THE VACCINE TREATMENT OF TUBERCULOSIS IN CHILDREN.

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THE scientific investigations regarding tuberculin treatment, which we owe to the brilliant researches of Sir A. E. Wright and his co-workers, have placed in our hands a remedy the value of which is now assured, and which requires only the confidence of the profession to give it the recognition it so justly deserves. The results of the old empirical methods of injection have left behind a feeling of distrust which still clings persistently to the very name tuberculin. The profession ought to realize how widely different is the treatment as at present carried out. Formerly we dosed by rule of thumb, often with unfortunate results; now, thanks to the discovery of opsonins, the dose of tuberculin, its effects, and the most suitable intervals for injection can be studied with scientific precision. This discovery has, in short, brought treatment with tuberculin, and with bacterial vaccines generally, within the realm of safe therapeutics, and the clinical success that has attended the employment of that treatment has firmly established its position. Thus, though we are indebted to opsonins for the modern vaccine and tuberculin treatment, yet, be it noted, this treatment does not stand or fall with the opsonic theory, but rests on a clinical basis. At present the determination of the opsonic power of the blood remains a fairly accurate measure without which tuberculin and other vaccines cannot be intelligently or safely used; but other and less laborious methods of determining dosage may perhaps be found, and the days of the "opsonist" pass. Whether this happens or not, the therapeutic position of the vaccines (including tuberculin) is now assured; the vaccines have come to stay. The time is coming, or perhaps has come, when the practitioner who omits to suggest tuberculin in the treatment of localized tuberculosis will be open to justifiable reproach from his patient.

The cases which form the basis of this paper were treated some at the East London Hospital for Children, Shadwell, and some at the City of London Chest Hospital, Victoria Park. My thanks are due to my senior colleagues on the staff of the former hospital for their kindness in placing beds at my disposal, and to Sir Hugh Beevor at the latter hospital for a similar courtesy. The scientific work in connexion with the treatment is carried out by myself in the laboratories of the City of London Chest Hospital, and I am indebted to my friend Dr. George W. Ross for my initiation into the details of the methods at present used in Sir A. E. Wright's laboratory.

THE OPSONIC INDEX IN TUBERCULIN TREATMENT.

The opsonic index is a measure of the resistance to microbic invasion of the patient's blood serum as compared with that of a healthy individual. Thus, if the index is 0.5, the resistance is only one-half what it should be; if it is 1.2 or 1.3, it is greater than normal. The object of tuberculin treatment is to raise the opsonic power—that is, the resistance to infection—and to maintain it at the higher level for as long a period as possible. In the case of the tubercle bacillus the index does not often rise above 1.5, and any figure at or above 1.0 is satisfactory. The chart shows the effect of a tuberculin injection on the opsonic index. Immediately after injection, a short rise, which may be called "prenegative," is observed (not seen in all cases) followed immediately by a "negative phase"; this gives place later to a "positive phase," at the end of which the index again sinks.

In most of the cases treated the opsonic index was low before injection, 0.6 or 0.7 being a common figure, but in some the index was already high. There is a natural tendency to believe that if the index is already high, and especially if it fluctuates, no advantage will be derived from tuberculin treatment. In such a case it is presumed that the lesion is not strictly localized, but the tuber-

culous focus so open to the blood stream that the patient inoculates himself from his own lesion. Such auto-inoculation is increased with any increase in the local blood supply, and a corresponding fluctuation of the opsonic index can be shown as a result of exercise, or of manipulation of the diseased area (in tuberculous peritonitis, for example). Under such conditions it does not seem rational to use tuberculin, and at the beginning I steadfastly re-

The effect of tuberculin on the opsonic power. From Case II, tuberculous joint disease. A = "prenegative rise"; B = "negative phase"; C = "positive phase."

used to undertake such cases. I was, however, persuaded to take over one apparently hopeless case with a high opsonic index, and the improvement was so striking that I am now inclined to give such cases a trial and to disregard the original index, except as an indication for rest during treatment. The opsonic power steadies under the injections, and, though it may rise no higher, still clinical improvement is manifest.

DOSAGE.

At the beginning I was persuaded to give doses which I have since learnt were excessive. My first cases received 300 mg. irrespective of age, and though there was generally a rise of opsonic power accompanied by improvement in the lesions after the first injection, subsequent injections produced a prolonged negative phase, and the local conditions got worse. It was soon easy to see, even with these comparatively small doses, how much harm may be done with tuberculin in inexperienced hands. As the result of experience I have come to regard 200 mg. as an average adult dose, and fractions of this must be given to children according to their size. On the whole, I find children stand rather larger doses in proportion to their weight than adults; I commonly give 120 mg. to a child of 1 year, 200 mg. at 5 years and 300 mg. at 10 or 12 years of age. It is always safer to begin with a

comparatively small dose. With regard to the intervals at which injections should be given, I started with the belief that it was best to wait over the period of raised index before reinoculating; I now prefer to shorten the intervals when possible, and, as long as the reaction is prompt, to reinject at intervals of about two weeks. As a result of the smaller doses and shorter intervals I am obtaining much better results in my later than in my earlier cases.

It has been stated by some that tuberculin may be given safely without opsonic determination. In children this is certainly not so; even with the help of the index the dose is often difficult to fix, and individual idiosyncrasy must be considered. It is also stated that after the dose has been fixed, the opsonic index may thenceforth be disregarded. Even this is not altogether safe advice; I have seen susceptibility increase suddenly after more than six months' treatment, so that the dose had to be reduced to one-half and then one-third of its original strength. The result of continuing the earlier doses would have been a dangerously prolonged negative phase. At the present time I begin a case with two examinations of the opsonic index, one before exercise and one after, to determine whether any auto-inoculation is taking place. I then inject and examine the index twenty-four hours, seventy-two hours, one week, and two weeks afterwards, to determine the negative and positive phases and their duration; and if I consider the result satisfactory, I afterwards examine the index once weekly, or in some cases only once between the injections.

No additional treatment has been used in the cases described, but there is good reason to suppose that other forms of treatment on general lines may often be advantageously combined with tubercle vaccination.

SOME DETAILS OF TREATMENT.

All cases should remain quiet for a day or two after injection; later, in purely localized cases, there is advantage in activity. With lesions not strictly localized, or where the local disease is widespread, much harm may be done by injudicious exercise; all such cases must be kept strictly at rest. The necessity for this may often be indicated by fluctuation of the opsonic index; a steady curve is attained only when complete rest is enforced.

Injection with tuberculin should be postponed during acute intercurrent illness. One of my cases was unfortunately injected the day before an attack of mumps, the index fell to 0.4 and remained at that figure for a couple of weeks, though no ultimate harm resulted. On the other hand, two cases (one an adult) injected immediately after influenza suffered no harm but reacted normally.

CONCLUSIONS.

The conclusions at which I have arrived from a study of my cases are as follows:

1. That in tuberculin we have a most valuable remedy for localized tuberculosis. There is nothing dramatic in its effects, but, with proper dosage, a steady uphill progress occurs both in the local conditions and in the general health. That this improvement corresponds with an increase of opsonic power I have satisfied myself by observing the alternate improvement and relapse in superficial lesions with the rise and fall of the opsonic index of the blood.

2. That tuberculin, especially suitable for localized tuberculosis, is also of value in many cases of less localized infection, especially if nutrition be not greatly impaired. Many of my cases appeared hopeless from the outset, being either chosen by myself for the purpose of testing the limitations of tuberculin—Case I, abdominal tuberculosis, and Case III, tuberculous glands—or handed over to me because other treatment had failed—Cases II and III, abdominal tuberculosis, and Case I, psoas abscess. With marked wasting and general illness no good results should be expected; yet even under such conditions tuberculin is occasionally the turning point in a downhill course—Case III, abdominal tuberculosis—so that unless the lesions are known to be widespread it is still worthy of trial.

3. That tuberculin cannot take the place of surgical procedures but should be used in conjunction with these. Especially must caseous material, unless small in quantity, be removed, and this should be done at a time when the opsonic index is at a high level. On the other hand, many cases would escape the necessity for

surgical measures if tuberculin were given sufficiently early.

4. That the secondary infection, always present with open tuberculous lesions, generally lessens with improvement in the tuberculous process. The advantage of and occasional necessity for a second vaccine is a point to which I am devoting my time at present.

5. That tuberculin treatment should only be undertaken by those who have given it special study. This must be obvious to all who remember the results of its use in the old days.

TUBERCULOUS DACTYLITIS AND SUPERFICIAL ABSCESES.

These are most suitable cases for tuberculin treatment if taken early. The three cases described were among my first, and at the beginning were treated with doses which I now regard as excessive. Two of the three did well; the third had widespread lesions, and died of accidental diphtheria with empyema.

CASE I.

A. G., 4 years of age, showed scars of three superficial abscesses, an open sinus $\frac{1}{2}$ in. deep over a metatarsal bone; and enlargement of one finger with sinuses on each hand. This trouble had been present for twelve months. The opsonic index before injection was 0.8, and the first injection ($\frac{1}{1000}$ mg.) was given on June 26th; the index rose steadily to 1.3, and the sinuses had healed by July 3rd. After the second injection on July 17th the sinuses opened again, the dose of tuberculin having proved too large. Subsequently, after a third injection ($\frac{1}{1000}$ mg.), the sinuses healed permanently.

Number of estimations of the opsonic index, 21. Injections, 3.

CASE II.

W. B., 1 year of age, showed two superficial abscesses on the right foot, two enlarged fingers with sinuses on the right hand, and on the left hand one diseased finger and a superficial abscess. These lesions had been present for six months, and the sinuses grew a white staphylococcus. The opsonic index was 0.5 and 0.6 before injection. The first injection ($\frac{1}{1000}$ mg.) was given on June 26th, and the index rose to 1.3; the lesions had nearly healed by July 17th. A second injection of $\frac{2}{1000}$ mg. (too large a dose) caused a depression of the opsonic power, with reopening of some of the lesions. The most appropriate dose was difficult to find in this case, but eventually all the lesions healed except one finger where there was some dead bone. The child became an out-patient, and unfortunately contracted measles, of which he died at the beginning of December.

Estimations of the opsonic index, 28. Injections, 7.

CASE III.

E. H., 14 months old, showed lesions of the left foot and hand, and a large abscess over the left elbow. The opsonic index before injection was 0.5, and the first injection ($\frac{1}{1000}$ mg.) was given on June 26th; the index rose to 1.2, and the lesions improved, but before reinjection a tuberculous abscess of the left buttock appeared. After the second injection the index began to fluctuate, and continued to do so to the end. The foot and hand got well, but the abscess remained. The child suffered with diarrhoea, and on September 4th had nasal diphtheria, developed an empyema, and died.

Estimations of the opsonic index, 18. Injections, 3.

TUBERCULOUS GLANDS.

These cases are eminently suitable for tuberculin treatment, and the two uncomplicated cases mentioned below have done well. Case I was treated at a distance, the blood and tuberculin for injection being sent through the post; it was one of my earlier cases, and I had some difficulty in finding the best dose. The child now reacts well to inoculation, and his general health is excellent. Case II illustrates the necessity of removing caseous material when present in quantity. Case III was a wasted infant with enlarged glands, but also with generalized tubercle of which he died, though the glands got smaller before death.

CASE I.

J. C., 2 years of age, was treated in conjunction with Dr. Lauder Smith, of Wells, Somerset. The child had a bad family history; there were moderately enlarged glands in both posterior triangles (one of which had softened), one enlarged submaxillary gland, and some enlarged glands in the axillae and groins. The opsonic index before injection was 0.68 and 0.78, the first injection ($\frac{1}{1000}$ mg.) was given on July 26th, resulting in a long "negative phase," during which the softened gland discharged itself. After the second injection ($\frac{1}{1000}$ mg.) the abscess healed, and subsequently he has reacted excellently to doses of $\frac{1}{1000}$ mg., his opsonic index rising to 1.4 to 1.8. He has lately been brought up to town to see me, and I find the glands considerably smaller, and his general nutrition greatly improved.

Estimation of the opsonic index, 27. Injections, 10.

CASE II.

N. L., 10 years of age, showed a softened gland the size of a cherry under the chin, and enlarged glands in the right posterior triangle, the largest being about the size of a cherry. The opsonic index before injection was 0.8, and the first injection ($\frac{1}{3000}$ mg.) was given on September 5th; there was tenderness of the glands a few days later, and by September 26th the largest in the posterior triangle had shrunk to one-half of its former size. The second injection was given on October 3rd, and during the "negative phase" the softened gland began to discharge its contents. This continued at intervals into December, and, since much dead material remained, it was scraped away; two weeks later the wound had completely healed. She has reacted well to injection throughout, the opsonic index rising to 1.1 to 1.5; the glands in the neck are smaller and the child in excellent health.

Estimations of the opsonic index, 12. Injections, 6.

CASE III.

E. P., 16 months old, one of twins, was wasted and ill with signs in the left lung, and masses of glands on both sides of the neck, the largest being the size of a chestnut. The opsonic index before injection was 0.8, and the first injection ($\frac{1}{3000}$ mg.) was given on November 16th, but with no opsonic response. The child continued to lose weight steadily, though the glands diminished in size, and he died on January 8th.

Estimations of the opsonic index, 10. Injections, 4.

PSOAS ABSCESS.

This case was handed over to me owing to lack of improvement under ordinary treatment. The child was pale and wasted; under tuberculin treatment she has become rosy and plump and is still gaining weight rapidly, but there remains a deep sinus which grows a pure culture of *Staphylococcus aureus*. Her opsonic index to this organism is high (2.0), but if the sinus does not heal I intend vaccinating her against the staphylococcus as an addition to tuberculin treatment.

CASE.

E. B., 5 years of age, had a psoas abscess three years ago and has worn a spinal jacket ever since. In March, 1906, a second abscess was opened, and the discharge has continued since with loss of flesh and anaemia. The opsonic index before injection was 0.8 and 0.7; the first injection ($\frac{1}{3000}$ mg.) was given on July 9th, and treatment has been continued up to the present time with the result described above. She is now receiving $\frac{1}{3000}$ mg. of tuberculin every two weeks, and her index usually rises to 1.0 to 1.2.

Estimations of the opsonic index, 20. Injections, 11.

TUBERCULOUS JOINT DISEASE.

The slow course of these cases renders it very difficult to draw conclusions as to the value of tuberculin treatment. On general grounds one would believe that to keep the opsonic index high was to do good, but more than this it is difficult to say. The cases I have treated have disappointed me somewhat, but I do not feel that they represent all that can be done. Perhaps more attention should be paid to secondary infections in these cases; I hope to collect material for a more decisive statement on this point later on. In Case I I suspended the treatment, as the child was getting about the ward and the opsonic index fluctuating; under such conditions I felt I could do her no good. Case II improved considerably in general health, but there was not sufficient time to note any alteration in the local condition. Case III was a very acute tuberculous process, and received only three injections. He has now returned from the country with a secondary streptococcal infection, and I am recommending tuberculin, and preparing to make a streptococcal vaccine.

CASE I.

E. L., 11 years of age, showed old tuberculosis of the right elbow and recent tuberculosis of the right ankle, with an open sinus, from which cultures of *Staphylococcus aureus* and *albus* were obtained. The opsonic index before injection was 0.4 and 0.9; the first injection ($\frac{1}{3000}$ mg.) was given on June 26th, and others following it on July 20th ($\frac{1}{3000}$ mg.) and August 17th ($\frac{1}{3000}$ mg.). The patient reacted well to these injections, the index rising to 1.1 to 1.3, but the "negative phase" was longer in each case than I should now permit, that is, the dose was relatively excessive, and I do not think the local condition was noticeably improved. About the time of the third injection she was permitted to get about the ward on the other foot, and as this rendered her condition unsuitable for tuberculin treatment I did not reinoculate. On October 5th an abscess appeared on the left elbow, and I have since lost sight of the case.

Estimations of the opsonic index, 22. Injections, 3.

CASE II.

A. B., 10 years of age, showed disease of the left hip-joint, but no sinuses. The opsonic index before injection was 0.6,

1.0, and 1.1; the first injection ($\frac{1}{3000}$ mg.) was given on July 9th, and subsequent inoculations on July 20th ($\frac{1}{3000}$ mg.) and September 11th ($\frac{1}{3000}$ mg.). At the beginning the opsonic index after tuberculin fluctuated more than I liked; this was due, I discovered, to overmuch movement of the joint, and after the adjustment of a long splint the opsonic power of the blood remained steady. The patient improved in general condition, and was the picture of health when sent home in October, but I do not know whether there was any change in the local condition.

Estimations of the opsonic index, 20. Injections, 3.

CASE III.

A. N., 6 years of age, developed a large tuberculous abscess over the left hip, which was opened on July 6th. The opsonic index before injection was 1.1, 1.1, and 1.0 on three different occasions; the first injection ($\frac{1}{3000}$ mg.) was given on July 9th, and the second ($\frac{1}{3000}$ mg.) on July 30th. Before the second injection was given his index had fallen, and the wound, nearly healed, broke open and began to discharge. Later the discharge became offensive, and continued in considerable quantity. On October 15th the head of the femur was resected. No injections were given after September 18th, and by December 14th the condition was worse. At this time culture showed a pure growth of streptococcus, to which the opsonic index of the patient's blood was 1.5. The child soon after was sent to Bognor; since his return (January 25th) tuberculin injections have been resumed.

Estimations of the opsonic index, 26. Injections, 4.

ABDOMINAL TUBERCULOSIS.

This represents a mixed group in which, for the most part, the lesions are widespread and accompanied by constitutional disturbance. Conclusions as to the effects of any form of treatment in abdominal tuberculosis are open to many fallacies, and not too much reliance must be placed on a few isolated cases. Nevertheless, Case III appears to be a definite score for tuberculin, and Cases IV and V have progressed admirably. Case I I regarded as hopeless from the outset owing to the marked wasting and the early age of the child. Case II was handed over to me because the patient was doing badly on other treatment; I do not think tuberculin has done her any good. Case III also was handed over to me because the child was going downhill. The result, however, has been strikingly different from Case II, seeing that the patient has steadily gained ground ever since the beginning of the treatment. Case IV is improving rapidly, but might, of course, have shown improvement with other methods of treatment. Case V is very interesting, being an acute tuberculous infection of serous cavities (peritoneum and pleura). This rapidly cleared after the first injection, but appeared again four weeks later, tuberculin having been withheld. After the second injection it again cleared, and, the injections being continued, the child has remained well.

CASE I.

J. B., aged 2 years, ill and wasted with frequent stools; showed enlargement of the abdomen with adherent coils of intestine and masses, but no fluid. The opsonic index before injection was 1.4 (after abdominal examination), and 0.6 and 0.7 on two other occasions. The first injection ($\frac{1}{3000}$ mg.) was given on July 6th, and was followed by a prolonged "negative phase," but the patient reacted to $\frac{1}{3000}$ mg. on July 20th, and to $\frac{1}{3000}$ mg. on July 30th, the index rising to 1.1 to 1.4. In August she had a bad attack of vomiting and diarrhoea, and thereafter her temperature remained high and fluctuating; she continued to waste, and died on September 5th.

Estimations of the opsonic index, 18. Injections, 4.

CASE II.

R. B., 4 years of age, has had abdominal tuberculosis and enlarged glands since June, 1905, and in June, 1906, was getting markedly worse. The abdomen showed tuberculous masses but no fluid. The opsonic index before injection was 2.0 and 1.2. The first injection ($\frac{1}{3000}$ mg.) was given on July 9th, the second ($\frac{1}{3000}$ mg.) on July 30th; by August 28th her general condition had improved. Subsequently her index began to fluctuate, and in November she went to the hospital convalescent home for a long stay, but lost flesh considerably while there. Since then she has not improved; she has suffered with diarrhoea, and her stools contain a large growth of short streptococcus. Her opsonic index to this streptococcus (January 4th) was 1.5, to staphylococcus 1.8. There is perhaps a secondary infection present, but her general condition is too bad to make any further inoculation desirable.

Estimations of the opsonic index, 22. Injections, 7.

CASE III.

E. J. was a child, aged 5 years, wasted, with large abdomen showing adherent coils and general resistance but no fluid. The opsonic index on July 24th was 1.3, and since it was high I did not advise treatment. The child steadily lost

weight under other treatment, and at the beginning of October I was again requested to try tuberculin as a last resort. On October 5th the index was 1.2, and I injected $\frac{1}{1000}$ mg. The child immediately improved in spirits and weight, but on October 13th had a severe gastro-enteric attack and nearly died. Since then she has steadily improved on fortnightly doses of $\frac{1}{1000}$ mg., and her weight rose from 1 st. 11 lb. on October 26th to 2 st. 7 lb. 6 oz. on December 30th. From January 11th, however, she again began to lose weight, and on February 2nd a tuberculous mastoiditis was discovered and treated by operation. Tuberculin was continued, the wound healed rapidly, and her weight, which had sunk to 2 st. 6 lb. on February 19th, had risen to 2 st. 8 lb. by February 26th, and the child continues to improve.

Estimations of the opsonic index, 14. Injections, 9.

CASE IV.

A. G., aged 6 years, wasted and anaemic, showed some enlargement of glands, and peritonitis of the dry variety. The history dates from January, 1906. The opsonic index before injection was 0.8, the first injection ($\frac{1}{1000}$ mg.) was given on November 13th, and subsequent inoculations at intervals of about two weeks. The weight on November 11th was 1 st. 13 lb. 6 oz., steadily rising to 2 st. 5 lb. 5 oz. by February 17th, the child being now rosy and fairly plump. Treatment continues.

Opsonic indices, 9. Injections, 6.

CASE V.

J. T., 9 years of age, was brought to me for wasting on August 20th. I considered the child tuberculous, but a careful examination discovered no lesion. Ten days later he returned with abdominal pain and swelling, and there was free fluid present in the abdomen. I admitted him to hospital, and on September 5th there appeared also a small effusion in the left pleural sac. The opsonic index before injection was 0.86; the first injection ($\frac{1}{1000}$ mg.) was given on September 5th, and by September 19th both the pleural and peritoneal effusions had disappeared, and he was gaining weight. His opsonic index remaining at about 1, I postponed the second injection till October 13th, with the result that by this date a fresh peritoneal effusion had formed, and pleural dullness was returning. After the second injection ($\frac{1}{1000}$ mg.) the signs again began to subside, so that by October 24th there was no longer any evidence of ascites, and the pleurisy had cleared; the remaining abdominal enlargement and resistance to palpation gradually improved till, by September 7th, the organs appeared to be quite normal. He has remained well since, and is steadily gaining weight.

Opsonic indices, 17. Injections, 8.

PHTHISIS.

Only one case of phthisis has been treated, and this patient was chosen not because she seemed suitable for tuberculin, but because no other treatment offered a chance of improvement. The disease was too advanced for sanatorium treatment, so tuberculin was given a trial. The patient has been seven months under treatment and has held her own; the physical signs are much as at first, but with fewer moist sounds in the lungs. Her weight at the present time is 4 st. 12 lb., and I think she is better nourished than at first, but unfortunately her weight was not taken at the outset.

CASE.

J. L., 12 years of age, had a history of twelve months' duration. There was finger-clubbing and involvement of the whole left lung and the apex of the right. Her index before injection was 1.1, 0.8, 1.15, 0.8 on four separate occasions. The first injection ($\frac{1}{1000}$ mg.) was given on July 20th, and $\frac{1}{1000}$ mg. at intervals since. In January her index to streptococcus was 1.15 and to staphylococcus 2.0. She was treated in the wards for the first five or six weeks, went to the convalescent home for a time, and has been treated as an out-patient since October.

Opsonic indices, 16. Injections, 8.

THE INFLUENCE OF ANTITUBERCULOUS SERUM ON THE OPSONIC INDEX.

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VERY encouraging reports have been made as to the value of Marmorek's antituberculous serum by a large number of Continental writers; indeed, in looking through the available literature, scarcely any entirely adverse verdicts are to be found. Some authors write enthusiastically in favour of the remedy. Thus Richer states that it

is a true antitoxin, and temporarily inhibits the growth of the bacilli; Frey calls it undoubtedly a specific antitoxin, and Ullmann holds that it is superior to all other remedies yet devised against tuberculosis. It seems, therefore, advisable that more extended trials should be made of the serum in this country, and that records of the results obtained should be published, so that more complete statistics may be available for estimating the true value of the remedy. The following brief communication deals with one point only in the action of the serum—namely, its effect on the opsonic index of the blood, since in so chronic a disease as tuberculosis only a prolonged course of treatment can afford a basis for definite conclusions as to the value of any remedy, and such a trial was impossible in the circumstances in which we were situated.

The patients selected for this trial were all suffering from advanced tuberculosis of the lungs. This was in accordance with advice kindly given by Dr. Marmorek himself, it being difficult to estimate the effects of any

remedy in early cases, which often improve wonderfully under open air and plentiful feeding alone. One of our cases was probably hopeless from the outset; the others appeared capable of improvement, but had made little or no progress while in hospital. They were all febrile cases, such being chosen in the hope that the effect of the serum might be rendered visible on the temperature chart. In accordance with the advice of Dr. Marmorek the most recent method of administration of the serum, rectal injection, was chiefly employed; but in one case subcutaneous administration was used as a control.

CASE I.

C. B., aged 18 years. Tuberculosis of the right upper lobe and of the whole of the left lung. Very ill, vomiting at times, and suffering from abdominal pain, weakness, and emaciation. Going downhill; practically a hopeless case. Serum was given per rectum in daily doses of 5 c.c. from August 27th to September 15th. The patient's temperature appeared to fall a little during the first part of the course, and he looked and felt better, the pain being at first less, but returning towards the