompanying copious expectoration. The diarrhoea too was very troublesome up till the day before he died, being due to tuberculous enteritis, and the sweating continued to the very last. Pain in both sides continued, and of course, the pneumothorax was heralded by a great increase in the pain, and dyspnoea. The temperature from being intermittent became more remittent.

I am very much afraid that the serum was the means of hastening the process of destruction in the lungs. The pneumothorax pointed, of course, to more or less rapid breaking^{down} of the lung tissue. The patient, with such an active process going on in his tissues, would be inoculating himself, and the adding of a vaccine to an already loaded system was like adding fuel to a fire.

Unfortunately a post-mortem examination was not granted by the friends.

Case 9. J.M'G. M. Age 19. Occupation lorry driver.

Family and Social History.

In this case the phthisical tendency is marked, his mother and several brothers having died of phthisis.

Previous History. 1.10.05.

He has had no illnesses of any consequence, till his present one began, 5 months ago.

Present Illness. 1.10.05.

This present illness began in the beginning of June of the present year, and he attributes it to a severe cold, brought on by exposure to wet, and to want of proper attention—the proverbial "neglected cold". Cough was the most troublesome feature, but he never appears to have been troubled with much expectoration, or from later facts, it would be better to say, that he did not trouble much with expectoration. He seems to have been in the habit of swallowing it. What sputum there was, was of a light yellowish colour, and was never blood-streaked. He has also had night sweats. There has been a progressive loss of flesh, how much he cannot say. His appetite all along has been fairly good, but his digestion has not been perfect, certain articles of diet, meat for example, causing indigestion. At no time does he appear to have been very bad, and since admission he has been improving, his cough becoming less frequent, and the amount of expectoration lessening. He also sleeps well during the night, the cough only troubling him slightly. His temperature chart also shows a great improvement. On admission in August 1905, he had an intermittent temperature, for about a fortnight, too, it was an inverted one.

After nine weeks residence in hospital, however, it became absolutely normal. On admission his weight was 8 stones.

Present Condition. 1.10.05.

General. This patient's general condition is good, being well-nourished, and having a good colour.

Respiratory.

Left Lung - Anterior.

Inspection and Palpation. Over the apex there is a diminution in the movements, with flattening, not marked, however. The vocal fremitus is also slightly increased.

Percussion. Dulness is present in the supra- and infra-clavicular spaces, and it is well localised.

Auscultation. The respiratory murmur is harsh and bronchial in character. During inspiration clicking rales are to be heard, down to the third interspace, and also above the clavicle where they are also heard during expiration. The vocal resonance is increased - broncophony. In the axilla the breathing is of the bronchial type, clear with no rales.

Right Lung - Anterior.

Here there are also physical signs, but slight, compared with those in the left apex. Thus there is no dulness, but auscultation reveals the presence of a few clicking rales, above the clavicle, during inspiration. The respiratory murmur is clear, but is intensified.

Left Lung - Posterior.

At the apex is slight dulness, reaching to the level of the 1st. dorsal spine. In that area the respiratory murmur is accompanied by clicking rales. Elsewhere the respiratory murmur

is clear, only approaching the bronchial type. Vocal fremitus^{an} and resonance are both relatively increased, in the above area. Nothing else in the lungs calls for note.

Sputum. It has been noted as regards the sputum, the small quantity. Indeed patient did not require a spit cup. This had been a feature all along. He says he never had any expectoration.

Cardiac. There is nothing abnormal in the heart.

Digestive. His appetite has been fairly good, but he has had attacks of indigestion. He has not had diarrhoea.

Temperature. On admission the temperature was intermittent, and for a short time it was inverted, but after nine weeks it became normal. Its further course will be noted under treatment

Treatment and results.

This certainly seemed a good case for the tuberculin treatment. All the signs physical and otherwise pointed to an early stage, and although at first the temperature was an intermittent one, by the time the serum was started, the case had become an afebrile one. In spite of these things, however, I have to record a fatal result, but one which differed from the other fatal terminations, in very many ways, as will be seen.

This case was admitted to hospital in the beginning of August 1905, and at that time the disease was advancing, as evidenced by his intermittent temperature and sweating. After being in an ordinary ward for a short time, he was transferred to a shelter, to undergo the complete open-air treatment. Under such conditions he improved steadily, his temperature becoming quite normal in nine weeks, his cough becoming less trouble-

some, and the sweating stopping. He also increased in weight.

On October 31st. the injections of serum were started, and the patient altogether had 40 injections.

I must say he did no good under the treatment, from the very first, but I would not like to put the the whole blame on the serum, from the after course of the case.

His cough seemed to give him no great trouble all along, and there still continued to be no sputum, and this when the lungs were beginning to break down. The temperature did not give much evidence of mischief going on; only very occasionally did it rise to 100F, and on one occasion, after the injection of the No 4 strength, it rose to 101F, evidence of a reaction. However it soon came down to normal again. Towards the end of the injections it became a little more irregular again, going up at night. It continued more or less irregular, till a week before death, when it became subnormal. At no time did it rise above 101F, and only to that point on two occasions. The last injection was given on January 3.

In January 1906 he began to be troubled with sickness and vomiting and diarrhoea. No food would remain in the stomach, not even milk, at times. This condition continued with short remissions, but always getting worse, till death occurred on April 5th. With these gastro-intestinal symptoms was a rapid wasting. No treatment seemed to have any affect on the diarrhoea, or only for a very short time. The motions were very watery and offensive and occasionally contained blood. The appearance of the case now, gave rise to a suspicion of enteric fever, but the blood examined for the Widal reaction, gave a negative result. The urine now became loaded with al-

bumen. Severe headache was complained of, and very soon marked indications of meningitis set in, and eventually the patient passed into the typhoid state with subnormal temperature and died.

Examination of the chest, in the latter part of March showed signs of cavity formation in the left lung. The right lung also, now showed signs of breaking down. The following is a summary of what was found post-mortem:-

The body was extremely emaciated. Both lungs were bound down, by firm pleural adhesions, the ^{left} more so than the right. In removing the left lung, a large cavity occupying the apex was opened into. It was filled with a pus-like fluid. This cavity occupied the greater part of the apex, and the condition of its walls showed that it was a rapidly advancing process. Connect- with it were several small cavities also in an active state. The lower lobe was congested, and presented several small case- ous nodules. The right lung also presented cavity formation, but to a smaller extent than the left one. The middle lobe was also involved, and the lower one the least of all.

Both kidneys were enlarged, and presented well-marked amy- loid disease.

Intestines. Here there was very extensive tubercular ulcer- ation. Several tubercular ulcers were present in the ileum, and also in this part of the intestine were numerous small nodules, under the mucous membrane. These extended right along the ileum, to the jejunum, becoming less numerous, and being absent altogether from the duodenum. In the colon there was extensive ulceration of a tubercular character. This condit-

ion was most marked in the caecal region, and had given rise to great thickening. This condition extended right along the colon to the sigmoid flexure.

In describing this case I have tried to emphasise the fact that all along, there was no sputum, or at least nothing to speak of, even when the condition in the lung was bound to be giving rise to material requiring expectoration. The patient must have been swallowing it, and the intestinal tract would in this way become affected. Once started, the malnutrition it would give rise to, would tend to hasten the process in the lungs, and from the lungs, the meninges would also be infected. From observation of a very large number of cases of tuberculous phthisis, diarrhoea due to tubercular ulceration of the intestinal tract, seems to be one of the worst complications, few if any ever recovering from it. It is usually a late manifestation of the disease, occurring when the condition in the lungs is far advanced, that is to say where you have cavity formation. In the present case however, the disease in the lungs was not far advanced when the intestine became affected, but, once the intestine was affected, the disease in the lungs advanced very rapidly.

Case 10. W.M. M. Age 17. Occupation an india-rubber worker.

Family and Social History.

There is nothing definite to be derived from the family history. His social circumstances and surroundings were poor, four persons living in a single a room. His occupation, also was an unhealthy one.

Previous History. 7.10.05.

From childhood he has been the subject of chest affection. Every winter he would suffer from bronchitis. He has also had one attack of influenza.

Present Illness. 7.10.05.

He dates his present illness from the month of July this year. At that time he had to leave off work. However his cough dates back a good number of years. In July he began to expectorate and to feel out of sorts, and not equal to his work. The least exertion rendered him breathless. Occasionally, too, his sputum would be blood-streaked, and he had periodical sweats. Loss of flesh, however, has not been at all marked. About the same time his stomach began to trouble him; he was not able to retain his food, and his appetite was not so good as formerly. Since admission, in August till the commencement of the serum treatment on November 2nd. 1905, on the whole he has improved. His cough is not so troublesome, and he can sleep well at night. His cough begins to be more troublesome towards morning. He still has occasional sweats, and his expectoration is more abundant, but is expelled with less difficulty. It has become darker in colour too, but has not been streaked with blood, since coming under treatment. At first he

was confined to bed, but has been going about lately.

Present Condition. 7.11.05.

General. Patient is very unhealthy looking and very anaemic, suffering from acne. He is soft and flabby looking. His present weight is 7sts.2lbs.

Respiratory.

Left Lung - Anterior.

Inspection and Palpation. The movements here are defective, there is flattening and also an increase in vocal fremitus.

Percussion. Over the apex there is dulness, extending downwards into the cardiac area, and also into the axilla. It is most marked in the supra-clavicular space, and least marked towards the sternal end of the clavicle.

Auscultation. The respiratory murmur is cavernous in type, most markedly, in the supra-clavicular region. In the same space, numerous moist bubbling rales are heard, both during inspiration and expiration, but during expiration they are more crepitant in character. The vocal resonance is greatly increased - pectoriloquy. Below the clavicle you have also the above signs, but not in such a heightened degree - thus, the rales are more crepitant in character during inspiration, and during expiration they are crepitant. The respiratory murmur is not so markedly cavernous, and the vocal resonance also not so much increased.

Right Lung - Anterior.

The movements are good, and there is no dulness.

Auscultation. All over the lung, the respiratory murmur

is broncho-vesicular in type, with no rales. The vocal resonance is also slightly increased. The middle lobe presents pretty much the same characters as the upper one. Just above the nipple there are a few rhonchi.

Left Lung-Posterior.

Percussion. The lung is absolutely dull from apex to base, not a clear area to be found. One could imagine it was a lobar pneumonia.

Auscultation. At the apex, there are very evident signs of cavity formation, thus the respiratory murmur is cavernous in type, and is accompanied by abundant moist rales, both during inspiration and expiration; the vocal resonance is also very much increased - pectoriloquy. These signs are even more marked than they are in front, and they extend downwards, in a lessening degree, to the lower angle of the scapula.

At the base you get evidences of fluid, thus, there is a board-like dulness, a distant muffled respiratory murmur, oegophony at the upper limit of the accumulation, while over the dull area, a diminished vocal resonance.

Right Lung - Posterior.

There is no dulness, but the respiratory murmur is harsh in character, but with no accompanying rales. A few rhonchi are to be heard at times.

Sputum has been copious, and of a dirty greenish colour, but not nummular. Examination for tubercle bacilli gave a negative result.

Cardiac. Heart is normal.

Digestive. Stomach is very easily upset. On admission the appetite was poor, but it has been improving till now.

Temperature. The presence of a temperature has not been a prominent feature in this case. It was slightly irregular, of a hectic character at first, but before serum treatment was started, it had become quite normal.

Treatment and results.

Judging from the physical signs in this patient's chest, one would be inclined to think it a most unsuitable case for tuberculin treatment. The disease was advanced, and there was an undoubted mixed infection. But there is this to say in favour of the treatment being used in this particular case, that it was ^{an} a-febrile one, and that apparently the disease was not in an active state. However one would imagine it would be very easy to start the process again, by inoculation.

The injections were started on November 2nd. 1905., and the patient had only 32 of them, the fewest of any of the cases, of course excepting those which ended fatally.

From the behaviour of the case, I have no doubt that it was tubercular, although the tubercle bacillus was not found in the expectoration. I have said that before treatment had started, there was no temperature, but immediately the injections were started, the temperature began to rise. This was quite well marked in the first week, when four injections were given. However in the second week, when three were given, on not a single occasion was there a rise above normal. Apparently the system had become accustomed or immune. The same applies, with the exception of one rise, to the third week when four were

given. In the second week, the absolutely afebrile one, there was a gain in weight of four pounds. In the third week however, there was a drop of two pounds again, in all probability caused by the single rise in the temperature. In the fourth week again if we leave out the last day of it, there was still no temperature. During these four weeks the injections were only given every second day, but after that they were given every day, and immediately a very decided reaction was obtained, more marked than at first, the temperature on one occasion reaching 102.6F. There was also pretty severe local reaction at the site of injection, not due to any outside infection. The serum itself was also sterile.

I gave injections on three consecutive days, and the reaction lasted for eight days. When the temperature had been normal for two days I repeated the injection, and immediately the temperature rose to 102.4F. However I continued the injections the following two days, and the reaction became less and less. I then allowed an interval of three days, during which there was no temperature, when I gave a fresh injection, which was followed by still less of a reaction.

When the daily injections were started, there was also a complaint of sickness made by the patient; he also had a slight haemoptysis. The sickness continued for three weeks i.e. during the period of greatest reaction.

After this the injections were given gradually, allowing two days to intervene, then one, till they were given daily, the reaction becoming less and less, till in the ninth week of the treatment, although given every day, the temperature never

once rose above normal.

During the period of reaction, there was a loss of weight, and during the afebrile periods there was a gain, as one would expect.

I have entered thus fully into this case, as it best shows the action of the serum to be that of a vaccine. The accompanying charts will make the above points more distinct.

Since the treatment was stopped the patient has gone on improving. His weight is now 9sts.5lbs. an increase of over 2sts.

The condition of his chest the last time it was examined was as follows:-

The right lung showed no physical signs of disease at all. The left however, seemed very much as reported at first examination viz. consolidation and softening at apex and fluid at base. Rales were numerous both in front and behind at apex, with increased vocal fremitus and resonance.

Case 11. M.B. F. Age 22. Occupation a machinist.

Family and Social History.

As far as she knows there has been no tubercular disease in her family. Her social surroundings were poor - five persons living in two small apartments. For six years she has been a machinist, and in a dusty atmosphere.

Previous History.

As a child she had measles. She has nearly always had a "cold", Summer and Winter, since childhood. Sleep was always

good, till the present illness started, but has been more or less disturbed since. Her appetite has been always poor, and it has got even worse since she turned ill.

Present Illness. 2.11.05.

Present illness commenced in November 1903, with cough which has steadily become worse. Two or three months after this cough had started, she had a bluish glairy spit, which afterwards became yellow. The quantity too, has also increased. Since January 1905, she has sweated a good deal. Previous to November 1903, she says she had no sweats. In August 1905, for the first time she put up a little blood - one or two spits of pure blood. She spat blood for the second time, two or three weeks ago, a little more than on the first occasion. In March 1905, she had pain on deep breathing in the region of the right shoulder. She began to lose flesh, most markedly from April or May of this year.

Present Condition.

General. This patient is thin and emaciated with prominent ribs and bones. Her colour is pretty good.

Respiratory.

Inspection and Palpation. The respiratory movements are very defective, over both apices, left and right being very much alike. Vocal fremitus is also slightly increased over both.

Right Lung - Anterior.

Percussion. At the apex there is dulness distributed as follows:- clavicular region dull, 3rd. not quite so dull;

4th, space clear.

Auscultation. In the 1st. space the respiratory murmur is tubular, and is accompanied by a "click" on inspiration, and crackling rales, both during inspiration and expiration. In the 2nd. space the respiratory murmur is cavernous, with some crackling rales. In the 3rd. space the respiratory murmur is not quite tubular, but is accompanied by abundant rales, crackling in character. The vocal resonance is increased all over, and in the 2nd. space it is pectoriloquy.

Left Lung - Anterior.

Percussion. There is dulness in the supra-clavicular region, and extending to the first space. Below that the note is clear.

Auscultation. In the 1st. space the respiratory^M is tubular in character, and at the inner end of the space it is almost cavernous. Accompanying it are abundant crackling rales, and also some rhonchi. In the 2nd. space the breath sounds are not so tubular, but are accompanied by abundant crackling rales. Below this the rales are very numerous, and in addition there are rhonchi. Vocal resonance is much increased.

Right Lung - Posterior.

Percussion. The note over the apex is of slightly impaired resonance, but is not dull. The base shows no dulness.

Auscultation. At the apex, the respiratory murmur is bronchial in character. Accompanying it are numerous rales, crackling, down to the lower angle of the scapula. At the base are a few rales, and occasional rhonchi. The vocal resonance is

increased at the apex.

Left Lung - Posterior.

Percussion. At the extreme apex there is slight relative dulness, but the base is clear.

Auscultation. The respiratory murmur is bronchial in character, and is accompanied by numerous crackling rales, down to the level of the lower angle of the scapula. The base is clear, only at times showing a slight wheeziness on expiration.

The vocal resonance is increased at the apex.

Sputum is very copious, and contains tubercle bacilli.

Cardiac. The heart is normal.

Temperature. The temperature is typically hectic, with intermissions ranging from 97F in the morning to 102F in the evening.

Treatment and results.

This case very much resembled Case 8, and the remarks that were applied to it, might quite well be applied to this one.

The injections were started on November 2 1905, and the patient only had 11, when they were stopped altogether, as she was apparently getting worse, and very much weaker.

For the first week, when four injections were given, the temperature went up slightly. Towards the end of the second week, when she had six, it began to be lower, and with a very few exceptions, it continued lower, till the end of the third week, when the serum was stopped altogether. She also made complaint of sickness at times. At her own request, she was taken out by friends on December 9, but died two days later.

Before she did go out, her cough had become very much worse; the throat had also become affected. Her breathing became very difficult, at times requiring her to sit up.

In this case I have not much doubt that the treatment by serum, was the means of hastening the process. It was a case of inoculating a person, who was too fully inoculated. There can be no doubt that such cases are not suitable for this form of treatment. But I think there could not have been any hope for this case, by any form of treatment. Tuberculous phthisis in females seems to run a more rapid and acute course, than in males, perhaps on account of their having less power of resistance, or from the fact of their being later in undergoing treatment. They appear to hang on longer than men, hoping against hope, for improvement, before seeking advice or treatment.

Case 12. E.B. F. Age 19.

Family and Social History.

Patient only knows of another member of the family being a "bleeder", one of her brothers. Family history otherwise is unimportant. Her social surroundings were poor.

Previous History and Present Illness.

Except for the presence of the enlarged glands, she all her life has enjoyed good health. She first noticed the swelling in her neck when she was seven years of age, and they have got gradually larger since then. When she was fourteen years of age, she had one of the glands removed by operation, but there was so much difficulty with the bleeding, that no further operative measures were attempted. She herself has noticed her

bleeding propensity, e.g. she would have great difficulty in stopping the bleeding from a simple cut finger. Also when she was about 14 years of age, spots appeared on her legs, subcutaneous haemorrhages, which have left brownish stains. She is subject to periodical attacks of erysipelas of the face, dating from her operation.

Present Condition.

General. Except for the presence of the enlarged glands, she looks very healthy - her colour is good, and she is very well developed and nourished. Her chest is quite healthy, as is also her heart. She takes her food well, and makes no complaint of anything.

Special. There is a very great enlargement of the cervical glands. For the most part they are freely moveable, with no skin involvement. They look as if they could be readily shell-ed out, but on account of the haemophilia, an operation, particularly in this region, would be a very serious matter. Strange to say, too, she never makes any mention of the bleeding, when operation is spoken of. Indeed she has been on the operating-table, when a nurse recognised her as the patient who had caused so much trouble, at a former operation. Six large glands can be felt, in front of the sterno-mastoid muscle, one large one extending over the cheek. In the supra-clavicular space, is another large one, about the size of a plum, and also freely moveable. No enlarged glands exist in any other part of the body. Her present weight is 9stones4½lbs.

Treatment and results.

On account of the bleeding tendency, this was thought to

be a good case, in which to try the effects of sero-tuberculin. Its behaviour in this case is particularly interesting, although a conclusive result was not obtained, only marked improvement in the glandular condition.

She had the first injection on October 31 1905, but she only had 15 in all, on account of the severe reaction, that was being set up. From October 31 till November 28, she had twelve injections of No. 1 and No. 2, and in that time there was absolutely no reaction, the temperature remaining quite normal. Also in that time improvement in her condition was apparent, the glands were smaller, and felt looser. You seemed to be able to make out a commencing lobulation, as if the connective tissue between the lobes were contracting. In that time, too, her weight increased from 9sts. $4\frac{1}{2}$ lbs. to 9sts. 10lbs. On November 13, she had a return of her erysipelas, but it was very slight, and soon passed off.

On November 28 she had the first injection of No 3, and it was followed by a very decided reaction, both local and general. The arm at the point of injection became very red and swollen, spreading upwards and downwards, and closely resembling erysipelas. She had a rigor, her temperature running up to 102.6F, with headache sickness and vomiting. She also felt very drowsy. These symptoms gradually passed off, so that on December 2, the temperature was normal, when I gave her another injection, but with a return of the symptoms, the arm becoming red and swollen, then the rigor. On this occasion, however the reaction was not so severe. This time she also complained of her throat feeling painful and dry, and again she

was very drowsy. By December 5, the temperature had reached normal again, and her arms, where the injections were made, were improving. During the period of reaction she lost 4 lbs. fully, in weight. Round the glands a slight redness was noticed, and also slight softening. On December 17, I gave her the 15th. and last* injection, but this time only one third of the dose. However the same severe reaction occurred, arm, red and swollen, where injection was made, followed by a rigor, headache &c. By the 20th. the temperature had again reached normal, and the arm was slowly improving. She was also steadily putting on weight, being 9sts. 7 lbs.

The glands were undoubtedly much smaller than when the treatment was started, but were still of considerable size.

She went out shortly after.

This case again, I think proves the nature of the serum to be that of a vaccine, and I imagine if the treatment had been continued, very gradually increasing the strength and frequency of the injections or inoculations, a good result would have followed.

Conclusions.

It now only remains to sum up the various results obtained, and to draw conclusions from these results.

In describing the cases, I have tried merely to record facts, without any prejudice, one way or other, but I suppose, when a person takes up any new form of treatment, prejudice must, to a certain extent creep in.

To begin with, I will discuss the cases which ended fatally.

Three of these, I think, might very well be bracketed together, as presenting very similar characters and features.

These are, Case 1, G.W. Case 8, P.M'C. and Case 11, M.B. These three cases all exhibited an advanced stage of the disease, and what was more, and worse, a rapidly advancing condition, evidenced by the high temperature. The hectic temperature also showed them to have reached the stage of mixed infection. In such cases auto-inoculation is going on to a large extent, hence outside inoculation, instead of being beneficial, is harmful. It was rather strange, or perhaps it was not at all strange, that two of these cases should have died suddenly, one death being due to haemoptysis, the other to pneumothorax. The third case may have died suddenly also, but death took place in her own home. Were these results brought about or hastened by the sero-tuberculin? It is very easy to think that they were. Both haemoptysis, the late form at any rate, and pneumothorax, are caused by more or less rapid destruction of lung tissue, and we have seen that tuberculin, in such cases as the above will tend to bring about such a destruction. Vaccines in such cases are quite contra-indicated. What is required in such cases, is a body which would neutralise the toxins being formed i.e. an antitoxine. In these cases too, where the infection is a mixed one, the use of antistreptococcal serum might be of value.

Case 4 F.D. may be dismissed in a few words. Along with his chest trouble, he had well marked cardiac valvular disease, and also kidney mischief. The lung trouble was not such as to cause death, and indeed during the serum treatment, an improve-

ment was seen in it . Death was due to failure of compensation of the heart. Otherwise a good result might have been looked for in this case.

Case 9 J.M'G. seemed a suitable one, for serum-therapy, disease in the lungs was not advanced, and when the treatment was started there was no temperature. However the intestinal infection occurring secondarily, from the swallowing of the sputum, was sufficient to counteract any good effects obtained at first, and to bring about a fatal termination.

In Case 2, A.S. and Case 7, R.E. the results on the whole were rather unsatisfactory, but improvement was seen in both, although physical signs were present in both, after treatment. They complained much less of subjective symptoms, and both testified to feeling very much better.

In Case 3, F.M. and Case 10, W.M. the physical signs were very well marked, the disease was advanced; but in one at any rate was not acute. In both great improvement was noted, but unfortunately in Case 3, a relapse occurred. An improvement, however, even although only temporary, was I think gratifying. It rendered the patient's condition much more comfortable, and his existence much more pleasant.

The three cases remaining were cases of local tuberculosis, one of which had in addition disease of the lungs.

The two joint cases were completely cured, and were very much improved in their general condition. The lung complication in the one, was also greatly improved, although a few physical signs were still present. The third case, with enlargement of the cervical glands was improved, locally and

generally, but the treatment was not completed, on account of the severe reaction set up by the serum, to which the patient objected.

I think on the whole, therefore the results were gratifying, or at any rate, such as to lead one to use the serum, in certain cases. Apparently the most suitable cases are local tubercloses, such as tubercular joints, ulcerations and tubercular glands. In tuberculous phthisis, I would also expect good results, but the earlier in the course of the disease that the inoculations are started, the better. It would also seem to be beneficial in the more advanced cases, with no temperature. It is perhaps hopeless to look for cure in such cases, but even improvement, although only for a time, is always something. As has been said it is quite unsuitable in acute advancing febrile cases.

From a such a small number of cases, it is difficult to form any very definite opinion or conclusions. However one would imagine that if a certain result were obtained, with a certain treatment, in a certain class of case, a similar result would be obtained in other similar cases. Unfortunately this is not always the case, the personal factor, the idiosyncrasy, has to be taken into account.

But every small collection of cases, adds to the number, and to the evidence for or against any treatment.

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The original sources have been given, but these were not consulted in every case.

For the general matter the first works were consulted.