tuberculosis in children. With the above technique I have not failed so far to obtain a positive reaction in any case of tuberculous meningitis, acute miliary tuberculosis, massive abdominal tuberculosis, and acute pulmonary phthisis.

Case 1.—Mary F., aged 11 years; acute phthisis. Admitted June 3rd, 1921. Great emaciation and weakness. Large hard mass of glands in the right side of neck; signs of consolidation and catarrh in the right lung. Cutaneous test, performed June 5th, was negative two days later; the child was not seen again until June 23rd, when the reaction was positive. A second test, done on June 23rd, was positive. July 25th: emaciation and weakness extreme; tubercle bacilli in sputum; third cutaneous test positive. Death, sixteen days later. No post-mortem examination.

Case 2.—Charles S., aged 13 months; pulmonary and miliary tuberculosis. Admitted December 3rd, 1921, with fever, emaciation, and weakness. Signs of consolidation in right middle lobe of lung; rapid progress of disease. Cutaneous test, made nine days before death, positive. Post-mortem examination showed tuberculous bronchopneumonia of right middle lobe; miliary tubercles in both lungs, liver, and spleen; and tuberculous mediastinal glands.

Case 3.—Francis C., aged 15 months; general tuberculosis. Admitted February 1st, 1922, in extreme weakness and emaciation; death in twelve days. Cutaneous test positive six days before death. Post-mortem examination showed tuberculous cervical and mediastinal glands; large miliary tubercles in both lungs, especially the left; tuberculous ulcers in intestine, and tuberculous mesenteric glands; miliary tubercles in liver, spleen, and kidneys.

These cases have been selected because of the extensive or acute nature of the disease, and also because a positive test was obtained in an extremity of weakness and emaciation and within a few days of death.

McLean and Jeidell,⁸ in a report on 3,742 Pirquet tests in young children, found 44 negative reactions in cases proved to be tuberculous by autopsy or by the discovery of tubercle bacilli during life. The technique of the test was as follows:

"Two light scratches were made approximately 1/4 in. in length and 2 in. apart. Into one scratch the tuberculin (undiluted O.T.) was lightly rubbed with a toothpick having a flat end; the other scratch was used as a control. In doubtful cases the test was repeated. It was not usually considered negative until forty-eight hours after application."

Dunn and Cohen,⁴ in reporting failures of the test in a considerable number of cases of tuberculous meningitis, peritonitis, and miliary tuberculosis, give no account of the technique of making and reading the test. It may be presumed that it was carried out in a similar way. There is no doubt that their experience of failure in advanced tuberculosis is amply confirmed by other investigations employing a similar technique.

My own experience with a different technique is as yet small compared with that of the investigators mentioned, but it has included every type of tuberculous case, and it suggests that when care is taken to apply tuberculin thoroughly to the skin, and that when the standard of a negative test in severe disease with weakness and emaciation is not the absence of reaction in one or two but in seven days, the Pirquet test does not fail even in massive tuberculous disease. If further experience should confirm this, the clinical significance of a negative test will be increased; it will then absolutely exclude tuberculous disease. But the technique of the test will require modification on the lines laid down in the present paper.

One other point may be briefly mentioned. I am not as yet prepared to say that with this improved technique positive tests can be obtained in acute illnesses, such as pneumonia or measles, with an underlying tuberculous infection. At present I am trying to collect evidence on this point. In any case, the point is not of clinical importance; a considerable personal experience of such cases with the ordinary technique has shown me that a positive reaction can be obtained soon after the crisis of the acute illness.

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THE THERAPEUTIC USE OF TUBERCULIN.

BY

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VIEWS on the use and value of tuberculin are so various, discrepant, and contradictory that no final judgement can be reached until the actual protocols of evidence are produced and submitted to a close and searching analysis and criticism by a judicial tribunal that recognizes the distinction between evidence and comment or assertion. Guessing in the process of diagnosis and uncertainty in the evaluation of essentially different methods of treatment should be excluded.

The diagnosis must be based upon the presence of tubercle bacilli in the discharges from the affected parts or organs; and since in all but pulmonary cases in adults and in all cases in children it is impossible to determine whether the disease is due to the bovine or to the human type of bacillus, these cases should be excluded. Pulmonary tuberculosis in adults with tubercle bacilli in the phlegm is almost invariably due to the specific action of the human type of bacillus, and therefore constitutes the ideal material for determining the value and trustworthiness of tuberculin in treatment and even in diagnosis. Another cogent reason why pulmonary tuberculosis should be selected for this investigation is that this is the prominent lesion in almost 90 per cent. of all the serious forms of tuberculosis in man; and of the remaining 10 per cent. at least half may be reasonably traced to pulmonary tuberculosis.

Long ago I laid it down that in testing the value of any method of treating pulmonary tuberculosis, logic required that no other system should be used. At the Tuberculin Dispensary we allowed patients to continue their life as usual, neither insisting upon the "open window" nor using drugs, and only giving extra food when it was quite obvious that the patient had not the money to buy enough food to maintain normal nutrition. Pulmonary tuberculosis is, however, a very variable disease, because both soil and seed vary. Inherent qualities, often inherited, in the individual, age, local conditions of the lungs, sometimes created by certain infections, such as measles, whooping-cough, and influenza, which may convert a latent into an active process of tuberculosis, and general biochemical anomalies in the tissues, blood, and lymphatics (deficiency of endocrines, deficient calcium, malnutrition), are among the factors in the soil that favour definite disease. The seed also varies in quality, virulence, and quantity, but there is no clinical way of measuring these variations. Accordingly one must not draw conclusions from the results, whether good or bad, in a few cases, must not select cases, and must not publish anything short of a series of at least fifty consecutive cases in various stages of the disease treated exclusively with the remedy to be tested.

After a full course of treatment the cases must be examined regularly two or three times every year for three years, and then once a year at least for another three to five years. Anything less than supervision for five years spoils the investigation, because it is well known that early stages of tuberculosis without any treatment may not become serious for four or five years. For cases treated in the second stage five years may be considered ample, but in my investigation there has been supervision for eight years and more. The control of these cases is very difficult among the poor, who constantly change their home; and during the war the difficulties were intensified. Nevertheless this exacting condition is essential, because the sure test of the value of any method lies in the duration of life after treatment has begun. The length of life, ability to work, sense of energy, the state of the pulse and appetite, even the appearance of the patient to the practised eye, and especially the evidence in changes in the quality and amount of the phlegm, furnish more useful evidence of improvement than the most meticulous description of physical signs. Paying due respect to these exacting conditions, I am prepared to produce evidence which goes to prove that the method, which I have evolved from a continuous experience since the earliest days of tuberculin, yields results far better than any I have seen published in any English, German, or American literature. Tuberculin has not had a fair trial in England, except at the hands of myself and a few of my pupils, who soon learnt from experience that tuberculin, used in accordance with definite principles, is quite free from danger, and that the timid use of tuberculin is a poor substitute for

the method of increasing doses, controlled exclusively by a meticulous regard for the clinical signs, manifested in variations in temperature, in weight, and in pulse rate.

The value of tuberculin treatment cannot be accurately assessed in children affected with enlarged cervical glands. The reasons are obvious to those familiar with the varying nature of glandular swellings in children, especially between the ages of 5 and 15. At this age period children are liable to suffer from many sorts of gland swellings, quite independent of tuberculosis. Further, except by operation and laborious investigations, one cannot say whether the swelling is due to infection with human or bovine tubercle bacilli or with other infective agents.

In certain cities, notably Edinburgh, the bovine tubercle bacillus is shown to be a very common cause of enlarged cervical glands, and the concentration of these forms of gland tuberculosis in children's hospitals may give a wholly wrong impression of the prevalence of tuberculosis in children even in Edinburgh. There is certainly some evidence that in children over 5 years of age the bovine type of tubercle bacilli causes lesions more prone to regress and to become fibrotic than those induced by the human type. In Edinburgh especially any deductions based upon the effects of tuberculin in tuberculosis of the cervical glands in children must be suspect.

Statistics show that in children between the ages of 5 and 15 the mortality from tuberculosis is one-third to one-fifth of that in the earlier years of life, and one-fifth to one-tenth of that in the later years. It would seem that at this period the human tissues acquire a special resistance, and at no other period is this natural resistance greater. I have suggested that this remarkable immunity during these years is due to mild infections with bovine tubercle bacilli in early life. The great prevalence of general tuberculosis, and of tuberculosis of the udder in dairy cows, justifies the assumption that very few children can be expected to escape the risk of infection with bovine tubercle bacilli by the lymphatics of the mouth and cervical glands and other sections of the alimentary tract. These mild infections explain, too, why so many young children, all of whom drink cow's milk, give a von Pirquet reaction. The value of this reaction as a diagnostic test must therefore be discounted; it is just the cutaneous expression of these mild infections. These lesions tend to regress at this period. My own inclination is to the view that if the lesions do not regress the infective agent is more likely to be the human type of bacilli. Certainly the frequency of a von Pirquet reaction does not indicate the frequency of infection by the human type of tubercle bacillus. But the main point I wish to urge is that with so many indeterminate variants in the processes of gland tuberculosis in children, especially between the ages of 5 and 15, children of this age furnish about the very worst material for affording clear evidence as to the value of tuberculin either in diagnosis or treatment. Hundreds of children between these ages are taken to the seaside, and of course improve, because at these ages the natural tendency is towards improvement. No harm is done. Margate is better than London, if people can afford it, but it is not proved by any means that Margate air has cured the tuberculosis because the symptoms and signs regress. The symptoms and signs would have regressed if the child had stayed in London. The test of the value of Margate air must be made at a time of life when this disturbing age factor is eliminated. In like manner Sir Robert Philip's opinions¹ must remain suspect until he gives proof that the subjects of his experiments with inunctions of tuberculin did not belong to this age period, distinguished by an extraordinary phase of immunity.

With much that Sir Robert Philip has stated I agree; I have expressed the same views again and again. But good observer though Petruschky is, I do not approve of his method of dosage, and I do not trust his method of inunction. The test of the relative value of different methods of using tuberculin depends upon the duration of life after treatment in a series of cases of similar character. Years ago I came to the conclusion that the minimum dose for securing permanent results was at least 0.6 c.cm. of the stronger preparations. This opinion is based upon more than twenty-five years' continuous experience in hundreds of cases, in various stages. Shortly before his death, when I related this experience to Professor Koch, he said:

"That is remarkable. We have proved, by complement fixation tests, that 0.5 c.cm. must be given before antibodies can be demonstrated in the blood; while not less than 0.3 c.cm. neutralizes a pre-existing von Pirquet reaction."

I have also shown, by some experiments independently controlled, that, after large doses, the opsonic index may be raised to 2 and even 3, and there is no negative phase of any duration. Moreover, in 1906, I proved, by Arnet's method, that, after large doses of tuberculin, a great improvement occurs in the character of the leucocytes, which probably play a part in the production and action of antibodies. Apart from these laboratory methods I have shown that the subcutaneous injection is a simple, painless, and accurate means of exhibiting tuberculin. I can produce the protocols as evidence at any time, and, while my methods may be far from perfect, I can only be convinced by the details of protocols in evidence that Sir R. Philip can in any way approach the success I have achieved by large doses given subcutaneously.

Subcutaneous injections, given properly and in the proper place, are not painful; and young children, properly handled, rarely ever shed a tear. Ten years' experience at the dispensary proves this. The subcutaneous method is painless, and is free from danger in competent hands; my thirty years' experience convinces me of this. And after three years' experience at my Tuberculin Dispensary, all the doctors assisting me wrote to the BRITISH MEDICAL JOURNAL and subscribed to this view. The subcutaneous method is the best way of giving large and progressively increasing doses—perhaps the only way—as all of the tuberculin passes into the circulation. There is no way of telling how much tuberculin may be absorbed by inunction, and Sir R. Philip does not mention any maximum dose. It would vary with the type of skin, sex, age, temperature, and other conditions. Possibly inunction has an advantage when the lesions are localized in the cervical glands. The lymphatics of the skin drain certain areas, and the lymph makes straight for the associated glands of these areas. Hence inunctions would favourably affect these glands harbouring the bovine type of bacillus. But the dominating purpose in the treatment of tuberculosis in man is, not to treat these mild conditions due to bovine tubercle bacilli, but to treat all tuberculous lesions in the body, and above everything the more dangerous lesions, associated with the presence of the human strain of bacillus, in the lungs, kidneys, deep glands of the body, and in serous membranes. On anatomical grounds I cannot see that inunctions can be as effective as subcutaneous doses in tuberculosis of bones or joints. Tuberculin is not a counter-irritant.

Except in lupus and tuberculosis of the cervical glands, tuberculosis is mostly situated in parts which can be best approached by large doses through the general circulation. No doubt in subcutaneous injections tuberculin travels also by the lymphatics, and may cause the lymphatic glands to swell; but the crux of the argument is the success achieved by the methods in question. In cases of pulmonary tuberculosis treated in 1910, 1911, and 1912 at the Tuberculin Dispensary, these are the results:

In cases in Stage I, with tubercle bacilli in the phlegm, no death was known to have occurred in any case from tuberculosis in the succeeding ten years. In cases in Stage II, with tubercle bacilli in the phlegm, 67 per cent. were proved to be alive nine years later. In fact in Stages I and II, after a period of nine years, 72 per cent. were still alive and able to work.

The success or failure of any method depends exclusively upon the results obtained in these stages of the disease (Stages I and II). If Sir R. Philip will produce the protocols of any similar consecutive cases of pulmonary tuberculosis, with tubercle bacilli in the phlegm, treated by the percutaneous method (inunction), I am ready to produce my protocols and leave the decision in the hands of an unbiased tribunal.

Dr. William Gordon² has given a comparison of results, four years after treatment, at different sanatoriums in cases (open and closed) in Stage I as follows:

Frimley	...	...	...	...	15 per cent. dead
Midhurst	...	...	...	...	20
"London cases" (Dr. Bardswell)	...	...	...	...	31

The Brompton Hospital Reports show that in 86 cases in Stage I with tubercle bacilli in the phlegm treated in 1905, 1906, and 1907, and checked by after-examinations up to 1912 (four to seven years after treatment), the results were 23 dead and 29 lost sight of. This is equivalent to 23 deaths out of 57 cases in the course of the four to seven subsequent years—a death rate of over 40 per cent.

In 1910, 1911, 1912, and part of 1913 I treated with large doses of tuberculin (TA) alone (as a rule a final dose of 1 c.cm.) 106 early cases, of which 16 had tubercle bacilli in

the phlegm, and I had not a single death from tuberculosis to record down to the year 1920. Moreover, I had one striking control case.

A young boy was brought to us. He had positive physical signs at one apex, and at the Lister Institute a few tubercle bacilli were found in his phlegm. We treated him for two months and he gained 2 lb. and improved very much. Unfortunately we notified the case. Thereupon a lay visitor went to the house and urged the mother to take the boy to Brompton Hospital. I lost sight of the boy for more than a year, when the mother told me the tragic story. At the instance of the lay visitor the boy went to Brompton and was six weeks in the hospital for observation. The mother was then told that the boy had not tuberculosis. (Tubercle bacilli had been found by us.) When I saw the boy again he was in a hopeless third stage, and he died in a few months. Our diagnosis was tragically confirmed.

Thus the only early case that we were not allowed to treat died within two years; surely a striking control. These results obtained by me in England almost exactly tally with the results I have published in my book.³ My records in Australia and London are quite good enough to give me unswerving faith in large doses of tuberculin given subcutaneously as easily the best remedy for tuberculosis in all its forms.

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THE TREATMENT OF PNEUMONIA.*

BY

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PNEUMONIA causes more deaths than tuberculosis, and more people die from it between the ages of 35 and 55 than at any other period. It carries away insidiously the aged without an acute attack. The death rate is put at 20 per cent, and with influenza at 30 per cent. This means one death out of every five or six patients; annually over 40,000 persons die from it.

Pneumonia at its outset is a septicaemia caused by a diplococcus. All its symptoms are the result of the influence of the bacillary toxin on the nervous system. Its entrance is always at some local focus of the lung evidenced early by dullness and diminished air entry, but its spread is often very rapid. Hence the importance of the early localization and diagnosis and active measures.

The early attempt at defence is consolidation, to limit the focus of infection; the organisms are surrounded, and there is a leucocytosis whereby the phagocytic action of certain blood-cells destroys the organisms. It must be remembered that the lungs contain a larger number of leucocytes than any other organ, except the marrow (their birthplace) and the spleen (their grave). The clotting of the fibrinous exudate in the alveoli which gives rise to consolidation, and the attack by emigration into this of the leucocytes shows an attempt on the part of Nature to localize the infection and prevent its spread. But leakage occurs, and before consolidation takes place certain organisms and toxins have already spread to the blood, causing the acute septicaemic symptoms. Nature's third attempt at defence is the formation of antibodies. Let me summarize the main principles, as it appears to me, on which we should go in attempting to counteract the septicaemia.

There is acute nerve exhaustion from intoxication. This demands absolute rest. The least movement of the patient is exhausting, especially any efforts by himself. Once the diagnosis is made he should not be moved for examination. He should not be allowed to do anything, and bed pans and urine glasses are essential. With this acute nerve exhaustion there is nerve exhaustion to the heart from the poisoning of the vasomotor centre and of the heart muscle. Therefore the importance of rest is especially demanded by an organ called upon to do extra work by the resistance to the circulation in the lung alveoli. A patient may fall back dead on attempting to sit up. The consolidation of the lung alveoli lessens the oxygenation of the blood, and has therefore thrown out of action a defensive auxiliary of the blood. This demands free ventilation around the patient.

The high temperature, the rapid breathing, rapid pulse, the

pain, all add to the patient's discomfort, and therefore it is essential that his comfort and his environment should be attended to by a skilled nurse, or one to whom all the particulars of the necessary details are made plain.

Various lines of treatment have been adopted in the past:

1. Active bleeding and purgation; its ancient history and objects are well known, and I need not dwell on this.

2. Poulitices and expectorants may be said to have died out.

3. "Expectant" treatment may be summed up as doing what each individual fancies best. Where groups of cases have been treated by certain definite drugs it has not infrequently been claimed that some of them were "specific"; types of cases may vary greatly in severity, according to the virulence of the organism, or the influence of the locality, or of the acquired natural resistance, so that claims founded on statistics are of little value. I believe at present there is no specific drug for this disease. Any drug to be specific, or any combination of two drugs to deserve such a claim, must show equal results in the hands of any practitioner anywhere. By the expectant treatment thousands of lives are lost annually.

4. "Chloroform" treatment has been used in America. Its object was to give rest to the inflamed lung. It has not had, so far as I know, a long run. It aids, in my opinion, the basic factors causing the distress, and can have no influence on the intoxication.

5. The application of ice has been advocated by many, the late Dr. David Lees among others, and has been tried in Dublin hospitals. It demands the earliest recognition of the disease—the localization at its earliest site. Two ice-bags are placed so as to include between them the inflamed lung. It has a scientific and rational basis, and good results have followed its use. The pneumococcus is very sensitive to changes of temperature, and will not live below 28° C., nor above 42° C.—the optimum being 37.5° C. The greater the virulence of the organism the more marked its sensitiveness to temperature. The ice inhibits its multiplication, lowers the patient's temperature, adds to his comfort, and is helpful to sleep. I have often used ice in high temperatures with benefit. In general practice no doubt public opinion would be shocked, but it is of great use to give ice to suck. Chills do not occur. It takes time to reduce high temperatures by rubbing with ice, but the sensation is comforting. I have often seen and used ice for the hyperpyrexia of sunstroke, the whole naked body being on blocks of ice and rubbed with ice.

6. The object of lung puncture is to cause a local accumulation of polymorphonuclear leucocytes by setting up a focus of irritation in the pneumonic areas and so stimulating phagocytosis. It is applying to the lung Kraske's principle in the local treatment of erysipelas, his treatment for the latter disease being to make superficial incisions about an inch or two from the spreading margin all round the affected part. It is considered analogous to laparotomy in the ascitic variety of tuberculous peritonitis. This line of treatment demands accurate determinations of situation and area of consolidated patches; a hollow needle or trocar about two inches long is put into the consolidated patch and left there for thirty seconds. If more than one patch is present, and frequently general practitioners get these cases with many, the largest is selected, and if there are several large patches other punctures are made. Strict asepsis is essential, and the best sites are said to be the axillary lines. Striking results have been claimed by its advocates, but as a method for general practice it does not seem desirable with other measures yet available.

7. Studies at the Rockefeller Institute of Medical Research (referred to in the memorandum on pneumonia issued by the Local Government Board in 1919) led to the recognition of four types of pneumococcus; so far antipneumonia serum has been found effective only in cases due to Type 1. In so acute a disease we cannot afford to wait for the determination of the type, and as the serum has to be injected every eight hours it is out of court in general practice.

A bright hope lies in the success attending vaccine treatment. Recovery depends on the patient providing sufficient antibodies against the bacteria and their toxins in the blood; this and this only is the specific treatment available. Early diagnosis is essential: given during the first twenty-four hours, brilliant results have been obtained. A vaccine must be used early, and it is not necessary to wait for a vaccine to be prepared. By the use of vaccine we are helping Nature, and by accumulating antibodies in the blood we have them available for the lung when the fibrin has been liquefied. In other septicaemias (streptococcus, staphylococcus, gonococcus, *B. coli*, etc.) vaccines have been successful. Should we not

* A paper read before the North Middlesex Division of the British Medical Association.