to drive the patient to seek medical advice, cure is out of the question. Venesections do some temporary good—and are useful at critical moments—but frequent repetitions hardly prove acceptable or satisfactory. Calomel still holds its ground as perhaps the best single drug. The high-frequency current (diathermy) is the best of the "symptomatic" remedies, but too often I fail to persuade the *x*-ray specialists to take much interest in invisible results. In the long run intermittent courses of calomel, diet, regulated life, diversions of mind, and an annual visit to one or other of certain spas seem at present to be all we can do. C. A.

THE CUTANEOUS TUBERCULIN TEST (PIRQUET):

WITH REFERENCE TO ITS FAILURE IN ADVANCED
TUBERCULOUS DISEASE IN CHILDHOOD.

BY

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THE cutaneous tuberculin test (Pirquet) is now accepted as a delicate indicator of tuberculous infection in childhood—so delicate, indeed, as often to reveal a latent focus, buried out of reach of clinical methods of detection, and producing no effect upon sound health. On the other hand, it is common doctrine that the test fails in a considerable number of cases of advanced and widespread tuberculous disease in childhood. It is enough to say that these failures of the test are admitted by Pirquet himself,¹ by Calmette,² and are confirmed by many published investigations, of which those of McLean and Jeidell,³ and Dunn and Cohen,⁴ may be quoted as representative and recent.

It would seem rash to question such weighty scientific teaching and general clinical experience, and in a previous communication to the *BRITISH MEDICAL JOURNAL* (1909)⁵ I have myself subscribed to the frequent failure of the test in advanced tuberculous disease. But for some time I have used a more careful technique in the performance and reading of the Pirquet test, and with this I have not failed to obtain a positive reaction in any case of severe tuberculous disease proved to be such by the discovery of the bacillus or by *post-mortem* examination. It seems worth while, therefore, to describe this technique and to give some examples of its results.

TECHNIQUE OF THE PIRQUET TEST.

There is great variation in the directions given for the performance and reading of the test. Undiluted tuberculin is now generally advised, but a dilution is permitted by Calmette and others. For the preparation of the skin, multiple scratches or a single scratch, or the use of a dental burr or small chisel (Pirquet), are variously recommended. The test is advised to be read as positive or negative in twenty-four hours, or at latest forty-eight hours, though it is admitted that late reactions may occur after this time. The control test is made by a similar lesion on the dry skin and the application of a drop of normal saline. The technique which I now use, and which is, I think, more thorough and less free from error, is as follows:

1. *Undiluted Old Tuberculin (O.T. Koch) must be used.*—In my first series of cases, published in the *JOURNAL* in 1909, a 25 per cent. dilution of old tuberculin was used, and it is very probable that some of the failures there recorded were due to this. Calmette himself still advises such a dilution. In another paper⁶ I have published photographs showing the simultaneous use of undiluted tuberculin and 25 per cent. dilution in two cases, and the diminution of the test in the one case and its failure in the other with the diluted tuberculin. It is necessary, therefore, to emphasize the importance of using undiluted old tuberculin for the cutaneous test.

2. *Preparation of an Area of Skin to Ensure Contact of the Tuberculin with Vascular Tissue.*—The method of the single scratch, or of a number of scratches, is too haphazard. Pirquet's method of placing a drop of tuberculin on the skin and of making a lesion by rotating through it a small drill or borer, may also fail to reach and expose the vascular cutis. I always use the following method: A small circular area of skin on the front of the forearm is chafed with the sharp point of a darning-needle until the epidermis is removed and the pink cutis vera is exposed. Care is taken to avoid bleeding. The eye of the needle is now charged with un-

diluted old tuberculin, and pressed into the prepared vascular surface with a rotary motion. A small bruised pit is thus formed from which the tuberculin is rapidly absorbed. This procedure is similar to that advised by Pirquet; but it differs in the careful preliminary excoriation of the skin, and thus renders more certain the contact of tuberculin with the skin capillaries; this difference is enough, I think, to secure success in cases where the tuberculin reaction is feeble. In seven cases in which both methods were tried side by side the reaction was positive in five with the method just recommended, and in only two with Pirquet's method. The reaction is a vascular reaction, and it is only after a careful removal of the tough epidermis that contact with the blood vessels of the skin can be ensured.

3. *The Time-Reading of the Test.*—The routine in clinical work is to read the test as positive or negative at the end of twenty-four hours, and later observations are seldom made. This is another source of fallacy. It may be granted that in a large majority of cases a positive reaction is visible after one day; but it is quite common for the reaction to be delayed until the end of two or three, or rarely four days. Therefore, though a test may be pronounced positive at the end of one day, it is never safe to record it negative until four days have elapsed. I shall give presently an example (Case 1) of how easy it is to make mistakes when, in the routine of clinical work, the arm is examined after twenty-four hours, is recorded as negative, and is never looked at again.

In a previous paper⁵ I suggested the definition of a positive reaction as a "red papule that persisted for seven days." Since that was written in 1909 my subsequent experience has confirmed me in this definition. Calmette² states that the reaction generally disappears in "a few days." I have watched the behaviour of many positive reactions for weeks. Even in feeble reactions I have never failed to see a dark discoloured papule at the end of two weeks; and it is common to see clear evidence of a positive reaction at the end of a month. The tuberculin cutaneous reaction is a chronic enduring reaction: it may be slow in appearing, but it is always long lasting; and in that respect it shows its kinship to the slow inflammation of a true tuberculous process. There need be no fear that if a test has not been read until after a week a positive reaction may have come and gone in that time. It is worth repeating that while a positive reaction may be recorded after a day, a negative reaction (and this is the more valuable clinical aid) may not be accepted until at least four days have elapsed. It would be a safer, though perhaps less convenient, way to read the test at the end of a week rather than at the end of a day. In all important and doubtful cases the practice of observing the arm daily for a week is to be recommended.

The size of the papule is of little importance. It generally exceeds 5 mm. with the above technique; but in a few cases is less than that, and yet is to be regarded as positive if it persists for a week.

4. *The Use of a Control.*—Up to a few months ago the control I used was a 50 per cent. solution of glycerin and water. Since then I have used normal horse serum, which has proved a more severe control, as it gives not seldom a small inflammatory papule. This, however, has always disappeared in four days. But its appearance makes it necessary to delay the recording of a small or doubtful positive reaction until this time has elapsed; if this is not done, pseudo-reactions, sometimes called traumatic reactions, may be accepted as true positives. It will thus be seen that the practice of reading the cutaneous reaction at the end of one day may introduce two kinds of fallacy: it may omit late and feeble positive reactions which may develop after a day; and it may include false positive reactions which will have disappeared in a few days. But the use of a normal serum control ought to guard against the latter fallacy.

There are obstinate critics who argue that any albuminous substance rubbed into the skin may produce an inflammatory reaction, and who put no faith in the specific character of the tuberculin test. Such an argument can neither be proved nor disproved. But *post-mortem* evidence, which has now been produced in great amount, makes it reasonably certain that a positive cutaneous reaction indicates a tuberculous focus in the body.

Alleged Failure of Test in Advanced Tuberculous Disease.

I shall now cite a few examples from my own experience to show that, with the technique just described, positive reactions can be obtained in cases of massive and advanced

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.

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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