

A STUDY OF  
THE RELATIVE EFFICIENCY OF  
FOUR TUBERCULIN SKIN TESTS.

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## INTRODUCTION

Although it was as long ago as 1890 that Robert Koch introduced Old Tuberculin, only within comparatively recent years has the practical application of this great discovery been realised to the full.

There have been many reasons to account for this tardiness in development. On the one hand the supporters of the then orthodox teaching, if not openly antagonistic to Koch, were quietly cynical as to whether anything would come of this new discovery, while on the other hand many hailed it as the cure for a scourge which for centuries had taken its toll of the civilised world.

However, with the passage of years there has been consolidated from the systematised scientific examination of Old Tuberculin, a vast amount of evidence to demonstrate the essential value of this substance, leaving us eternally indebted to Koch for his discovery. From those studies, not only has our understanding of the clinical course of Tuberculosis been clarified but we have been given a product that will prove of immense value in the future eradication of Tuberculosis from civilisation.

## HISTORICAL RESUME OF THE EVOLUTION OF THE VARIOUS SKIN TESTS.

It has been demonstrated by experiments upon animals, as well as by observations on the human subject, that tuberculous infection whether apparent, latent or concealed, results in a specific hypersensitive state of the tissues to tuberculin. This phenomenon is the foundation of all tuberculin skin tests.

Originally the test was performed by Koch by the subcutaneous injection of tuberculin, resulting in sensitive subjects in reactions which have been classified as local, at the site of injection, focal, in the neighbourhood of foci of tuberculous infection in the tissues, and general, manifested by pyrexial upset. The last named reaction was the diagnostic feature of the Koch test.

It soon became apparent that these reactions could be very hazardous, exacerbating latent or active disease and consequently other methods of investigation had to be devised.

In 1892 Escherich (Hart, 1932) introduced a modification of Koch's original technique, which in its various forms has been used mostly in Austria and Germany. It consisted in injecting superficially

in the subcutaneous tissues dilutions of tuberculin in doses varying from 0.01 mgm. to 10 mgm., a positive reaction being characterised by local redness and oedema. This test, which for obvious reasons had to be conducted with extreme caution, gave accurate results but lacked facility in its application to large numbers of patients not under constant observation.

The scarification or scratch test was evolved by Pirquet in 1907. Because of its ease in performance and freedom from danger in the form of severe local or general reactions, this test became very popular.

About the same time Calmette and Wolff-Eisner started to use the conjunctival reaction brought about by dropping tuberculin into the conjunctival sac, but because of the pain resulting in positive cases and the danger of damage to the eye, this test has rightly been abandoned.

Elaborate technique and the infliction of pain are definite objections if they can be avoided without in any way taking from the accuracy of the test. So we find in 1908 Moro introduced the percutaneous test by which tuberculin was introduced into the tissues of the skin by inunction. However, although desirable in one respect this test failed in accuracy.

What has become recognised as the most accurate test in the detection of tuberculin sensitivity was announced in the same year by Mantoux. It consisted in the intradermal injection of tuberculin dilutions.

Unfortunately no test had been devised comparable in accuracy to the Mantoux test, at the same time eliminating pain and elaborate technique. Thus we find various attempts brought forward to solve the problem in the form of the Patch Tests.

Actually in 1908 there was devised the Percutaneous Tuberculin Plaster Test which did not receive the notice it merited until interest was re-aroused by MalMBERG (1931) who claimed for it almost as accurate results as for the Mantoux (1 mgm.) test.

In 1930 encouraging results were obtained in Germany by Vollmer (1937) who used adhesive tape on which tuberculin had been allowed to dry. Similar findings were obtained by Grozin (1933).

A further modification of the test advocated by MalMBERG was used by Wolff (1934) who applied to the skin a mixture of tuberculin and dead tubercle bacilli under adhesive strapping.

As will be shown later all these tests suffered from very obvious technical defects. With this in view Vollmer and Goldberg (1937) introduced "A New Tuberculin Patch Test" for which they claimed accuracy comparable to a carefully performed Pirquet

test. They went further with this excellent adaptation of the Patch Test and developed more recently another Patch Test which they have found so far directly comparable to the Mantoux (lmgm. ) test in accuracy.

Such then is a brief review of the evolution of the various Tuberculin Skin Tests in use at the present day.

#### THE DESIRABLE QUALITIES OF A TUBERCULIN SKIN TEST.

In the selection of a tuberculin skin test there are certain attributes which it must as far as possible possess. Hart (1932) states with reference to this subject "--- it should be safe, easily performed, capable of quantitative application, sufficiently sensitive to detect every tubercle infected individual ---". To this should be added the further requirements of freedom from pain, cheapness and long life.

To find such a test or combination of tests was the problem which confronted one at the outset of this investigation into the relative accuracy of the four tuberculin skin tests commonly in use.

#### CHOICE OF MATERIAL.

Many of the investigations into the comparative accuracy of these tests recorded in the literature have been conducted on frankly tuberculous subjects, but one would imagine that a more stringent examination would be to apply the tests to those who have been merely in contact with tuberculous infection, but who show no definite clinical evidence of disease as elicited by ordinary physical examination, for in those the greatest variation in sensitivity is to be expected. Accordingly for the purpose of this survey one hundred and fifty healthy contacts were examined.

The age groups were as follows:-

Age in Years	TUBERCULIN REACTION			
	Negative		Positive	
	Male	Female	Male	Female
0-1	1	0	0	0
1-5	7	7	12	11
5-10	9	5	28	19
10-15	2	5	13	18
15 & over	0	1	1	11
Sex Totals	19	18	54	59
Class Totals	37		113	
Grand Totals	150			

GENERAL PROCEDURE.

A card index system was used in recording the name, age, sex, probable source of infection, X-Ray screening report and the results of the various skin tests.

The Moro, Pirquet, Vollmer and Mantoux (0.1 mgm.) tests were applied simultaneously to each case. This technique would appear in no way to invalidate the results as Willis(1934) has stated that this point, though insufficiently studied, is not important as previous experience inclined him to the opinion that such a procedure had no effect on the reaction to any of the concurrent injections. The tests, except in the case of doubtful reactions, were read at the end of forty-eight hours. If no reaction resulted from the Mantoux (0.1 mgm.) test it was repeated using the 1 mgm. dose. It was reasonably assumed that a case reacting positively to a Mantoux (0.1 mgm.) test would also be positive to a Mantoux (1 mgm.) test.

DESCRIPTION OF THE TESTS USED WITH DISCUSSION OF RELEVANT LITERATURE.THE MORO TEST

As originally used by Moro equal parts of old tuberculin and lanolin were rubbed into the skin of the chest or the abdomen over an area of 5 cm. diameter, a resulting crop of papules indicating a positive reaction. By this technique accuracy considerably less than that obtained generally by the Pirquet test was reported by Hamman and Wolman, quoted by Hart (1932).

Lovett (1929) by improving the technique, obtained results comparable to, if not of greater accuracy than those obtained by the Pirquet test. The method consisted in rubbing a piece of concentrated old tuberculin the size of a pin head into the skin previously defatted by scrubbing with ether until hyperaemia resulted. The test was read in forty-eight hours, a positive reaction being similar in appearance to that obtained from the original Moro test.

The German literature contains references to the Moro test, but most of the evidence is of an inconclusive nature. Seier (1932) using the method obtained results with Moro's test comparable to those obtained with the Pirquet and Mantoux tests. Landau and Mossbach (1928) recommended the Moro test ~~and~~ in diagnosis. Hamburger (1928) evidently realising the inadequacy of the Moro test even when performed with very concentrated tuberculin suggests that it be

Followed if necessary by the Escherich subcutaneous test.

Friedman, Black and Esserman (1933) in trying out various tuberculin skin tests on tuberculous children found both the Pirquet and Moro tests quite unreliable.

Madsen (1935) in comparing results obtained from the use of the Mantoux, Pirquet and Moro tests on a large number of persons found the Moro test satisfactory up to the age of 11 or 12 years but thereafter it gave a wide difference when compared with the Mantoux results.

Malmberg (1931) already referred to in connection with the Patch Test obtained with the Moro test results inferior to those obtained by his own method.

Parish (1938) considers the Pirquet and Moro tests inferior to that of Mantoux.

#### RESULTS OBTAINED IN THE PRESENT SERIES.

For the present series a 50% Moro Ointment as supplied by Smith, Edinburgh was used. After defatting the skin in front of the sternum with ether until hyperaemia resulted, a piece of this Tuberculin Ointment about the size of a pea was massaged into the skin with 100 rubs over an area 3" square. This should not be exceeded as a brisk reaction of any size can be extremely irritating. The parents were instructed not to wash the area until after the test had been read along with the others at the end of forty-eight hours. Positive reactors showed a crop of papules occasionally accompanied by hyperaemia. The rash gradually faded within the course of a week, some late desquamation being frequently noted. One case was seen to give a delayed response, five days elapsing before the appearance of the typical rash. The other test results in this case were not delayed. No control was used with this method.

Age did not appear to have significant effect upon the reaction. The average age of those reacting positively to the Moro test was 7.4 years, whereas the average age of those reacting negatively to the Moro test and positively to one or other of the additional tests was 9.9 years.

Of the 150 cases tested by the Moro method 77 reacted positively and 73 negatively, the latter group including 37 cases which failed completely to give a response to any of the other tests.

MORO AND PIRQUET TESTS COMPARED.AGREEMENT

Both positive	44
Both negative (including 37 non-reactors)	<u>66</u>
	110

DISAGREEMENT

Moro positive, Pirquet negative	33
Moro negative, Pirquet positive	<u>7</u>
	40

MORO AND VOLLMER TESTS COMPARED.AGREEMENT

Both positive	76
Both negative (including 37 non-reactors)	<u>51</u>
	127

DISAGREEMENT

Moro positive, Vollmer negative	1
Moro negative, Vollmer positive	<u>22</u>
	23

MORO AND MANTOUX (0.1 mgm.) TESTS COMPARED.AGREEMENT

Both positive	75
Both negative (including 37 non-reactors)	<u>46</u>
	121

DISAGREEMENT

Moro positive, Mantoux (0.1 mgm.) negative	2*
Moro negative, Mantoux (0.1 mgm.) positive	<u>27</u>
	29

(\*Both of these cases reacted positively to the Mantoux (1 mgm.) test.)



MORO AND MANTOUX (1 mgm.) TESTS COMPARED.AGREEMENT

Both positive	77
Both negative (including 37 non-reactors)	37
	<u>114</u>

DISAGREEMENT

Moro positive, Mantoux (1 mgm.) negative	0
Moro negative, Mantoux (1 mgm.) positive	36
	<u>36</u>

From the above figures it will be seen that the efficiency of the Moro test lies somewhere between that of the Pirquet and Vollmer tests; but on account of its results differing so much from those of the Mantoux it should not be used as a diagnostic method. However it appears to be a better test than that of Pirquet. This impression is confirmed by the work of Monrad (1914) and (1933) on a total of 16,400 children.

ADVANTAGES

- (1) Ease of application.
- (2) Long keeping power.
- (3) Painless to the patient.
- (4) Causes no local damage or general reaction.

DISADVANTAGES

- (1) Failure to give accurate results.
- (2) Consumes more time than other methods.

THE PIRQUET TEST

This test was first described by Pirquet in 1907. Through a drop of tuberculin placed on the cleansed forearm a small superficial wound, not deep enough to cause bleeding, was made in the skin by means of a scarifier. The tuberculin was either allowed to dry or covered by a dressing and the test read in from 24 to 48 hours. A positive result is indicated by the appearance in forty-eight hours of a papule of at least 5 mm. diameter. At first Pirquet used diluted tuberculin but later abandoned this in favour of undiluted fluid with which more accurate results were obtained.

It is obvious from the different factors operating in such a test that variation in results should be marked. The chief causes of this variation are:-

- (1) The type of instrument used.
- (2) The pressure with which it is applied.
- (3) The brand of tuberculin employed.
- (4) The time allowed for drying.
- (5) The tenderness of the skin.

The relative sensitivity of the Pirquet and Mantoux tests has frequently been the subject of enquiry. Hart (1932) gives a concise summary of investigations reported on between 1909 and 1929, indicating that the Pirquet test is definitely inferior to the Mantoux. Of a total of 4, 787 clinically tuberculous patients no reaction to the Pirquet test was obtained in 16% and 23% if only children are considered. Amongst the higher degrees of error found may be quoted that of Tisal and Brown (1926) who found the corresponding value as high as 41.9%. Greengard and Nichamin (1934) report it as 34.6%.

More recently Slater and Jordan (1932) in a comparative study of the two tests in school children concluded that the Mantoux gives superior results to the Pirquet test.

Gleich (1932) working with coloured children found the Pirquet test less sensitive than the Mantoux.

Aronson, Zacks and Poutas (1933) concluded that in determining the incidence of tuberculous infection the Mantoux was superior to the Pirquet test quoting a large literature in support of their findings.

Friedman, Black and Esserman (1933) in comparing various tuberculin skin tests found the Pirquet test quite unreliable.

Madsen (1935) states that the Pirquet reaction is inferior in sensitivity to that of the Mantoux.

Steele and Willis (1937) in comparing results obtained by various methods of application of the newer Purified Tuberculin Products found the Pirquet test inferior to that of Mantoux.

Parish (1938) in an article on Tuberculin in Diagnosis states that the Pirquet test is less accurate than the Mantoux.

RESULTS OBTAINED IN THE PRESENT SERIES.

In this series the original technique of Pirquet was employed using undiluted tuberculin supplied by Bayer, London. The scarifier was identical with that designed by Pirquet. Along with the other reactions this test was read only at the end of forty-eight hours. A positive result consisted in the appearance of an indurated papule at least 5 mm. in diameter. Erythema was variable in extent but usually much greater than the induration. No control was used.

Of the 150 cases tested by the Pirquet method 51 reacted positively and 99 negatively, the latter group including 37 cases which did not react to any of the tests applied.

PIRQUET AND MORO TESTS COMPAREDAGREEMENT

Both positive	44
Both negative (including 37 non-reactors)	66
	<u>110</u>

DISAGREEMENT

Pirquet positive, Moro negative	7
Pirquet negative, Moro positive	33
	<u>40</u>

PIRQUET AND VOLLMER TESTS COMPARED.AGREEMENT

Both positive	50
Both negative (including 37 non-reactors)	51
	<u>101</u>

DISAGREEMENT

Pirquet positive, Mollmer negative	1
Pirquet negative, Vollmer positive	48
	<u>49</u>

PIRQUET AND MANTOUX (0.1 mgm.) TESTS COMPAREDAGREEMENT

Both positive	50
Both negative (including 37 non-reactors)	47
	<u>97</u>

DISAGREEMENT

Pirquet positive, Mantoux (0.1 mgm.) negative	1
Pirquet negative, Mantoux (0.1 mgm.) positive	<u>52</u>
	53

PIRQUET AND MANTOUX (1 mgm.) TESTS COMPARED.AGREEMENT

Both positive	51
Both negative (including 37 non-reactors)	<u>37</u>
	88

DISAGREEMENT

Pirquet positive, Mantoux (1 mgm.) negative	0
Pirquet negative, Mantoux (1 mgm.) positive	<u>62</u>
	62

Here again it is obvious how inaccurate the results of the Pirquet test can be. They are as low as any quoted in literature, and can be accounted for only by too superficial a scarification having been made. A test subject to such variation can never be of scientific value and may even be misleading unless controlled by other more accurate methods. The Pirquet test was inferior in efficiency to any other attempted.

ADVANTAGES

- (1) Ease of application.
- (2) Long keeping power.
- (3) No elaborate equipment required.
- (4) The scarifier is easily sterilised in a flame.
- (5) No untoward local or general reactions result.

DISADVANTAGES

- (1) Excessively liable to variation of application.
- (2) Very painful if done properly.
- (3) Not capable of accurate quantitative application. Hart (1932).
- (4) Even when properly applied it gives results inferior to those obtained from the Mantoux test.

THE PATCH TEST

From time to time various Patch Tests have been suggested for use in eliciting the tuberculin reaction but most of these have suffered from various technical disadvantages. A Patch Test appears to have been described for the first time in 1908. Unfortunately the method fell into obscurity until revived again by Malmberg (1931). The technique was as follows; Tuberculin Ointment of strength 3 of the State Serum Institute, Copenhagen was applied to the skin under adhesive plaster for 24 hours, the test being read at the end of 72 hours. In a series of 2,154 children up to the age of 15, tested by Monrad (1936), it was found to give more accurate results than the Moro test. In a further series of 1,720 children where this test was compared with the Mantoux (1 mgm.) 358 cases reacted positively to the Mantoux test. In only 17 of these were both patches negative. In 1,362 cases both plasters and intracutaneous test were negative. Therefore in a total of 1,720 children only 17 or 1% were not detected by the plaster and found by the Mantoux (1 mgm.) test. When expressed as a percentage of the Mantoux positive cases the error is 5%. The method of preparation of this ointment is given by Jensen (1938).

Adhesive strapping on which drops of old tuberculin had been allowed to dry was used by Vollmer in Germany for Patch Test purposes. Satisfactory results were obtained and the findings confirmed by other workers (Vollmer and Goldberg 1937).

Malmberg and Fromm (1931) developed this idea further by incorporating the tuberculin in the adhesive element of the Patch (1 drop per sq. cm.). It has been suggested as a disadvantage in this method that insufficient tuberculin could be combined with the adhesive matrix to give satisfactory results. But Anzen (1935) using this Plaster Test on 2,183 patients up to 15 years found it positively consistent with the Pirquet test in 307 cases and negatively consistent in 1,838 patients (98% conformity). In 0.5% the Plaster was positive and the Pirquet test negative. In febrile states the Patch Test was more sensitive than the Pirquet Test. Of the patients in whom both the Plaster and Pirquet Tests were negative, 806 were further tested by the Mantoux method (the doses varying from 0.1 to 5 mgm.). Of this number 11 (1.25%) reacted positively. The Plasters keep at least two years. Wolff and Hurwitz (1937) found this method expensive in widespread use. They also complain of the soft messy character of the Patches.

Seier (1932) using the method of Nathan and Kallos of applying tuberculin soaked pads to the skin under waterproof for 24 hours, claimed results equal to those obtained by the Mantoux test.

Grozin (1933) working on Vollmer's idea places a few drops of tuberculin on the skin covering it with a 3 cm. square of adhesive tape pressed down round the edges.

Wolff (1933) introduced a further modification. A pin-head sized drop of highly concentrated tuberculin mixed with dead tubercule bacilli in an absorbable base was applied to the skin under adhesive tape for 48 hours when the test was read. Accuracy practically equal to that obtained from the Mantoux (0.1 mgm.) test was reported in 800 children examined. Wolff and Hurwitz (1937) further report agreement between their ointment Patch Test and the Mantoux (0.1 mgm.) on 1,075 cases in 98.2%. The method is inexpensive and the ointment keeps for at least two years. Discrepancy occurred only in latent cases.

Vollmer and Goldberg (1937) described a "New Tuberculin Test". This consisted in applying to the skin a strip of adhesive plaster bearing three squares of filter paper, the two outer squares having been soaked in old tuberculin and dried while the middle one was used as a control having been soaked in glycerine broth and similarly dried. The Patch was applied for 48 hours when it could be read or better still at the end of 72 hours when all reaction from the tape had subsided. The natural moisture from the skin dissolved the tuberculin thus bringing about the typical cuti reaction. A positive reaction was characterised by a crop of papules or vesicles or merely erythema with some oedema in the region of the tuberculin squares whereas the control square gave no reaction save in pseudo cases where the result was recorded depending on contrast. This test they found equal to, if not better than, the Pirquet test in eliciting positive reactions. Of 209 tuberculous children examined by this method almost 90% showed conformity between the results of the Patch Test and those of the Pirquet Test. Of the 22 (10%) in whom the results did not conform 15 showed a positive reaction to the Patch Test and a negative reaction to the Pirquet Test. The following advantages were claimed for the test -

It is painless and does not excite nervous children.

It consumes less time.

It does not involve the use of instruments and their sterilisation nor is the skin traumatised by needles or scarifiers.

It can be performed without help by a nurse or an assistant.

In contrast to all other Patch Tests it creates a sharply defined area of reaction and prevents uncontrollable spread of tuberculin over the skin - a common complaint where ointment or wet tuberculin tape tests are used.

It eliminates the danger of infection.

It has never been known to stimulate a focal or general reaction.

The Patches keep for at least a year.

More recently Vollmer and Goldberg have increased the potency of the tuberculin content of the Patch Test by four-fold and it was with this product that the present series was tested. Not infrequently one finds when the Mantoux (0.1 mgm.) test is used routinely as the initial test dose severe local reactions, sometimes accompanied by fever and general malaise, occur. It was in an attempt to replace the Mantoux (0.1 mgm.) test that Vollmer and Goldberg increased the potency of their Patch Test.

In a series (not yet published) of 169 tuberculous children tested by the two strengths of Purified Protein Derivative and the Patch Test they obtained the following results:-

Number	P.P.D.1	Patch 1.	P.P.D.2	Patch 2.
164	Positive	Positive	not done as not necessary.	
1	Negative	Positive		
2	Negative	Negative	Negative	Negative
1	Negative	Negative	Positive	Negative
1	Negative	Negative	Positive	Positive

In a further series (not yet published) of 118 non-tuberculous children simultaneous testing was first done by the Pirquet and Patch methods. The negative reactors were retested by the Mantoux (1 mgm.) method. Results were as follows:-

Number	Pirquet	Patch	Mantoux (1 mgm.)
106	Negative	Negative	Negative
8	Positive	Positive	not done
2	?	Positive	not done
2	Negative	Positive	Positive

In this series just quoted the Mantoux (1 mgm.) test did not reveal a single case of tuberculous infection which had not been discovered already by the Vollmer Patch Test. No general reactions were noted.

Since the completion of the present series Hart (1938) has reported a comparative study of the results of the Vollmer and Copenhagen Patch Tests and the Mantoux Test on a series of 536 children of the hospital class. His results are as follows:-

Number	Vollmer	Copenhagen	Mantoux (1 mgm.max.)
436	Negative	Negative	Negative
95	Positive	Positive	Positive
1	Positive	Negative	Positive
1	Negative	Positive	Positive
3	Negative	Negative	Positive

(a) Twenty-eight gave a reaction to the Mantoux (0.01 mgm. or less). All gave markedly positive Patch Tests (Vollmer and Copenhagen).

(b) Sixty gave a reaction to the Mantoux (0.1 mgm.) test. All gave positive Patch Tests to both Vollmer and Copenhagen, less intense than in (a).

(c) Twelve gave a reaction to the Mantoux (1 mgm.) test. Three failed to react to either Patch. In two cases the Patches did not agree.

#### RESULTS OBTAINED IN THE PRESENT SERIES.

In the present series the Vollmer Patch Test was applied to the back between the shoulders after cleansing the skin with ether. The site was found to be usefully inaccessible in any attempt of the child to remove or scratch the test when itching occurred. The results were read along with the other tests at the end of 48 hours except in the case of doubt. A positive reaction appeared as a sharply circumscribed, infiltrated and reddened square with tiny papular or in sensitive cases even pustular elevations. Pseudo reactions were read in the usual way by contrast. Three cases of delayed reaction were noted, which fact supports the advisability of reading the test not sooner than 72 hours after application.

Most positive reactions faded after a week or so but many persisted for longer, showing slight desquamation and pigmentation, rather like the changes observed in the fading of a positive Schick reaction.

Even in the most sensitive reactors no case of excessive local disturbance was noted. A defaulter who kept the Patch on for a week and reacted positively did not show excessive eruption of the skin at the end of that time.

In the cases which showed a positive reaction to the Mantoux (0.1 mgm.) test but not to the Patch Test, the size of the Mantoux reaction was amongst the smallest noted, being on the average 2 cm. in diameter and always of a mild character. Where for the sake of accuracy a Mantoux (1 mgm.) test was also done no excessive reaction occurred.

One case of a pseudo-positive reaction was noted in this series the control showing a faintly papular eruption. (see plate)

Of the 150 cases tested by the Vollmer method, 98 reacted positively and 52 negatively, the latter group containing 37 cases which did not react to any of the tests applied.



VOLLMER AND MORO TESTS COMPAREDAGREEMENT

Both positive	76
Both negative (including 37 non-reactors)	<u>51</u>
	127

DISAGREEMENT

Vollmer positive, Moro negative	22
Vollmer negative, Moro positive	<u>1</u>
	23

VOLLMER AND PIRQUET TESTS COMPAREDAGREEMENT

Both positive	50
Both negative (including 37 non-reactors)	<u>51</u>
	101

DISAGREEMENT

Vollmer positive, Pirquet negative	48
Vollmer negative, Pirquet positive	<u>1</u>
	49

VOLLMER AND MANTOUX (0.1mgm.) TESTS COMPAREDAGREEMENT

Both positive	95
Both negative (including 37 non-reactors)	<u>45</u>
	140

DISAGREEMENT

Vollmer positive, Mantoux (0.1mgm.) negative	3
Vollmer negative, Mantoux (0.1mgm.) positive	<u>7</u>
	10

VOLLMER AND MANTOUX (1 mgm.) TESTS COMPAREDAGREEMENT

Both positive	98
Both negative (including 37 non-reactors)	<u>37</u>
	135

DISAGREEMENT

Vollmer positive, Mantoux (1 mgm.)negative	0
Vollmer negative, Mantoux (1 mgm. )positive	15
	<hr/> 15

From the above figures it can be seen how superior the Vollmer test is to any other excepting the Mantoux. But even when compared with the Mantoux test the Vollmer shows little deviation, more particularly from the Mantoux (0.1 mgm.) results.

When reduced to percentages the findings are as follows:-

(a) Of 102 Mantoux (0.1 mgm.) positively reacting cases 95 (or 93%) were Patch positive.

(b) Of 113 Mantoux (1 mgm.) positively reacting cases 98 (or 87%) were Patch positive.

(c) Of 150 cases examined only 4 were found to react to the Mantoux (0.1 mgm.) test which had not already reacted to the Vollmer test (97% efficiency for the Vollmer test).

(d) Of 150 cases examined only 15 were found to react to the Mantoux (1 mgm.) test which had not already reacted to the Vollmer test (90% efficiency for the Vollmer test).

One can see therefore that as yet the Vollmer test is not perfected but when used in conjunction with a Mantoux (1 mgm.) control there are many advantages over the repeated Mantoux testing with several dilutions.

These figures are considerably lower than those obtained by Hart (1938). Of his Mantoux positives 96% gave Vollmer positives whereas in the present series the corresponding figure was 87%. There is a possible explanation for this discrepancy in the fact that Hart read his tests at 72 hours whereas most of the present series were read at 48 hours for the sake of convenience of out-patients. The conclusions reached however in both instances are the same, namely that a negative Vollmer reaction does not exclude tuberculous infection and should be followed in all cases by a Mantoux (1 mgm.) test which if negative excludes tuberculous infection for all practical purposes.

ADVANTAGES

- (1) It is painless and does not excite nervous children.
- (2) It consumes less time.
- (3) It does not involve the use of instruments and their sterilisation, nor is the skin traumatised by needles or scarifiers.

ADVANTAGES (contin.)

- (4) It can be performed without help by a nurse or by an assistant.
- (5) In contrast to all other Patch Tests it creates a sharply defined area of reaction and prevents uncontrollable spread of tuberculin over the skin.
- (6) It eliminates the danger of infection.
- (7) It has never been known to stimulate a focal or general reaction.
- (8) The Patches keep for at least a year.
- (9) It eliminates the necessity for repeated graded injections.
- (10) It eliminates the danger of sloughing and permanent scar formation.

DISADVANTAGES

- (1) It is not as sensitive a test as the Mantoux.
- (2) Other disadvantages which were not found to be of any account in this series are quoted e.g. severe reaction and even vesiculation in sensitive subjects, time taken for the reaction to fade, and false reactions where folliculitis of the skin is present.
- (3) One very important objection to the use of this test is the cost.

Single Tests	..	..	..	1/3
10 Tests	..	..	..	10/3
100 Tests	..	..	..	42/-

subject to the usual Medical and Hospital discounts.

But since the basic materials are cheap there is no reason why with increased usage the cost should not fall. In an abstract from the German literature mentioned in the British Medical Journal Sept. 10th, 1938, page 80, some idea can be obtained of how tuberculin paper tests may be prepared and stored economically.

THE MANTOUX TEST

It was in 1908 that Mantoux introduced his intradermal tuberculin test and since then the technique has altered little.

From the literature already quoted in connection with the relative efficiency of the Moro, Pirquet and Vollmer tests it can be seen that the Mantoux test gives by far the highest number of positive reactions. Hart (1932) submits ample evidence to show that this efficiency is not only relative but absolute.

To facilitate accuracy in the intradermal injection of tuberculin dilutions a special syringe and needle must be employed.

It has been advised that a separate syringe be used for each dilution because of the adhesive nature of the stronger solutions of tuberculin, but in the present series this refinement of technique was not considered necessary. The syringe was carefully washed out with ether when there was any change in the dilution used.

Hausman and Neumann (1926) investigating the action of light on tuberculin found that the shorter wave lengths destroyed the potency of higher dilutions. Accordingly these were stored in dark coloured bottles.

As regards the keeping power of tuberculin dilutions the literature is full of conflicting opinions. To quote extremes, Smith (1929) advises that they be changed every two days, whereas Fernbach (1932) found a 1:8 dilution had changed little in six years, and in 25 years only half its potency had been lost, at 20 deg.C. in the dark. Much of what has been stated is rendered useless by the fact that little systematised study has been done and much prejudice allowed to over-rule. This problem was the subject of enquiry by the Health Organisation of the League of Nations (Paris 1933). Douglas and Hartley (1934) examined tuberculin dilutions under varying conditions for potency and stability. They found no loss in the potency of the 0.5% phenol saline dilutions kept at room temperature for 53 days. It was the practice in the present work to change these dilutions once monthly.

It should be understood that the volume of fluid injected intradermally in each case was 0.1 cc. 0.1 cc. of 1:1000 Old Tuberculin =t 0.1 mgm. O.T.  
0.1 cc. of 1:100 Old Tuberculin =t 1 mgm. O.T.

#### RESULTS OBTAINED IN THE PRESENT SERIES

Having previously noted how few contacts reacted to the Mantoux (0.01 mgm.) test, an initial strength of 0.1 mgm. Old Tuberculin was given along with the other tests. This was read at the end of 48 hours and if no reaction occurred a dose of 1 mgm. Old Tuberculin was next administered in the same way, the reaction being read at the end of a further 48 hours. The minimum standard adopted as a positive reaction was an erythema of at least 10 mm. or an induration of at least 5 mm. diameter. No control for the Mantoux test was used for Hart (1932) states there is no material need for such a procedure unless the 1 mgm. dose of Old Tuberculin is exceeded. A-typical non-specific reactions occur in only 0.5% of injections made with 1:1000 or 1:100 dilutions. Moreover 1 mgm.

was considered a sufficiently  $\approx$  high maximum dose of Old Tuberculin. Hart (1932) found that in tuberculous cases when a maximum of 0.1 mgm. O.T. was used the error was 4% or 6% for children aged 0 - 5 years.

In the present series only one case of general upset was noted, being characterised by malaise and headache which passed off in a day. The Mantoux (0.1 mgm.) reaction was very pronounced but disappeared satisfactorily.

Three cases showed vesicle formation in the Mantoux (0.1 mgm.) test, one being as large as a hazel nut. In no case did severe sloughing occur. Such a complication may leave a permanent scar (see plate).

Of the 150 cases tested by the Mantoux (0.1 mgm.) method 102 reacted positively and 48 negatively, the latter group containing 37 cases which did not react to any of the tests applied.

With the Mantoux (1 mgm.) test, 113 reacted positively and 37 negatively. None of this last group of 37 cases reacted to any other tuberculin test.

The figures for the comparison of the Moro and Pirquet tests with the Mantoux have already been given under the appropriate headings but on account of their differing widely they will not be quoted here.

#### MANTOUX (0.1 mgm.) AND VOLLMER TESTS COMPARED

##### AGREEMENT

Both positive	95
Both negative (including 37 non-reactors)	<u>45</u>
	140

##### DISAGREEMENT

Mantoux (0.1mgm.) positive, Vollmer negative	7
Mantoux (0.1mgm.) negative, Vollmer positive	<u>3</u>
	10

#### MANTOUX (1 mgm.) AND VOLLMER TESTS COMPARED

##### AGREEMENT

Both positive	98
Both negative (including 37 non-reactors)	<u>37</u>
	135

DISAGREEMENTS

Mantoux (1 mgm.) positive, Vollmer negative	15
Mantoux (1 mgm.) negative, Vollmer positive	<u>0</u>
	15

MANTOUX (0.1 mgm.) AND (1 mgm.) TESTS COMPAREDAGREEMENT

Both positive	102
Both negative (including 37 non-reactors)	<u>37</u>
	139

DISAGREEMENT

Mantoux (0.1 mgm.) positive, (1 mgm.) negative	0
Mantoux (0.1 mgm.) negative, (1 mgm.) positive	<u>11</u>
	11

It will be seen from the figures given above how essential it is as yet to control all other skin tests by the Mantoux method. When the Mantoux test is used alone it is further advisable to use dilutions up to at least 1:100 strength if reasonable accuracy is expected.

ADVANTAGES

- (1) Accuracy of a higher order than by any other tuberculin skin test is obtained.
- (2) This accuracy is not only relative but absolute.
- (3) The method is not expensive especially when large numbers have to be examined.

DISADVANTAGES

- (1) To avoid reactions of a severe nature several dilutions must be employed and this unnecessarily increases the amount of work.
- (2) Elaborate equipment is required.
- (3) The dilutions do not keep for long periods.
- (4) Pain, though transient at the time of injection, frequently gives trouble when the reaction is at its height.
- (5) Co-operation of the patient is essential. Only from experience can one realise how difficult it can be to perform a Mantoux test even with assistance upon a rebellious child.

GENERALCONCLUSIONS

From what has been written it is obvious that as yet the ideal Tuberculin Test has not been found.

The Moro and Pirquet tests, unless controlled by the Mantoux, are much too misleading in their inaccuracy to be used as diagnostic methods.

Where accuracy alone is considered the Mantoux test gives by far the most satisfactory results.

The Vollmer test approximates in efficiency to the Mantoux (0.1 mgm.) test.

There is much to be said in favour of a combination of Vollmer and Mantoux (1 mgm.) testing. While giving results of the highest order this technique would be found more acceptable to both patient and doctor by safely eliminating repeated intradermal injections.

An attempt should be made to increase still further the potency of the Vollmer Patch Test so as to approximate its efficiency to that of the Mantoux (1 mgm.) test.

For the occasional testing of patients in General Practice the Vollmer Patch Test should prove very useful because of its simplicity and long life. Patients reacting negatively to this test may be safely retested using the Mantoux (1 mgm.) method. In the latter test tuberculin can be replaced by Purified Protein Derivative Material with advantage since it keeps for a long time in the dry state. Tablets of equivalent diagnostic power to that of 1 mgm.O.T. are available. (5 mgm. P.P.D./cc. =t International Standard Old Tuberculin)

SUMMARY.

A short historical resume is given of the evolution of the Tuberculin Skin Tests commonly in use to-day.

An attempt is made by the study of the reactions from those tests on 150 tuberculosis contacts to assess the relative efficiency of each test.

Of the Mantoux (1 mgm.) positive reactors -

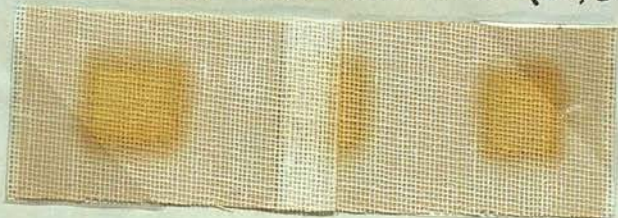
87% were Vollmer positive  
45% were Pirquet positive  
68% were Moro positive.

actors - Of the Mantoux (0.1 mgm.) positive re-

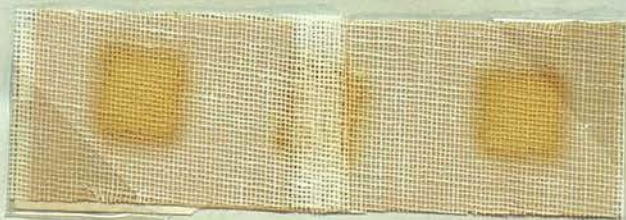
93% were Vollmer positive  
49% were Pirquet positive  
74% were Moro positive.

A method of combined Vollmer and Mantoux testing is suggested with in view the simplification of technique and the elimination of unnecessary pain.

VOLLMER PATCH TEST (LEDERLE)



BACK.



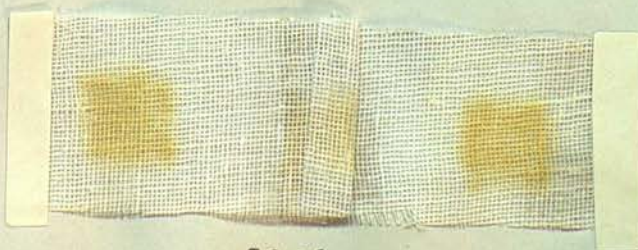
FRONT.



↑  
TEST.

↑  
CONTROL.

↑  
TEST.



GAUZE.



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APPENDIX

PLATES

Dufaycolor Transparencies should be viewed against bright diffuse day-light or in a viewing box giving similar day-light illumination.

- Plate 1. This shows a typical positive Vollmer reaction. The erythema and papulation are well demonstrated.
- Plate 2. This shows a more diffuse erythematous reaction with feeble papulation. The control area between the erythema patches is quite pale.
- Plate 3. This is of interest, as in addition to a bright positive Vollmer reaction, it shows a pseudo reaction in the control area. There is no difficulty in deciding the reading.
- Plate 4. This shows a permanent scar 1" in diameter on the arm of a child tested with an initial Mantoux (0.1 mgm.) dose. Such a danger is obviated by the use of Vollmer Patch Tests.

(ii)

I.

PLATE. I.



Typical Positive Vollmer Reaction.

II.

PLATE. II



Positive Vollmer Reaction - Diffuse Erythema.

III.

PLATE III



Positive Vollmer Reaction - with Pseudo.

IV.

PLATE IV



Permanent Scar from a Mantoux (0.1mg) test.

CASE INDEX

No.	Name	Age	Sex	Moro	Pirquet	Voëlmer	Mantoux 0.1mg	Mantoux 1 mg	X-Ray	Infect. Source
1	S.A.	9	M	+	-	+	+		N	S. O.
2	A.A.	11	F	-	-	+	+		IHS&L	"
3	M.A.	15	F	+	+	+	+		RA	F. L.
4	M.A.	7	F	+	+	+	+		N	M. L.
5	A.A.	6	M	+	+	+	+		IHS	"
6	F.A.	3	M	+	-	+	+		N	"
7	G.B.	7	M	+	-	+	+		N	F. L.
8	J.B.	5	F	+	+	+	+		RB	"
9	E.B.	3	F	+	-	+	+		N	"
10	J.B.	1	M	-	-	+	+		IHS	"
11	C.B.	8	F	+	-	+	+		IHS	"
12	W.B.	4	M	+	+	+	+		IHS	"
13	J.B.	13	F	-	+	+	+		N	G. L.
14	A.B.	9	M	-	+	+	+		N	"
15	M.B.	5	F	-	-	-	-	-	ND	F. L.
16	J.B.	3	F	-	-	-	-	-	ND	"
17	A.B.	6	M	+	-	+	+		N	B. O.
18	M.B.	13	F	+	-	+	+		N	"
19	D.B.	6	F	+	+	+	+		LB	F. L.
20	M.B.	3	F	+	-	+	+		N	"
21	H.B.	2	F	+	-	+	+		N	"
22	S.B.	3	F	+	+	+	+		N	M. L.
23	G.B.	9	M	-	-	-	-	-	ND	S. L.
24	C.B.	17	F	-	-	-	+		N	"
25	W.B.	2	M	+	+	+	+		N	F. L.
26	D.C.	9	M	+	+	+	+		N	L. L.
27	H.C.	11	M	+	+	+	+		ND	U. L.
28	F.C.	11	F	-	-	-	+		N	L. L.
29	J.C.	11	F	-	-	+	+		N	S. O.
30	P.C.	7	M	-	-	+	+		N	"
31	J.C.	11	M	+	+	+	+		IHS	"
32	J.C.	9	M	-	-	-	-	-	ND	"
33	M.C.	13	F	+	-	+	+		ND	M. L.
34	J.C.	4	M	+	-	+	+		IHS	S. L.
35	A.C.	6	F	+	+	+	+		N	M. L.
36	W.C.	10	F	-	-	-	-	-	ND	M. O.
37	J.C.	10	M	-	-	-	-	+	ND	"
38	V.C.	13	F	-	-	+	+		ND	"
39	W.D.	1	M	-	-	-	-	-	ND	M. L.
40	G.D.	8	F	+	-	+	+		IHS	"
41	V.D.	13	F	+	+	+	+		N	S. L.
42	W.D.	16	F	+	-	-	-	-	ND	B. L.
43	J.E.	4	F	-	-	-	-	-	ND	F. L.
44	C.E.	2	M	-	-	-	-	-	ND	"
45	A.E.	12	M	+	+	+	+		IHS&L	B. L.
46	V.F.	15	F	+	+	+	+		IHS	B. O.
47	M.F.	9	F	-	-	-	-	-	ND	"
48	M.F.	8	F	+	-	+	+		N	"
49	G.F.	2	M	-	-	-	-	-	ND	"
50	D.F.	5	M	-	-	+	+		ND	"
51	J.F.	3	F	+	+	+	+		N	"
52	P.F.	1	F	-	-	-	-	-	ND	"
53	E.G.	12	F	+	-	+	+		IHS	F. L.
54	R.G.	10	M	+	-	+	+		N	"

(v)

No.	Name	Age	Sex	Moro	Pirquet	Vollmer	Mantoux 0.lmg.	Mantoux 1mg.	X-Ray	Infect. Source
55	J.G.	12	M	-	-	-	-	-	ND	F. L.
56	J.G.	15	F	-	-	+	+	-	IHS	M. L.
57	A.G.	2	M	+	-	+	+	-	IHS	"
58	M.G.	10	F	-	-	-	-	-	ND	B. O.
59	C.G.	3	F	-	+	+	+	-	N	"
60	M.H.	36	F	-	+	+	+	-	N	So.L.
61	S.H.	9	M	-	-	-	-	+	ND	B. L.
62	J.H.	13	M	-	-	-	-	-	ND	"
63	J.H.	10	M	-	-	+	+	-	IHS	F. L.
64	D.H.	21	F	-	-	+	+	-	ND	H. L.
65	J.H.	14	M	+	-	-	+	-	ND	M. L.
66	J.H.	6	M	-	-	-	-	-	ND	?
67	D.H.	5	M	-	-	-	-	-	ND	M. L.
68	G.H.	8	M	+	-	+	-	+	IHS	"
69	A.H.	13	F	-	-	-	-	-	ND	B. O.
70	M.H.	2	F	-	-	+	+	-	IHS	"
71	L.H.	8	F	-	-	-	-	-	ND	"
72	F.H.	6	M	+	-	+	+	-	N	"
73	M.H.	5	F	+	-	+	+	-	N	F. L.
74	E.H.	6	F	+	-	+	+	-	N	"
75	S.J.	3	F	-	-	+	+	-	N	M. L.
76	P.J.	6	F	-	-	+	+	-	IHS	"
77	J.J.	3	M	-	-	-	+	-	ND	F. L.
78	M.J.	10	F	+	-	+	+	-	ND	"
79	S.J.	2	M	-	+	-	+	-	ND	"
80	W.J.	8	M	+	+	+	+	-	ND	"
81	C.J.	5	F	+	-	+	+	-	ND	"
82	J.K.	5	F	+	+	+	+	-	N	"
83	P.K.	7	M	+	+	+	+	-	ND	M. L.
84	J.K.	4	M	-	-	-	-	+	ND	"
85	J.K.	13	M	+	+	+	+	-	IHS	"
86	H.M.	6	M	+	+	+	+	-	IHS	"
87	M.M.	14	F	+	+	+	+	-	IHS	F. L.
88	B.M.	23	F	-	-	-	+	-	ND	"
89	A.M.	3	M	+	-	+	+	-	ND	"
90	C.M.	16	F	+	+	+	+	-	RB	S. L.
91	A.Mc	16	M	+	+	+	+	-	IHS	F. L.
92	J.Mc	8	M	-	-	+	+	-	IHS	M. L.
93	T.Mc	13	M	+	-	+	+	-	N	B. O.
94	G.Mc	4	M	-	-	-	-	-	ND	"
95	A.Mc	2m	M	-	-	-	-	-	ND	S. O.
96	H.Mc	10	F	-	-	-	-	+	N	A. L.
97	M.Mc	11	F	-	-	-	-	-	ND	"
98	T.Mc	8	M	-	-	-	-	-	ND	"
99	R.Mc	5	M	-	-	-	-	-	ND	"
100	A.Mc	2	M	+	-	+	+	-	N	F. L.
101	C.Mc	6	M	-	-	-	-	-	ND	"
102	M.Mc	6	F	+	+	+	+	-	N	M. L.
103	J.Mc	6	M	+	+	+	+	-	IHS	F. L.
104	K.Mc	5	M	-	-	-	-	-	ND	M. L.
105	I.Mc	2	M	-	-	-	-	-	ND	"
106	E.Mc	6	M	-	-	-	+	-	ND	F. L.
107	E.Mc	9	F	+	+	+	+	-	LB	"
108	I.Mc	6	M	-	+	+	+	-	N	"
109	P.P.	5	M	+	+	+	+	-	IHS	M. L.

No.	Name	Age	Sex	Moro	Pirquet	Vollmer	Mantoux 0.1mg	Mantoux 1mg.	X-Ray	Infect. Source
110	R.P.	13	M	+	-	+	+		IHS	F. L.
111	P.P.	8	F	+	-	+	+		IHS	F. L.
112	T.R.	12	M	+	+	+	+		IHS	"
113	A.R.	11	M	+	+	+	+		N	"
114	G.S.	7	M	-	-	-	-	-	ND	S. O.
115	J.S.	6	M	+	-	+	+		ND	M. L.
116	I.S.	3	F	-	-	-	-	-	ND	"
117	A.S.	1	M	-	-	-	-	-	ND	"
118	G.S.	4	M	+	+	+	+		N	F. L.
119	J.S.	8	M	+	+	+	+		N	S. L.
120	E.S.	11	F	+	-	+	+		N	M. L.
121	B.S.	6	F	+	-	+	+		N	"
122	P.S.	8	F	-	-	+	-	+	IHS	U. L.
123	E.S.	5	F	-	-	-	-	-	ND	F. L.
124	W.S.	2	F	-	-	-	-	-	ND	"
125	J.T.	8	M	-	-	-	-	+	ND	"
126	R.T.	5	M	-	-	+	+		N	S. L.
127	A.T.	17	F	+	+	+	+		L	"
128	C.T.	12	F	-	-	-	-	-	ND	"
129	M.V.	1	F	-	-	-	-	-	ND	F. L.
130	M.W.	5	F	-	-	-	-	-	ND	L. L.
131	J.W.	4	M	-	-	-	-	-	ND	"
132	E.W.	2	F	+	-	+	+		N	"
133	M.W.	35	F	+	+	+	+		IHS	H. L.
134	E.W.	14	F	-	-	+	+		IHS	F. L.
135	J.W.	12	F	+	+	+	+		N	"
136	H.W.	8	F	+	+	+	+		IHS	S. L.
137	G.W.	11	M	-	-	-	-	+	ND	"
138	W.W.	5	M	-	-	-	-	+	N	M. L.
139	R.W.	3	F	-	-	-	-	-	ND	"
140	E.W.	4	F	+	+	+	+		N	"
141	J.W.	6	M	+	+	+	+		N	"
142	A.W.	9	M	+	+	+	+		IHS	"
143	T.W.	8	M	+	-	+	+		IHS	B. O.
144	J.W.	2	F	+	+	+	+		ND	M. L.
145	H.W.	14	F	-	-	-	-	+	ND	"
146	C.W.	13	F	+	+	+	+		N	S. L.
147	D.W.	13	F	+	+	+	+		IHS	"
148	A.W.	18	F	-	+	+	+		B	M. L.
149	A.W.	7	F	+	+	+	+		ND	"
150	N.W.	5	M	+	+	+	-	+	ND	"

KEY TO INDEX

X-Ray Abbreviations:-

B . . .	Increase in basal shadows.
L . . .	Shadow in either lung field.
N . . .	Normal appearance.
LB . . .	Left basal shadow.
ND . . .	Examination not done (negative reactors and defaulters)
RA . . .	Right apical shadow.
RB . . .	Right basal shadow.
IHS . . .	Increased hilar shadow.
IHS&L . . .	Increased hilar shadow with additional shadow in either lung field.

Infecting Source Abbreviations:-

A . . .	Aunt
B . . .	Brother
F . . .	Father
G . . .	Grandparent
H . . .	Husband
L . . .	Landlady
M . . .	Mother
S . . .	Sister
So . . .	Son
U . . .	Uncle
L . . .	Pulmonary lesion
O . . .	Lesion other than above.

PROBABLE SOURCE OF INFECTION

Of the 113 positively reacting cases 88 reported for X-Ray examination.

Of these 47 showed no lesion and 41 showed some lesion.

Increased Hilar Shadows accounted for 83%.

In the 88 cases examined there was evidence indicating that in 60% the probable source of infection was a pulmonary lesion in the parent.

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