A STUDY OF VON PIRQUET'S TUBERCULIN REACTION IN THE SURGICAL DISEASES OF CHILDREN.

ANALYSIS OF 223 CASES.

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THE cutaneous tuberculin reaction, which commonly goes by the name of von Pirquet, has received less attention here than on the Continent. The failure of Calmette's reaction to do all that was hoped of it has possibly prevented the cutaneous modification from receiving as fair a trial at the hands of clinicians as it deserves, and certain widespread errors with regard to the reaction have often prevented it from receiving a trial at all. The commonest of these is the statement frequently met with that all individuals over the age of 2 years, whether tuberculous or not, give the reaction; this I hope to show to be quite erroneous. Wolf-Eisner, in his work on the diagnosis of tuberculous disease, states that the cutaneous reaction is more delicate, and therefore less reliable when positive, than the ophthalmic, and seems to give the preference to the latter. He prefers, however, when possible, to observe both. Having known some unfortunate results from the ophthalmic reaction, I have confined myself entirely to the cutaneous form, which at any rate possesses the virtue of complete harmlessness.

The object of my experiments was to discover whether healthy individuals reacted, the effect of a previous reaction on a second one, the general reliability of the reaction, and, finally, whether or no any prognostic value could be attached to the type of reaction. My experience is limited to 223 cases, and to patients under 12 years of age.

Technique.

A small area of skin, conveniently on the arm, is sterilized, and a drop of a 20 per cent. solution of Koch's old tuberculin placed on it. The solution is usually in glycerine, and is kept in small capillary tubes similar to those used for vaccination and calf lymph. The skin is then lightly scratched through this solution until a slight hyperæmia is produced. The capillary plexus should not be opened, but I have not found that a small drop of blood interferes with the reaction in any way. A special instrument has of course been invented for this purpose, but I prefer a domestic needle. A control scratch is made through glycerine or normal saline, and a small dressing is applied for twenty-four hours.

The common type of positive reaction is as follows: In twenty-four hours the tuberculin scratch shows a slight hyperæmia and oedema extending a little beyond the actual scratches of the needle. The control scratch should be invisible. In forty-eight hours the spot is redder, and is very definitely raised so as to be palpable to the finger. On the third day it has begun to fade, and on the fourth day it is usually gone.

A.—Results of the Reaction in Healthy Children.

The reaction was tried on 48 children who had been carefully examined without any evidence of tuberculous disease being detected. They were chiefly cases admitted to hospital for radical cure of hernia, fracture, cleft palate, or infantile paralysis. In each case I ascertained that there was no family history of tuberculous disease. Their ages varied from 9 months to 11 years.

In every case the reaction was negative—that is, there was no difference between the tuberculin scratch and the control scratch. This fact is, of course, of primary importance if the value of the reaction is to be established. My first conclusion, therefore, is that in children who show no evidence of tuberculous disease a negative reaction may confidently be expected.

B.—Results of the Reaction in Cases known to be Tuberculous.

In all these cases the tuberculous nature of the condition was established by operation or *post-mortem* examination. In cases which were not obvious a microscopical examination was made. It was assumed, however, that lymphatic glands which showed definite evidence of caseation were

tuberculous. Cases merely diagnosed clinically as tuberculous are considered in the next section.

Of these cases known to be tuberculous there are 21 in my series.

Of these, 19 gave a positive reaction. They were:

Tuberculous cervical adenitis	...	11 cases
" joints	...	6 "
" periostitis	...	1 case
" meningitis (following mastoid disease)	...	1 "

Total ... 19 cases.

Two cases gave no reaction; they were:

Tuberculous peritonitis.	
Tuberculous hydrocele of tunica vaginalis.	

In the former of these the reaction was repeated, with a negative result. The fact that tuberculous peritonitis was present here was only discovered on the accidental prolapse of some omentum during the radical cure of a hernia. There were no clinical signs of the disease. From this one case of course nothing can be induced, but it is interesting from the fact that tuberculous peritonitis has always given a negative result with Calmette's reaction.

The tuberculous hydrocele was a case in which a small patch of granulations was found on the tunica vaginalis during a radical cure. On section, typical giant cells were seen.

The association of a tuberculous hydrocele with a similar form of peritonitis in children is fairly common, and this may quite reasonably have been the case here. Consequently all the known tuberculous cases gave a positive reaction with two exceptions, one of which was known to be, while the other probably was, tuberculous peritonitis.

Of the cases of tuberculous cervical adenitis referred to above as giving a positive reaction, one had been operated on two years previously for tuberculous peritonitis. There was no sign of this condition when I saw the case.

C.—Cases Clinically Diagnosed as Tuberculous.

Of these, there were 43 in my series, not including those referred to above, in which a pathological diagnosis was possible.

Thirty-four gave a positive reaction; they were:

Tuberculous hip	...	14 cases
" knee	...	2 "
Spinal caries	...	8 "
Tuberculous cervical adenitis	...	8 "
Lupus vulgaris	...	2 "

Total ... 34 "

These cases showed nothing in their course or termination to throw doubt on their tuberculous origin.

Nine cases gave a negative reaction. Of these, 8 eventually proved to be almost certainly not tuberculous. They were:

Syphilitic arthritis	...	1 case
Staphylococcal caries	...	1 "
Septic infection of cervical lymphatic glands	...	1 "
Congenital thickening of epididymis	...	1 "
Vesical calculus	...	1 "
Non-tuberculous arthritis of doubtful origin	...	3 cases

Total ... 8 cases.

The remaining case was one of spinal caries, and I believe this to be one of the four cases in my series in which the reaction was misleading.

Of the above 8 cases, 2 were diagnosed as "tuberculous coxitis," and their rapid cure by a short period of immobilization was in marked contrast to the progress of similar cases giving a positive reaction.

D.—Cases Clinically Doubtful.

Of these, there were 11.

Three of these gave a positive reaction. They subsequently proved to be:

Tuberculous caries of rib	...	1 case
Tuberculous coxitis	...	1 "
Lymphadenoma	...	1 "

Total ... 3 cases.

The case of lymphadenoma is the second of the four referred to as giving a misleading reaction.

Eight cases gave a negative reaction. They subsequently proved to be:

Simple vaginal hydrocele	...	2 cases
Septic cervical adenitis	...	2 "
Septic osteomyelitis	...	2 "
Sarcoma of kidney	...	1 case
Septic ext. iliac lymph glands	...	1 "

Total ... 8 cases.

Thus of a total of 123 cases the reaction was misleading in 4 only. Two of these were tuberculous peritonitis, 1 was spinal caries, and 1 was lymphadenoma, in which the reaction was positive. In this connexion it is interesting to remember that some pathologists have considered lymphadenoma to be a form of tuberculous infection.

Reaction on Repetition.

The diagnostic value of the reaction having been established, certain points of more academic interest come up for consideration. Prominent among these is the question of repeating the reaction. It has been stated that the result is always positive on the second attempt, and this has been attributed to the absorption of some of the tuberculin on the first occasion, and its subsequently causing a reaction to the second scratch. This is quite erroneous, as the following 14 cases in which I made the experiment show:

Reaction negative.	Repeated in 24 hours, again negative	Cases. ... 6
Reaction negative.	Repeated in 48 hours, again negative	... 1
Reaction negative.	Repeated in 5 days, again negative	... 7
Total	...	... 14

In 10 cases which gave a positive result I repeated the reaction (often many times), and the result was invariably still positive. The reaction may therefore be repeated without impairing its value, if for any reason it is found desirable to do so.

Reaction after Injection of Tuberculin.

Closely connected with the case of a repeated reaction is that of the reaction after a previous injection of tuberculin. The injection of tuberculin into a healthy person who gives a negative reaction will not cause a positive reaction to appear. This is proved by the following cases:

Eight healthy individuals were given an injection of tuberculin (500 mg.), and twenty-four hours later von Pirquet's reaction was done on six of them. It was in each case negative. Forty-eight hours after the injection the reaction was tried on the remaining two, and it was negative in these also.

But though the injection of tuberculin will not cause a positive reaction in a healthy individual, it will in certain cases curiously modify the type of reaction given by a tuberculous case. Before discussing this, a few words must be said about the types of reaction commonly seen.

The usual type which was referred to at the beginning of this article appears slightly on the first day, reaches a maximum on the second, and fades on the third and fourth. For convenience of description the intensity of the reaction will be represented by the following symbols: The sign + represents what I came to regard as the average amount of redness and oedema present in forty-eight hours. This is modified by qualifying adjectives written below, which indicate any divergence from the average. The sign - indicates no reaction. Thus, written symbolically, the common form of reaction would read as follows:

First Day.	Second Day.	Third Day.	Fourth Day.
+	+	+	+
Slight		Fading	Nearly gone

In other cases the type of the reaction is similar, but its intensity is much greater. Thus, I have frequently seen the following:

First Day.	Second Day.	Third Day.	Fourth Day.
+	+	+	+
Marked	Very marked	Marked	Fading

Or the reaction may run a perfectly even course, thus:

First Day.	Second Day.	Third Day.	Fourth Day.
+	+	+	+
			Fading

Reactions of the above types are commonly seen in the less serious forms of tuberculosis, such as glandular infec-

tions, in which the general health and the resisting power of the individual remain good. In more advanced cases, and especially in cases of joint disease with septic sinuses and evening temperature, the reaction frequently takes an entirely different type. Thus:

First Day.	Second Day.	Third Day.	Fourth Day.
+	+	-	-
	Nearly gone		

Here the maximum is on the first day, and the reaction has almost disappeared by the second. This condition may be so exaggerated that the reaction may have almost disappeared in twenty-four hours, and in doubtful cases, therefore, it is necessary to make an examination in eight or twelve hours, so as to be sure of not missing an early fleeting reaction.

In direct contrast to this is the reaction often seen in cases of old healed tuberculosis; thus:

First Day.	Second Day.	Third Day.	Fourth Day.
+	+	+	+
Marked	Very marked	Very marked indeed	Very marked indeed

Going on and only fading at the end of ten or fourteen days.

Wolf-Eisner regards the type of reaction seen as an important element in prognosis, and quotes a number of cases to prove his contention. My cases are not sufficiently numerous to enable me to speak with certainty on this point, but there is a fallacy in basing a prognosis upon the type of reaction owing to its great variability with the temporary condition of the patient. This variability seems to depend partly on the general health but mainly on injections of tuberculin, by autoinoculation or otherwise. From a prolonged series of observations it was found that an injection of tuberculin caused the reaction to take on the "early fleeting" type referred to, and it only returned to the normal in about seven days. Consequently, if the reaction be tested with a view to prognosis, it must not be done within a week of treatment by tuberculin.

Reaction with Bovine Tuberculin.

As it appeared a matter of some pathological interest the reaction was tried on a number of cases, using tuberculin made from the bovine as well as the human form of the tubercle bacillus. In fifteen such cases the reaction to the human and the bovine forms were exactly similar. Occasionally the intensity of the reaction was a little greater to one than the other, but the type was always the same. Moreover, the bovine reaction was similarly affected by injection of ordinary tuberculin. It was concluded, therefore, that as regards this reaction human and bovine tuberculin are substantially similar.

Reaction with Other Vaccines.

The reaction was tried in other forms of microbic infection (staphylococcal, streptococcal, and pneumococcal), using the corresponding vaccine in each case. In no case was any diagnostic reaction obtainable.

Summary and Conclusions.

1. Healthy children up to 12 years of age do not give von Pirquet's tuberculin reaction.
2. Tuberculous cases, with certain rare exceptions, do give this reaction.
3. The reaction has been of value in many doubtful cases.
4. The reaction may be repeated if desired without being modified or altered thereby.
5. A previous injection of tuberculin will not produce a reaction in a healthy patient.
6. An initial injection of tuberculin modifies the type of the reaction in a tuberculous case. The type returns to normal in about a week.
7. Bovine tuberculin behaves in an exactly similar manner to ordinary human tuberculin when used for the reaction. The reaction to bovine tuberculin is similarly modified in type by a subcutaneous injection of human tuberculin.