THE INTRADERMAL TUBERCULIN REACTION

with special reference to so-called surgical tuberculosis*

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The special interest of this paper centres around diseases of bones and joints and particularly the early diagnosis of tuberculosis of the hip joint. Tuberculosis of the hip presents a difficult problem; if the diagnosis is only made on definite text-book signs much valuable time may be wasted, yet if a provisional diagnosis is made early in the disease some non-tuberculous conditions will be included. There seems little doubt that it is better to begin treatment at once even at the expense of occasionally treating as tuberculous such conditions as coxa plana, slipped epiphysis or subacute septic arthritis of the hip.

In certain cases in spite of expert observation, good skiagrams and pathological investigations it is impossible to make a definite diagnosis for several months. The opening of the joint and demonstration of the tubercle bacillus is not always justified and the sceptic may point at the successfully cured cases and ask for proof that they were tuberculous.

As this early treatment of hip disease by immobilization in hospital is a serious step involving discomfort to the child, loss of schooling and a considerable expenditure of public funds, it is necessary in addition to a very careful clinical examination to collect all evidence which will assist.

I have used the intradermal tuberculin test since the beginning of 1928 and the results obtained until August, 1931, are used in this communication. More recent cases have not been used as their ultimate diagnosis may need revision.

The intradermal test was introduced by Mantoux¹ working in Paris in 1908 and by Mendel in Berlin in the same year. Mantoux injected into the layers of the skin of the forearm the equivalent of 0.01 mgm. of old tuberculin prepared by the Pasteur institute. He claimed that the technique of injection was as easy as giving an hypodermic injection and described the results as follows: 'Immediately after injection there is a small "boule d'oedema," which becomes absorbed and reappears after some hours as a raised papule. Later it becomes visible either white or rose coloured and in twenty-four hours is red in colour and around it is a white oedematous granite-like surface, and further outside this a rosy halo. In forty-eight hours it reaches its maximum and begins, as a rule, to subside, the size varying from a 50 centime piece to a 2 franc piece. The skin remains cool, but there is some tenderness on pressure.'

* Based on a thesis accepted for the degree of M.D. Cantab.

The method of obtaining the necessary dilutions is simple. A 1 in 100 solution is made by adding 0.5 c.c. of old tuberculin to 50 c.c. of normal saline and using for injection 0.1 c.c. of this solution, equivalent to 1 mgm. A 1 in 1,000 solution is obtained by adding 1 c.c. of the above solution to 9 c.c. of normal saline; here 0.1 c.c. is equal to 0.1 mgm. The control solution is obtained in the same way using glycerin broth instead of the tuberculin; the normal saline is sterilized and has 0.25 c.c. of pure carbolic acid in each 100 c.c.

In carrying out a series of tests by the Mantoux method, it has been found better to use two glass syringes, one for the injection of the tuberculin and the other for the controls. These are best sterilized by boiling and allowing them to dry before using and washing through with ether after use. In a few cases in which the same syringe was used for tuberculin and for the control solution, the control arm gave a very slight reaction. Even with careful use a small trace of the tuberculin may be left in the shoulder of the syringe or in the upper end of the needle.

The syringes used were white glass ones graduated in tenths of a cubic centimetre with a well-fitting coloured glass piston, supplied by Messrs. Allen and Hanbury. The needles were No 18 stainless steel, soft metal, with a rather short bevel.

The control arm has usually been injected first as it shows the child there is nothing to fear and should a mistake be made owing to the child moving, the injection can be repeated. For this, the right forearm is used after being washed with soap and water and swabbed with ether. When the arm is dry the skin is stretched by holding the forearm tightly with the left hand and the injection is made with the right. The needle is introduced almost parallel to the skin with the bevel of the needle showing as it enters the skin; when the bevel opening has disappeared into the layers of the skin the needle is turned so that the bevel faces deeply: 0.1 c.c. of the fluid is introduced and forms a small raised papule about $\frac{3}{16}$ in. across. The injection is made easier if the needles are kept in liquid paraffin when not in use, as even after boiling a fine film of paraffin remains and facilitates the introduction into the skin. The same technique is used for the injection of the tuberculin except that in most cases the left forearm is used.

Results.

A certain amount of experience is required to interpret the results. In a few cases in which the same syringe was used for the control and for the injection through a different needle, a small circular patch of erythema appeared on the control arm. In a few non-tuberculous cases a small circular patch of erythema about $\frac{1}{4}$ in. in diameter appeared on both arms. This was regarded as negative if slight, or indefinite if the reaction was greater in the test arm than in the control.

The size of the reaction varies somewhat in different states of the disease, but no prognostic significance is attached to the reaction in the present paper. The response is more marked in the stronger dilutions than in the weak. In 20 tuberculous cases injected both with 1 in 100 dilution and with 1 in 1,000 dilution, the reaction to the stronger dose, measured 2 days later, varied from $\frac{1}{4}$ in. to 3 in. making an average wheal of just over $1\frac{1}{4}$ in. in diameter, while in the weaker dilution the reaction varied from $\frac{1}{8}$ in. to $1\frac{1}{2}$ in., the average being a little over $\frac{1}{2}$ in. In a further series of twelve tuberculous cases injections were made simultaneously with dilutions of 1 in 250 and 1 in 2,500; the stronger solution gave a wheal of from $\frac{3}{8}$ in. to $1\frac{1}{2}$ in. the average being 1 in., while in the weaker dilution the reaction varied from a negative to $\frac{3}{8}$ in., the reactions being mainly too small to measure.

In thirty-two cases of tuberculosis the temperature was specially noted every four hours for three days after injection. Of those injected with 1 in 100 dilution, six ran a temperature above their usual level, the evening rise varying from 0.2° F. to 2.4° in one case; the remaining 14 were not affected.

Of twelve injected with a weaker dilution of 1 in 250 only two were mildly affected: in one the evening temperature which was usually 99° rose to 99.2°, while in another, normally afebrile, it rose to 99°.

I have never seen any ill-effects from an initial dose of 0.1 c.c. of 1 in 100 dilution of the tuberculin. On the other hand, I consider that 1 in 1,000 dilution is too weak for general use because in patients who are definitely tuberculous, but not seriously ill, this dilution gives such a weak response as to be inconclusive.

The results obtained in the few cases in which 1 in 250 dilution was used were very satisfactory and it is possible that this is the optimum dilution for the more chronic cases.

In three cases negative reactions were obtained with the weaker dilution although the patient was tuberculous and gave a positive response to the higher concentration.

The 243 cases here discussed are with five exceptions, children under 12 years of age. They are collected from the Hospital for Sick Children, Great Ormond Street, the Wingfield Orthopaedic Hospital, Headington, Oxford, the West Suffolk General Hospital, Bury St. Edmunds, and from private practice.

To facilitate discussion it is essential to group the cases and the classification adopted by Moncrieff² in his article on the interpretation of the intradermal test has been adopted as eminently satisfactory.

GROUP 1.—DISEASES OF BONES AND JOINTS.

	Age		Total.
	under 7.	over 7.	
Number of tuberculous cases giving a positive reaction	16	30	46
Number of suspected tuberculous cases giving a positive reaction and subsequently proved tuberculous ...	1	—	1
Number of suspected tuberculous cases giving a negative reaction and subsequently proved to be non-tuberculous	5	4	9
Number of apparently non-tuberculous cases giving a positive reaction ...	2	1	3
Number of tuberculous cases giving a negative reaction	—	—	—
Number of non-tuberculous cases giving a negative reaction	19	15	34
Indefinite cases	2	1	3
	<hr/> 45	<hr/> 51	<hr/> 96

Diseases of the bones and joints (96 cases).—This is one of the most important groups and the reaction has been more accurate than in any of the other groups except possibly of glandular affections. It is interesting also because many of these children were observed over a longer period of time, varying from three months to five years, and consequently the ultimate diagnosis has been more firmly established. It was unfortunate that in Moncrieff's² article on the interpretation of the intradermal reaction in which he has discussed its uses very fully he has only two cases of diseases of bones and joints; a fact which he himself comments on.

Of the 96 cases of affections of bones and joints, 46 were almost indisputably tuberculous and gave a positive Mantoux reaction. The clinical diagnosis was aided by a series of skiagrams and in many instances was further supported by the demonstration of tubercle bacilli or typical tuberculous tissue. These fall into the following divisions:—

Tuberculous hip	...	...	...	...	25
Tuberculous spine	...	...	...	...	15
Tuberculous knee	...	...	...	...	1
Tuberculous ankle	...	...	...	...	1
Tuberculous dactylitis	...	...	...	...	1

and in three cases the spine was involved with a second lesion in the hip, knee or wrist.

Thirty-four patients not considered to be suffering from tuberculosis gave negative reactions. These can be classified as follows:—

Congenital talipes	...	...	...	...	5
Mastoiditis	...	...	...	...	13
Spina bifida	...	...	...	...	3
Osteomyelitis	...	...	...	...	3
Sarcoma of spine	...	...	...	...	2
Fracture	...	...	...	...	2

and one case each of the following, coxa plana, osteochondritis of the femur, spastic diplegia, anterior poliomyelitis, multiple exostoses and congenital absence of the coccyx. These do not require much comment except to point out that if they had been tested before the diagnosis was established the reaction would have helped in elucidating the condition in the case of the coxa plana and of osteochondritis of the femur. Sarcoma of the spine is a relatively rare condition and a negative reaction would have reminded the observer of the possibility of sarcoma. These cases were not selected, but occurred in the course of a series of tests performed in hospital wards. No cases of proven tuberculosis in this group failed to react to the injection of tuberculin. This is a very significant point as it does not hold good in some of the other groups.

In one case, a boy of 2½ years, was admitted with a synovitis of the knee, which was not considered to be tuberculous. The Mantoux reaction was positive and at the end of a month in hospital he was considered to be tuberculous independently of the skin reaction.

Nine cases suspected of being tuberculous were under observation at the time the test was performed and gave a negative result. Two of these were cases of synovitis of the knee in boys of five and six respectively. They were treated by immobilization and by removal of all septic foci. In one case there was a biopsy of the knee joint and microscopic examination of the synovia. In neither case was any evidence of tuberculosis found, nor were there any bone changes. Both made a perfect recovery in a few months. They were considered to be of subacute septic origin, in one case the focus being the tonsils. Another case, aged $3\frac{1}{2}$ years, was admitted at a very early stage of hip joint disease, which was at first thought to be tuberculous, but which was proved by opening the joint on the sixth day to be due to an acute streptococcal infection. Two cases were difficult cases of subacute septic arthritis of the hip joint which quickly recovered after immobilization and the removal of septic foci. A boy of 12 was treated as tuberculous, but at a subsequent review six months later was thought to be suffering from a staphylococcal infection of the hip joint and the subsequent history of the case supported this view. Another case had multiple lesions of finger, knee and ankle joints, which were at first treated as tuberculous, but later proved to be a polyarthritis of septic origin.

In 1928, C. S., 5 years old, was in hospital as a case of tuberculosis of the right hip, the radiogram showing two foci in the head of the femur. I considered at the time that the Mantoux test in giving a negative reaction had failed, but in December, 1931, I wrote to Mr. G. R. Girdlestone, who replied—'the subsequent history of C. S. confirms the Mantoux tuberculin diagnosis. Apparently the result has been so satisfactory that there is a strong suggestion that the condition has never been tuberculous. . . . the clinical course has been more suggestive of a non-tuberculous infection.'

The same is true of V. C., 7 years old, who was being treated for tuberculosis of the left hip joint. He was reviewed by Mr. W. B. Foley also working at Oxford in 1932, who writes:—' . . . got full restoration of movements of the hip joint. His series of x-rays when I came to review them, I thought were rather more suggestive of slipped epiphysis than tuberculosis, and I think you will be fully justified in regarding him as non-tuberculous.'

Three cases who were not at the time being treated for tuberculosis gave positive reactions. One case of acute mastoiditis in a girl of three and a half years, who had in addition a gonococcal vaginal discharge had no obvious signs of tuberculosis, but nothing was known of the family history. Two other cases, one of arthritis of the temporo-mandibular joint in a girl of four and another in a boy of five with bilateral talipes equino-varus gave positive reactions. Both the children had spent a large part of their lives in hospital wards, but beyond this fact there is no adequate explanation of the tuberculous tendency. In none of these cases were skiagrams of the chest taken or any investigations made beyond a thorough clinical examination.

Three cases gave 'doubtful reactions.' In one case, R. G., with club feet, a mild reaction occurred both in the injected arm and also in the control arm showing that either the needle was not sterile or the child was sensitive to the protein of the media used both for the tuberculin and also for the control. H. H., a case of mastoiditis, gave a negative control and a slight reaction occurred in the arm into which the tuberculin was injected, but the reaction was so slight that it could not be classified as a positive. R. L. gave a very slight reaction in the control arm and a positive reaction in the arm used for tuberculin injection both in 1 in 100 and in 1 in 1,000 dilution. At the time he was thought to have a tuberculous hip, but five years later there is still some doubt as to whether or not the condition is tuberculous.

GROUP 2.—ABDOMINAL CONDITIONS.

	Age		Total.
	under 7.	over 7.	
Number of tuberculous cases giving a positive reaction	6	2	8
Number of suspected tuberculous cases giving a positive reaction and subsequently proved tuberculous ...	—	1	1
Number of suspected tuberculous cases giving a negative reaction and subsequently proved to be non-tuberculous	1	1	2
Number of apparently non-tuberculous cases giving a positive reaction ...	—	2	2
Number of tuberculous cases giving a negative reaction	2	—	2
Number of non-tuberculous cases giving a negative reaction	20	2	22
Indefinite cases	1	—	1
	<hr/> 30	<hr/> 8	<hr/> 38

Abdominal conditions (38 cases).—Eleven of the thirty-eight patients in this group suffered from some form of abdominal tuberculosis and nine of them reacted to the test. The two who did not react were very ill at the time of injection, one (J. L.) died less than a fortnight afterwards and at necropsy an enormous mass of caseating mesenteric glands was found; the other although very ill was removed from hospital by the parents. It is probable that both these cases would have reacted to a stronger dose of tuberculin. Happ and Casparis³ in their paper on the value of the intracutaneous tuberculin reaction in extensive tuberculosis state that they believe a failure to react to the tuberculin in miliary tuberculosis is due to a depression and not to complete loss of sensitiveness to tuberculin and that if high enough concentration is used a positive result can be obtained in practically all cases of tuberculosis. In the present series a larger dose than 0.1 c.c. of a 1 in 100 dilution of tuberculin has not been used because in those cases in which a lower dose gave a negative reaction, the diagnosis had already been established and therefore from a clinical standpoint the excessive dose was not justified.

In abdominal tuberculosis it might be argued, that, as the infection may have originated from infected milk bovine tuberculin should be tried. Tisdall and Brown⁴ in their series of 159 cases never found a case which reacted to bovine tuberculin, and which did not respond to human tuberculin. Gaisford⁵ used human and bovine tuberculin for a number of the 500 cases in his series and found no differences in their reaction. Tytler⁶ working on animals found the results were the same whether he used human or bovine tuberculin. He attributes the apparently weaker reactions of the bovine tuberculin to the more scanty growth of the culture from which the diluted tuberculin is prepared. He makes another interesting observation, perhaps worthy of comment here, that human cases, which react to human

or bovine tuberculin do not react to avian tuberculin or at most no more than to bacillus coli or other organisms. He considers it to be non-specific.

Twenty-two cases of abdominal disease not considered as tuberculous gave negative results. Two cases of abdominal disease not considered tuberculous gave positive reactions; one, A. D., suffering from acute streptococcal salpingitis was living with her mother, who had active pulmonary tuberculosis; the other, a boy of 11 years, was suffering from appendicitis, and had no signs of tuberculosis, or history of contact with tuberculous persons.

Two cases at the time of injection were under observation as tuberculous and gave negative reactions, the one proved to be a case of congenital idiopathic dilatation of the colon and the other a case of recurrent appendicitis. One case, A. J., gave a positive reaction, but was discharged without a diagnosis being made. One case, P. S., aged 11 years, seen in April, 1931, is worthy of comment; after influenza at his preparatory school during the previous term he developed a slight malaise with anorexia, loss of weight and an evening temperature between 99° and 100°. Just before his return home an attack of abdominal pain suggested the possibility of appendicitis. Careful clinical examination revealed nothing except a soft cardiac bruit, which had been noted two years previously; the urine and stools were normal both in appearance and on pathological examination. The blood count was somewhat suggestive of tuberculosis: R.B.C. 5,600,000, haemoglobin 72 per cent., colour index 0.64, W.B.C. 6,250; polymorphonuclear 32 per cent.; eosinophil 0.33 per cent.; basophil 1.33 per cent.; lymphocytes 61.34 per cent.; large hyaline 5.0 per cent.

A Mantoux reaction was positive and under an anaesthetic some hard abdominal glands were felt under the right costal margin confirming the diagnosis of early abdominal tuberculosis. After three months in bed in the open air he made an excellent recovery.

GROUP 3—INTRACRANIAL CONDITIONS.

	Age		
	under 7.	over 7.	Total.
Number of tuberculous cases giving a positive reaction	—	2	2
Number of tuberculous cases giving a negative reaction	1	1	2
Number of non-tuberculous cases giving a negative reaction	5	—	5
	<hr/> 6	<hr/> 3	<hr/> 9

Intracranial conditions.—In the present series this group is too small to be of much practical use, but it bears out what other observers have found, that the test is of little value in these conditions. A negative result in a normal dilution of the fluid is of no value in excluding tuberculosis and would not help in deciding between a case of meningococcal meningitis and one of tuberculous meningitis.

Of the nine patients in this group four were cases of tuberculous meningitis and two gave positive reactions, the other two who gave negative reactions died shortly afterwards, and post-mortem examination showed typical tuberculous meningitis. The remaining five patients not being treated as tuberculous gave negative results.

GROUP 4.—FEBRILE CONDITIONS.

	Age		Total.
	under 7.	over 7.	
Number of suspected tuberculous cases giving a negative reaction and subsequently proved to be non-tuberculous	1	—	1
Number of tuberculous cases giving a negative reaction	1	—	1
Number of non-tuberculous cases giving a negative reaction	3	—	3
	<hr/> 5	<hr/> —	<hr/> 5

Febrile conditions.—There are only five patients in this group, as many of the febrile cases naturally fall into one or other of the remaining seven groups. All five gave negative results: in two of these the test was useful in helping to exclude tuberculosis as the cause of an abscess in one case in the axilla and in the other in the groin. J. D. was at the time of injection suffering from miliary tuberculosis and did not respond; at post mortem the diagnosis of miliary tuberculosis was confirmed, signs of tuberculous meningitis being the most evident.

One case of typhoid fever gave a negative result during the febrile stage: the test was not repeated as perhaps it should have been to illustrate a point emphasised by Mitchell⁷, working in America, who found that a positive reaction of the skin to tuberculin is approximately two to four times as frequent during the convalescent, afebrile stages of such diseases as measles, diphtheria, scarlet fever, varicella, poliomyelitis, pneumonia and gastro-enteritis as it is during the febrile stages of these diseases. In general hospital work one does not see many of these cases on whom it is justifiable to perform the test and in private practice it has not been done for obvious reasons.

GROUP 5.—GLANDULAR AFFECTIONS.

	Age		Total.
	under 7.	over 7.	
Number of tuberculous cases giving a positive reaction	9	9	18
Number of suspected tuberculous cases giving a positive reaction and subsequently proved tuberculous ...	1	—	1
Number of non-tuberculous cases giving a negative reaction	3	—	3
Indefinite cases	—	1	1
	<hr/> 13	<hr/> 10	<hr/> 23

Glandular affections.—Of the twenty-three children in this group eighteen were straightforward cases of tuberculous adenitis, giving positive results with the diagnosis confirmed at operation. The test helped to reveal the cause of a retropharyngeal abscess of tuberculous origin and it is note-

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worthy that in three cases of septic adenitis the test was negative. One case who gave a positive reaction is classified as doubtful. He had a sinus in the neck, which was at first regarded as tuberculous and treated as such for a year. A diagnosis of branchial fistula was then made and excision performed, but as no microscopic examination of the tissue was made, the actual pathological condition must remain uncertain.

GROUP 6.—URINARY AFFECTIONS.

	Age		Total.
	under 7.	over 7.	
Number of tuberculous cases giving a positive reaction	—	1	1
Number of apparently non-tuberculous cases giving a positive reaction ...	2	1	3
Number of non-tuberculous cases giving a negative reaction	7	5	12
Indefinite cases	1	—	1
	<hr/> 10	<hr/> 7	<hr/> 17

Urinary affections.—Only one case of the sixteen in this group was frankly tuberculous and gave a positive reaction. Twelve cases, five of pyelitis, four of nephritis, one of cystic kidney, one of sarcoma of the kidney and one of cystitis gave negative results.

Three cases gave positive reactions without showing any clinical signs of tuberculosis. One was a boy with cystitis and a congenital abnormality of the membranous urethra and the other two were cases of nephritis. These three cases were not considered to be suffering from tuberculosis and no special investigations were made to exclude latent or healed infection of mediastinal glands. It is possible that the kidney condition in the two cases of nephritis was tuberculous for the tubercle bacilli are notoriously difficult to demonstrate, but that view was not held at the time of injection and the patients have since been lost sight of.

GROUP 7.—CHEST CONDITIONS.

	Age		Total.
	under 7.	over 7.	
Number of tuberculous cases giving a positive reaction	1	3	4
Number of apparently non-tuberculous cases giving a positive reaction ...	1	1	2
Number of non-tuberculous cases giving a negative reaction	8	3	11
	<hr/> 10	<hr/> 7	<hr/> 17

Chest affections.—In this group of seventeen patients four who were definitely tuberculous gave positive results, while eleven, who were not suspected of being infected gave negative results. Of the two remaining

cases, one child suffering from broncho-pneumonia gave a positive reaction, she came of a tuberculous family, but it is uncertain whether she was actually in contact with open tuberculosis. Dow and Lloyd⁸ working on tuberculous infection and its relation to contagion in children find that the incidence of a positive skin reaction in the first five years of life is five times greater in those who are in contact at home with open tuberculosis than in those who are not so exposed. The other case giving a positive reaction was one of asthma, but showed no signs of tuberculosis. The reaction did not appear to be due to a hypersensitivity of the skin to the protein of the media as the control was negative. In this connection it is interesting to note that Storm van Leeuwen and Varekamp⁹ working at Leiden found that most of their asthma patients reacted strongly to tuberculin with the von Pirquet test.

GROUP 8.—MISCELLANEOUS CASES.

	Age		Total.
	under 7.	over 7.	
Number of suspected tuberculous cases giving a positive reaction and subsequently proved tuberculous ...	1	1	2
Number of apparently non-tuberculous cases giving a positive reaction ...	3	5	8
Number of non-tuberculous cases giving a negative reaction	23	6	29
	<hr/> 27	<hr/> 12	<hr/> 39

Miscellaneous cases.—Of the thirty-nine remaining patients not included in the other groups none were at the time of injection diagnosed as tuberculous, but in two the positive reaction obtained helped to elucidate the condition. One was an unusual ulcer of the palate in a child aged eight months, which presented considerable difficulty in diagnosis, later some secondary glands appeared in the neck and microscopic section showed their tuberculous character. The other child was in hospital for the repair of a hare lip and cleft palate and was further investigated as a result of the positive intradermic reaction. An x-ray of the chest showed well-marked calcified peribronchial glands. Dow and Lloyd¹⁰ find that calcified peribronchial glands are frequent with a positive Mantoux reaction, but appear to attach very little significance to the finding. Twenty-nine children suffering from various non-tuberculous conditions gave negative reactions. There remain eight children, who gave positive reactions without at the time suffering from active tuberculosis.

A child, aged 5 years, was being treated for erythema nodosum and gave a very strongly positive skin reaction. This is interesting in view of a recent paper by W. R. F. Collis¹¹ who records the frequency of a positive skin reaction to tuberculin in erythema nodosum. Mackenzie believed that erythema nodosum was rheumatic in origin, while other observers have pointed out its association with tuberculosis. Collis believes that both these observations are correct in that both the tuberculous and the streptococcal infections play an important part. He suggests that erythema

nodosum is a type of hyper-reactive tissue response to various bacterial allergens and that the allergens responsible for erythema nodosum in London are commonly the tubercle bacillus and the haemolytic streptococcus.

E. S., a child aged 8 months, admitted as a case of marasmus was the ninth child of a father, who had undefined 'lung trouble,' the whole family of eleven living in two slum rooms. There were definitely enlarged glands present in both sides of the neck, which were probably tuberculous.

E. K., 10 months old, was admitted with a provisional diagnosis of anaemia and was, after investigation, diagnosed as suffering from tuberculous meningitis. There was a low erythrocyte count of only two million, the leucocyte count showed only 4,600 cells of which 66 per cent were lymphocytes: at post mortem nothing was found to confirm the diagnosis which must therefore remain uncertain.

A case of scleroderma and one of multiple deformities gave positive skin reactions as also did two cases of chorea and one case of rheumatism. The association between tuberculosis and the rheumatic diseases has been pointed out, but it is beyond the scope of this article to enter into a discussion of this interesting subject.

Discussion.

From the preceding analysis it would appear that the test is definitely more useful in the so-called "surgical" than in the medical forms of tuberculosis. Taking the whole series, 84 tuberculous cases gave positive skin reactions and 131 non-tuberculous cases gave negative reactions. In 17 cases the skin test was negative and the tentative diagnosis had to be revised, while in another 17 cases the skin test was positive without tuberculosis being the cause of the pathological condition for which the patient was under treatment; in five cases of tuberculosis the test was negative.

Analysing these cases from another aspect it will be found that of 136 children under twelve, who were not at the time under treatment for tuberculosis 119 (87.5 per cent.) gave negative results. Of these 136 children 95 were under 7 years old and in this age group 88 (92.6 per cent.) gave negative results. Of 41 children between 7 and 12 years of age 31 only (75.6 per cent.) gave negative results. Schlesinger and Hart¹² found in 1930 among hospital out-patients that one-fifth of the children under six years of age, not exposed to tuberculosis at home, gave positive skin reactions.

Of 89 tuberculosis cases 84 (94.3 per cent.) gave positive results; yet of 101 cases giving positive skin tests only 84 (84 per cent.) were tuberculous. Of the children under seven years of age 7 (4.8 per cent.) of a total of 145 children gave unexpected positives while between 7 and 12 years of age 10 (10 per cent.) out of 98 gave positive results, which were unexpected.

Conclusions.

The significance of a positive reaction.—The positive intracutaneous reaction means that the child has acquired a definite allergic reaction to the products of the tubercle bacilli and either has or has had tuberculosis. Children whose parents are tuberculous and who are exposed to open tuberculosis at home are much more liable to produce a positive reaction although they are not at the time suffering from active tuberculosis.

There seems to be little doubt that the younger the child the greater must be the significance attached to a positive result and that the older the child the less importance need be attached to it from a clinical aspect. The intradermal test, therefore, should never be allowed to establish a diagnosis of tuberculosis unless well supported by other evidence, but the test should take its place and a very useful place, in the balance of evidence for or against a diagnosis of tuberculosis.

The significance of negative reaction.—A negative skin reaction to an ordinary diagnostic dose of tuberculin (0.1 c.c. of 1 in 100 dilution) may mean:—

1. That the child has not been infected with tuberculosis.
2. That the test has not been properly performed or the tuberculin used is inactive.
3. That the child is already so ill with tuberculosis that its skin sensitivity is too much diminished to react.
4. That, although the child is suffering from tuberculosis, an inter-current fever, such as measles has caused a temporary diminution of the skin sensitivity and that if repeated during convalescence a positive result may be obtained with the same dose.

The findings here reported agree with those of Mantoux who wrote in 1910 'A negative test except in measles, meningitis and miliary tuberculosis and advanced cases with marked toxaemia is an argument of the first order in excluding clinical tuberculosis; contrary to most clinical methods the value of the intracutaneous test lies in its negative results.'

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