Thesis
on
"Tuberculosis in Relation to Measles
and other Infectious Diseases; a Study
of the Intra-Dermal Tuberculin Test"

Presented to the
Faculty of Medicine,
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by

JAMES STEWART WESTWATER,
M.B., Ch.B. (Univ. Edin.), D.P.H. (R.C.P.S.,
Eng.)

Park Hospital
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PREFACE.

Medicine being an Art as well as a Science, it is liable to reflect human failings and foibles, one of which is the weakness for a "fashion". It may be said that of the various tuberculin tests, the one associated with von Pirquet's name has been the fashionable one. Recently, however, the intra-dermal method of Mendel and Mantoux has bid fair to supplant the scarification test in popularity. If it is going to prove fashionable, it occurred to one that it might be of service to investigate its possible fallacies, particularly in relation to the acute infectious diseases.

Although the physician may be prone to "fashion" in technique, he is also a slave to dogma. A positive statement in medicine often acquires the authority of an established principle.

One such principle has been that tuberculosis is particularly liable to ensue after certain acute infectious diseases. Accordingly adopting the latest "fashion" in tuberculin tests, I set out as a devout believer to assess the value of the test in mitigating this grave sequel of events.
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Definitions.

"Allergy; sensitivity; reactivity" - used synonymously to indicate those specific reactions of the infected subject to bacillary protein.

"Anergy" - as used originally by von Pirquet, to indicate a loss or lack of allergy.

"Tubercular; tuberculous" - those adjectives, unless qualified, are applied to children with a sensitivity to tuberculin, such sensitivity being accepted as indicating tubercle infection, past or present; it does not imply active disease.

"Latent infection" - means infection without clinical evidence; it does not imply quiescence.
I. INTRODUCTION.

(1). Gravity of Measles and Whooping Cough.

(2). Purposes of the Investigation -
   value of the intra-dermal tuberculin test.

(a) Relation of measles and whooping cough to tuberculosis.

(b) Tuberculin allergy in acute infectious diseases.

(c) The value of the negative test.
(1). **The gravity of measles and whooping cough.**

As preventive medicine has advanced, controlling if not actually eliminating certain acute infections, there are two which have become gradually more prominent until they now appear as the most fatal of acute infectious diseases; they are measles and whooping cough. For some reason they have been long regarded by the laity as normal events in the natural history of the individual.

**Mortality.** The figures for the whole of England and Wales in 1931 show measles and whooping cough to rank with diphtheria, measles even surpassing it in gravity.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Total No.</th>
<th>Proportion per 1,000 deaths from all causes.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>3,288</td>
<td>7</td>
</tr>
<tr>
<td>Whooping cough</td>
<td>2,512</td>
<td>5</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>2,673</td>
<td>5</td>
</tr>
<tr>
<td>All tuberculosis</td>
<td>35,818</td>
<td>73</td>
</tr>
</tbody>
</table>

The acute respiratory infections approximate to the figure for tuberculosis; no doubt some deaths registered in the category of pneumonia are really late legacies of measles and whooping cough, so that these diseases probably have a larger mortality than their actual statistics show.

These figures are sufficient to direct attention to the gravity of diseases so long taken for granted as
benign medical events in any child's life. Included in the tables are the figures for tuberculosis, still high enough to warrant continued efforts to add to the successes already gained.

Now it is generally accepted that a source of the mortality in measles and whooping cough is the liability of the acute infectious diseases to predispose to or reactivate tuberculosis, and it was this belief that prompted this study.

Most authorities favour this view. Fishberg (1932) states... "in infants and children tuberculous broncho-pneumonia is infrequently a sequel of measles and whooping cough." Ker (1929) and Goodall (1928) subscribe to a similar opinion. Osler and McCrae (1928) however are non-committal, simply giving measles and whooping cough first rank among the acute infections lowering resistance.

MacNalty (1932), examining the figures of the incidence of tuberculosis in measles, is definitely sceptical, and concludes "until further evidence to the contrary is forthcoming, the influence of measles in directly favouring infection by the tubercle bacillus must be held to be dubious"; whooping cough, however, he considers capable of "igniting a latent Tb. lesion."

There is then some doubt in the matter, and the fact that measles and whooping cough are now the most dangerous of the infectious diseases makes any enquiry
into the causes of their considerable mortality and sequelae of some value.

(2). **Purposes of the investigation.**

(a). **Relation of measles and whooping cough.**

It is a principle of preventive medicine to discover the "bad risks" in any infectious disease. Applying this to measles and whooping cough it would be to discover the cases liable to the serious complications and therefore the cases liable to tuberculosis. How could this be done? By the use of the tuberculin test. Having had experience of the intra-dermal test at the East London Children's Hospital, Shadwell, I decided to try and assess its value in routine use in cases suffering from acute infectious diseases.

(b). **Tuberculin allergy in acute infectious diseases.**

The difficulty then arose that in certain of the infectious diseases the tuberculin sensitivity is weakened and even lost altogether. Although this has been known for many years, the maximum duration of any such effect does not seem to have been adequately determined. The first point then to settle was the degree of effect on tuberculin sensitivity in each disease, and then if possible determine how long it might last, and especially for how long a tubercular subject might remain completely insensitive to the test.
(c). The negative value of the tuberculin test.

Hart (1932) has adequately stressed the great importance of a negative tuberculin test in excluding tuberculosis.

It is agreed by clinicians that a positive result in itself does not mean active tubercular disease, although the younger the patient the more significant it is. The negative result, however, has become of much more value as the technique of the tests have improved, and it is now considered that in a patient with suspicious symptoms, a negative tuberculin test is of considerable significance.

There are certain fallacies, however, such as the low tuberculin allergy in acute forms of tuberculosis and in certain acute infections, notable measles, during which a sensitive subject may fail to react to the test.

Having determined the period in the acute infectious diseases during which a negative response might occur in a tubercle-infected patient, it would then be possible to test such cases at a period when the effect had passed off and thus be certain of selecting all the tubercular population in each disease. This was hoped to be of some value in measles and whooping cough for such cases could then be given special after-care and possibly avert the sequelae of tuberculosis reputed to ensue so commonly.
This study, then, sets out to answer the following questions: (1), to what extent may the intra-dermal tuberculin test be fallacious in acute infectious diseases? (2), what is the value of the test in these diseases? (3), what is the prognosis for the tubercular child suffering from an acute infectious disease? (4), is special after-care necessary for such children.
II. TUBERCULOSIS IN CHILDREN.

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Tuberculosis is a disease of such variety that it is necessary to define which form of the disease is implied before proceeding with any discussion.

1). Experimental tuberculosis.

The disease is primarily a lymphatic infection. This has been adequately demonstrated experimentally; from a primary inoculation there is a rapid spread from the site of infection through the lymphatic channels, and this spread is determined by the distribution of the lymphatic tissue of the animal (Krause, 1928; Scott, 1930). No matter where the site of inoculation may be, the infection ultimately involves all the main aggregations of lymphoid tissue. It is also characteristic of the primary infection that the local lesion heals without leaving a trace.

Following upon this lymphatic spread, allergy develops after a latent interval, and with it the characteristic feature of localisation of a re-infection typified in the Koch phenomenon.

2). Nature of tuberculin allergy.

This sensitivity has always been regarded as indicative of some resistance, although certain anomalies were difficult to explain. A primary overwhelming infection could prove fatal and no apparent sensitivity develop. It was supposed that the patient succumbed in the latent period before allergy and
therefore immunity was acquired. Further, von Pirquet found that in advanced cases allergy seemed to wane in the final stages of the disease, and considered that resistance weakened with the sensitivity.

On the other hand, cases can die of tuberculosis and retain their allergy to the end, which does not suggest that immunity is identical with resistance.

That this sensitivity to the bacillary protein was not identical with immunity was shown by Willis (1928); experimentally he found that a sensitized animal in time lost its allergy and yet retained its acquired resistance.

Rich (1929) elucidated the question and has demonstrated that an animal can be desensitized and yet it still retains its acquired immunity. Further, Rich has shown that this animal is better without its sensitivity, as the acute inflammatory reactions due to the intense irritation of the bacillary protein have a deleterious effect on the tissue cells, tending to facilitate the spread rather than arrest of infection.

Tuberculin allergy as indicated by the cutaneous response to tuberculin is therefore not an indication of immunity; immunity may co-exist, but is a separate entity. Is this allergic state analogous to the pseudo-reactions to the diphtheria bacillus?

Dudley (1929), by careful analysis has deduced that the
pseudo-reaction in the Schick test indicates recent contact with the diphtheria bacillus - the subject may or may not be immune to the exo-toxin. He showed that the reaction tends to wane from the time of infection. By analogy this would explain the significance of the reaction; it means tuberculin/infection past or present, active or quiescent, but it does not imply immunity. Also by analogy with the pseudo-Schick reaction, the more marked the response the more recent has been infection.

(3). Primary tubercle infection in children.

In children it is the primary lymphatic stage of the disease which is commonly observed. Whatever may be the portal of infection, the invasion is always lymphatic; an inhalation infection in the infant results first in the characteristic "benign infiltration", or "epituberculosis" - an example of Ranke's epithelioid tissue reaction in the lung parenchyma.

As Stewart (1932) has shown, it is this "benign infiltration" which later regresses to or from "Ghon's focus". Along with this primary lesion in the lung there is the involvement of regional glands at the hilum.

If the portal of entry be the alimentary tract, the mesenteric glands are first involved and often no focal lesion is to be found in the bowel itself. Once the infection reaches the lymphatic system, it tends to
spread throughout.

The fate of the child depends on the mass and repetition of infection; if slight, the lesions may regress without a trace except that a tuberculin sensitivity may persist; in others traces may be left such as a Ghon's focus or a calcified gland. On the other hand, if the infection is massive the child may succumb to an early generalisation, and meningitis is the usual termination to such cases.

The primary invasion is usually 'silent'; it is commonly symptomless. In a baby there may be a failure to gain weight; a short dry cough may direct attention to the lungs, and evidence of a primary infiltration may then be discovered. In the older child it is also commonly symptomless, unlike the focal disease of adults.

Clinically, then, primary tuberculosis is difficult to detect, and it is usually not until allergy has developed that it is detected. Sensitivity probably develops in 3-10 weeks, and with it that localising power, and the case enters on the second stage.

When a positive result is obtained, X-ray examination will often reveal evidence in the lungs and hilar glands, but clinical examination is usually fruitless.

Stewart (1932), valuing the tuberculin test at 100% in detecting tubercle infection, has assessed the
stethoscope at 1½.

Having found that a child gave a positive reaction, one relied largely on clinical findings as to the site of the infection. In some, typical small rounded glands would be palpable in the neck or in the mesentery of the abdomen. Mesenteric glands are readily palpable in thin subjects, but if the abdominal wall is well developed or the child at all fat, it is difficult to be certain. Radiological facilities not being available, no certain diagnosis could be made of enlarged hilar glands. D'Espine's sign one has not accepted without the means of confirming it; likewise the intrascapular and sternal dullness of itself is of little value. Occasionally faintness of breath sounds, limited to one lobe or one lung would give definite evidence, although this is also characteristic of the primary lymphatic infiltration of the lung; in the latter there is an impaired note over the affected lobe; also it is a condition to be expected most commonly in the first 2 years.

In a disease such as measles reliable clinical findings would be of value when the tuberculin test is not trustworthy. Small hard discrete and rounded cervical glands are well-nigh pathognomonic, but in cases of chronic otitis media or recurrent impetigo of the scalp, the upper cervical group of glands may show such features in a non-tubercular child.
Macgregor (1930), analysing 250 cases of autopsies on tubercular children, found only 23.5% with the cervical glands affected, so that only one out of four cases can possibly be recognised by examination of the cervical glands; 75% had lesions in the abdominal glands, but these are difficult to recognise clinically while the thoracic group can only be detected definitely by X-ray examination, which even then requires corroborative evidence in children, as calcification is unusual in early years. Accordingly the tuberculin test must be the main guide in detecting tubercle infection in children.

(4). Significance of the positive tuberculin reaction in children.

In this investigation I have chosen to investigate the behaviour of the sensitized children under 7 years, as over this age the positive reaction loses its significance. Although in the great majority of those under 7 years with a positive reaction I could not detect any clinical signs of tuberculosis, yet such cases cannot be said to be "latent" in the sense that the infection is necessarily quiescent and arrested. The younger the child, the more likely is the process to be active, but as it is primary and lymphatic, it is usually silent and symptomless. Macgregor (1930) in Edinburgh, found post mortem that in children under
a year, 100% of the tubercular lesions showed evidence of activity, and 96% of those in the second year.

It is of interest that the principle lesions were thoracic, indicating the importance of human infection; especially was this so in the first year.

Blacklock (1932) in Glasgow, similarly found that all the children under 2 years who showed tubercular lesions post mortem died from the tuberculosis. Thus it would seem that nearly all the children under 2 years infected with the tubercle bacillus die from the infection.

Macgregor and Blacklock both regard tuberculosis as a fatal disease at this age, a view sponsored by the Opie (1917). This is at variance with experience of clinicians.

Significance of a positive reaction in infancy.

As I have indicated, the pathologist regards tuberculosis as a fatal disease in infancy, but although clinical experience seemed formerly to corroborate this, recent work in America and on the Continent has shown that tubercle infection in the infant is by no means incurable. The mortality in children with a positive tuberculin reaction quoted by various authors is as follows:-
### Mortality

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 year</td>
<td><strong>78%</strong></td>
</tr>
<tr>
<td></td>
<td>Hempelman (1917).</td>
</tr>
<tr>
<td></td>
<td><strong>56%</strong></td>
</tr>
<tr>
<td></td>
<td>McLean and Jeidell (1922).</td>
</tr>
<tr>
<td></td>
<td><strong>53%</strong></td>
</tr>
<tr>
<td></td>
<td>Reuben and Smith (1924).</td>
</tr>
<tr>
<td></td>
<td><strong>63.7%</strong></td>
</tr>
<tr>
<td></td>
<td>Söderström (1928).</td>
</tr>
<tr>
<td></td>
<td><strong>80%</strong></td>
</tr>
<tr>
<td></td>
<td>Nonrad (1930).</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>66%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 years</td>
<td><strong>57%</strong></td>
</tr>
<tr>
<td></td>
<td>Hempelman (1917).</td>
</tr>
<tr>
<td></td>
<td><strong>37%</strong></td>
</tr>
<tr>
<td></td>
<td>McLean and Jeidell (1922).</td>
</tr>
<tr>
<td></td>
<td><strong>57.6%</strong></td>
</tr>
<tr>
<td></td>
<td>Söderström (1928).</td>
</tr>
<tr>
<td></td>
<td><strong>35%</strong></td>
</tr>
<tr>
<td></td>
<td>Nonrad (1930).</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>45%</td>
</tr>
</tbody>
</table>

The mortality is then still considerable, although not entirely fatal as the pathologists suggest. The average mortality under 1 year is 66%; from 1 to 2 years 45% prove fatal.

Certain provisos must be made, however. **Duration of contact is very important.** Bernard and Debré find that the fatal cases had usually been in contact 6 months and died as a rule within a month after isolation.

If the cases are segregated early, the prognosis is very much improved. Bernard and Debré find that in those under 2 years only 7.5% were fatal if isolated, whereas of those who had not been segregated 82% died. Lemaire had similar results, 4.5% only in the isolated
cases compared with 63% in the others.

In brief, then, the tuberculin test is the means of detecting tuberculosis in young children, and having done so, it is then essential to remove the child from the source of infection.
III. THE INTRA-DERMAL TUBERCULIN TESTS.

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Tuberculin tests.

1. Introduction.

The intra-dermal tuberculin test may be said to be a recent innovation in this country, but it was as long ago as 1908 that Mantoux and Mendel first described this method. However, at that time it was von Pirquet's test which found favour.

The introduction of the intra-dermal test for diphtheria by Schick, and of the similar toxin test for scarlet fever by the Dicks, appears to have been responsible for a revival of interest in the intra-dermal method.

Mendel (1908), using a special preparation - "arsen-tuberculin" - for intravenous therapy in tuberculosis, observed a characteristic reaction when some of the solution was accidentally injected into the skin, and he suggested the intra-dermal injection of tuberculin as a diagnostic method.

In the same year Mantoux also described the intra-cutaneous method. This test has been till recently neglected in favour of von Pirquet's method.

2. Comparison of the von Pirquet and intra-dermal tuberculin tests.

The von Pirquet test, so liable to variation according to technique and interpretation, has been
ound sufficiently sensitive for most workers.
McNeil (1923) found that with an improved technique, always using undiluted old tuberculin, reliable results could be obtained and the reaction elicited even in massive and advanced tubercular infection. It is interesting to find that in performing the test he insists on the excoration of the epidermis until the pink cutis vera is exposed, before rubbing in the tuberculin. This comes near to the method of injecting the tuberculin intra-dermally, except that it still lacks accuracy of dosage, necessitates pure tuberculin for sensitivity, and leaves a raw surface exposed.

McNeil stresses the importance of the persistence of the papule, and suggests reading the test at the end of a week, thus excluding the pseudo-reactions and including the delayed response. This is important as the relatively small papule of the von Pirquet test must be liable to differences in personal interpretation.

With the intra-dermal method, the reaction is larger and even the milder response is of sufficient size to allow accurate estimation of its character and persistence. Further, the method of scarification, in addition to lacking precision of dosage, is also more liable to pseudo-reactions, because of the trauma
and the possibility of secondary infection on the scarified area.

The intra-dermal test, on the other hand, has precision of dosage and there is the minimum of trauma, a scaled needle track preventing secondary infection, so that a uniform response is obtained. This is important in a comparative study.

Many comparative tables have been made illustrating the greater sensitivity of the intra-cutaneous test.

Mantoux (1910) found a difference of 12% in favour of the intra-dermal test, using the 1/1000 dilution, but a dilute tuberculin was also used for the scarification test. Since this original study, many other investigations have been made, using pure O.T. for the von Pirquet test. Hart (1932) has reviewed the literature and agrees with Cummins (1928) that in a dilution of 1/1000 O.T. the intra-cutaneous test is at least as sensitive as the scarification method using pure O.T.

3. Technique of the intra-dermal tuberculin test.
   (a). Type of tuberculin. Koch's Old Tuberculin was used throughout, using the standardized preparation of Burroughs, Wellcome & Co. Although there is no evidence of any difference in the protein or human and bovine O.T., some workers have claimed that in low
degrees of allergy the sensitive subject may only react to the specific protein of the infecting bacillus. In order to avoid such a fallacy, if such exists, I have used equal parts of human and bovine tuberculin.

Dilution. The standard dilution for the Mantoux test - 1/1000 - was used throughout, except in a small series of measles cases. The diluent usually adopted is 0.5% carbol-saline, but the carabolic tends to precipitate the protein. To obviate this, the special toxin diluent used for the Schick and Dick tests was adopted. Its composition is as follows:

Crystal borax 57 gms.
Boric acid 84 "
Sodium chloride 99 "} 1.5% in distilled water.

(Gleny and others, 1928).

The dilutions were made up fresh every three weeks as the tuberculin tends to deteriorate even when using the special toxin diluent. At first the solutions were made up in 5 cc. rubber-capped bottles, but with such a large quantity the repeated puncturing of the cap often led to contamination which gave rise to pseudo-reactions of an inflammatory nature, lasting 24 hours only. To avoid this, the tuberculin was prepared in 1 cc. sealed ampoules sufficient for 10 tests, and an ampoule once opened was discarded, whether all or part only had been used. By this means
I have been able to exclude all pseudo-reactions from the 1/1000 dilution.

Serial dilutions. Some prefer the method of repeated tests commencing with 1/10,000 dilution and repeating up to 1/100 or more. The 1/10,000 dilution avoids those intense necrotic reactions which very occasionally occur. I have found that usually in the highly allergic individuals who respond in this way there is a para-
tubercular condition such as paliytenular conjunctiv-
itis present, or a history of intimate and recent contact to warn one against using the standard 1/1000 dilution. I have found that even with precautions of freshness and sterility pseudo-reactions cannot be excluded, and they prove most difficult to differentiate from a mild positive response. One could only be certain of a true response in a 1/100 dilution if some oedema were present, and in such a case a response will also occur to 1/1000.

Instead of using a stronger solution I prefer to repeat the standard dilution of 1/1000 as the previous injection is an important factor stimulating allergy in considerable degree. (See Chap.IV, page 38, on Measles - "serial dilutions.")

(b). Technique. It is a tribute to the simplicity of the intradermal test that there has been such a flood of literature in recent years. No doubt the
Schick and Dick tests have done much to popularise the intra-dermal technique. A test difficult to perform, requiring a multiplicity of "props", beset with dangers of unpleasant reactions and difficult to interpret would not be so widely used.

The volar aspect of the fore-arm is the most convenient site. The skin surface is cleansed with ether or methyl alcohol. A convenient type of syringe is the "Vim" tuberculin syringe, made by the McGregor Co., U.S.A.; being longer than the ordinary 1 cc. syringe, it is easier to handle, the complete action of inserting the needle point and injecting the solution being carried out without changing ones grip. Further, this syringe is graduated to .001 cc., so that when one is making a comparative study of the size of the different reactions, one ensures accuracy of dosage. Being an all glass syringe it has an easy action without any leak past the piston. This is important, as it requires considerable pressure to raise the intra-dermal bleb, and if the piston does not fit tight, back some of the solution may leak between piston and barrel.

With the syringe held parallel to the skin surface, the needle - a fine short bevel type - is inserted into the skin.

One can ensure not going too deep by having the
bevel facing upwards and keeping it always in view, through the epidermis. The younger the child, the more difficult it is to do; the thinner the skin, the more liable is the needle to travel too deep and the more pressure is required to raise the bleb. The tuberculin is injected slowly by steady pressure, raising a white bleb or oedema about 5 mm. in diameter.

(c). Description of the reaction.

Usually within 24 hours a raised area of redness appears - not a simple erythema, but a maculo-papule due to an infiltration of the skin itself. It is always palpable. The reaction reaches its maximum in 48 hours when:

(i) In a mild reaction there is seen a dark red, well-defined maculo-papule measuring 15-20 mm. It is rare to find any reaction less than 5 mm. or greater than 20 mm. with 0.1 cc.

(ii) In a moderate reaction - in 48 hrs. an oedema can be observed in the centre; it is of light yellow tint and in more marked ones this oedema extends over the whole or the infiltrated area.

(iii) In a severe reaction there is actual vesiculation, usually on the 3rd day, sometimes with haemorrhage into it, and subsequent necrosis and sloughing of the part, but this is rare. Usually a desquamation only is observed 7 to 14 days after with pigmentation.
over a dull purple stain. The infiltration lasts a variable period, from 48 hrs. to 4 weeks or even more, persisting longer in more marked reactions.

It can be stated from experience of Schick and Dick reactions that the Mantoux reaction is absolutely characteristic. The closest resemblance is found in the pseudo-Schick reaction, but this has not the definition of outline - does not show oedema, but a brawny induration extending deeper with a surrounding erythema of wider area, whereas a tuberculin reaction has a definite margin, and although there may be a surrounding erythema, it also has itself a definite margin. Further, the colour of the tuberculin reaction is characteristic - rose pink, or it may be red, but not the deep red of a Schick or the scarlet tint of a Dick reaction.

The surrounding halo of erythema is a feature of the more intense reactions; it is found only in the 24 to 48 hours following the test, coinciding with the maximum response in the central area.

**Measurement of the reaction.** With 0.1 cc. I have found that the reactions vary in size from 5 mm. to 20 mm. in diameter; the usual size is 15 to 20 mm., and I have only rarely seen the infiltration exceed 20 mm. in diameter. Some workers describe much larger reactions, but they are probably including the
outer halo of erythema as well. Thus Dickey (1929) finds the average diameter to be 24 mm. He also found that the size of the reaction increases with each year of age up to 6. This is probably due to the increase in the thickness of the skin.

One finds that in younger children, the skin being relatively thinner and more dense, it is not possible to raise a wheal so readily nor of the same size as in the older subject. In the adult, the wheal from an intra-dermal injection of 0.1 cc. is 10 to 12 mm. in diameter, whereas in a baby one cannot raise a wheal larger than 7 to 8 mm. with the same quantity. The area over which the tuberculin is disseminated must affect the size of the subsequent reaction.

In a comparative study such as this it is necessary to have some standard by which to grade the reactions. As there is no accepted one I have adopted one for this investigation which indicates both the degree and the size of the reaction.

Size of the reaction. The standard quantity injected intra-dermally is 0.1 cc. and therefore in size results show a certain uniformity. Smith (1929) has shown that the area of the reaction is dependent on the quantity of the injection; 0.1 cc. produces a reaction about twice the size of 0.05 cc., and 0.1 cc. of 1/1000 dilution produces a reaction as large as 0.1 cc. or 1/1000
though less intense.

In reading results I estimated the mean diameter in millimetres.

Degree of response. The degree of response is of much more importance than size, although one finds that the more intense reactions are larger, up to the limit of 20 mm.

As the tests were all read by the same individual, then the results are comparable. I have found however, that size is of little value in comparing reactions, due no doubt to the variation in the age and therefore in the thickness of the child's skin.

To estimate the degree of reaction, the following categories were fixed:-

(+) = Erythema only; no infiltration.
+  = a raised pink or red area of infiltration.
++ = central part of the infiltrated area showing oedema.
+++ = whole of the raised area oedematous.
++++ = vesiculation.
+++++ = necrosis.

Thus "15 mm. +++" would signify a positive test of 15 mm. mean diameter, the area of reaction being wholly oedematous.

Surrounding the raised infiltrated area there may be the erythema - itself well-defined and pink in colour. It accompanies the more marked reactions, appearing
usually brightest at 24 or 48 hours, and fading quickly thereafter, being always gone after 72 hours. This erythema has been measured also; erythema or "E": 5 mm. signifies a halo of redness round the infiltrated area 5 mm. broad.

Degrees of response.

(+). The simple erythema not infiltrated can only be accepted as positive if it persists as a stain over 2 days at least; it is best confirmed by a second test.

(+). The mild reaction is an area of infiltration of the skin of pink or red colour, but sometimes barely tinted. It is a raised area of erythema - a maculo-papule.

(++). A moderate reaction shows in the centre of the raised area a yellowish oedema.

(+++). The more severe response shows the raised area becoming more and more oedematous until it extends over the whole of the infiltrated area,

(++++). In marked reactions there is actual vesiculation, often with haemorrhage into the little vesicles.

(++++)+ In the most severe of all superficial necrosis follows on the vesiculation, a dry slough separating in one or two weeks. This latter event is very rare, using 1/1000 dilution, and can be obviated by starting with a 1/10,000 dilution.
**Variations.**

1. **Delayed reactions.** The positive response may be delayed. There may be no reaction in the first 24 hrs. and a typical response in 48 hrs., usually at its maximum then. But positive reactions may be delayed much longer, no response occurring for three or four days or not even till two weeks or more. (See appendix - Delayed Reactions).

2. **Systemic effects.** The tuberculin, although injected into the skin, is absorbed into the circulation. Although the amount is so small as not to produce any severe systemic reactions, very occasionally there may be a febrile response lasting a few days.

   Evidence of the systemic effect is also found in the reactivation of a previous positive response after the primary reaction has faded, or a hitherto negative test on one arm is brought up positive by a test performed on the opposite arm.

**Controls.** For a period I used a control consisting of glycerin in broth proportioned and concentrated according to the method of preparing C.T. itself. With 1/1000 dilutions of this control I obtained no reactions.
IV. MEASLES

in relation to tuberculosis.

I. Introduction - History

II. Effect of Measles on Tuberculin Allergy
   (1). History
   (2). Review of the Literature
   (3). Personal Observations
   (4). Summary

III. Relation of Measles to Tubercle Infection
   (1). Review
   (2). Personal Observations
   (3). Summary

IV. General Conclusions
I. Introduction.

History. Although measles as a clinical entity was first differentiated from the other exanthemata by Rhazes in the 9th century, it is not till the middle of the 18th century that there is found reference to its association with tuberculosis; Hoffmann (1748) drew attention to this dread sequel of measles, stating:-
"Finite etiam morbo, si tussicula cum rancedine persistit nisco cito idoneis succaratur remediis, in phthisin et hecticam fit transitus."

It must be remembered that prior to Koch's discovery of the bacillus and the subsequent elucidation of the pathology, "phthisis" was a clinical syndrome, whose characteristics were "cough, difficulty in breathing, emaciation, hectic fever and sometimes purulent expectoration," and it is interesting to find Bayle (1838) stressing the necessity of diagnosing the disease before this clinical picture had developed, but he does not suggest that these symptoms and signs were not pathognomonic. It is easy then to imagine that the diagnosis or "phthisis" or "consumption" would be commonly applied to the protracted broncho-pneumonia of childhood; a broncho-pneumonia in a child can persist even over weeks, with increasing wasting
associated with "hectic fever, dyspnoea, cough, and sometimes expectoration." Even at autopsy those cases with early bronchiectasis following the pneumonia would seem to confirm the diagnosis as "cavitation," was thought to be the characteristic lesion of tuberculosis. Broncho-pneumonia being the common complication of measles and whooping cough, many such cases would probably be classified as "phthisis."

Of course there is no doubt a good number of cases must have been tubercular, as the disease was so rare and dissemination of the infection widespread and ever-present. Tuberculosis is active and fatal in the first 5 years; this is the common age period of measles and whooping cough, so that the association must have been very frequent indeed, as the tuberculosis mortality was much greater. For example, in the period 1861-1870 the mean annual death rate from tuberculosis in children under 5 years was over 5,000 per million living, whereas in 1927 it had fallen just under 1,000 per 1,000,000 (Pow and Lloyd: 1932).

It is obvious then that to the physicians measles and whooping cough must have appeared to be well worthy of this reputation as "phthisogenic" diseases.

With Koch's discovery of the tubercle bacillus many workers set out to investigate the relation of the two diseases more closely. The introduction of
the tuberculin reaction lent special interest when it was found that in measles there was a marked depression of the tuberculin sensitivity such that von Pirquet was satisfied that this explained the frequent activation or exacerbation of tuberculosis; he advanced the theory that the antibodies were used to combat the measles virus so that the tubercle infection could spread unchecked; the apparent loss of the tuberculin reaction in the acute and fatal stages of tuberculosis seemed to corroborate this. Studies of the behaviour of known tubercular children during measles in the light of the new knowledge of bacteriology showed that in active forms of tubercle infection measles could have an unfavourable effect, but in some of these studies post mortem findings of broncho-pneumonia in cases where tubercular glands alone might be found were yet classed as deaths from tuberculosis.

Debré and his co-workers (1926) in careful studies first cast doubt on the accepted "rôle néfaste" of measles - "la maladie tuberculissante"; at the present time opinion is divided and non-committal, so that it has taken half a century from the discovery of the etiology of tuberculosis to reach even the stage of doubting the belief of the earlier physicians that there was a particular relation between the two diseases.
II. **Effect of measles on tuberculin allergy.**

(1). **History.** In 1907 Preissich, using the von Pirquet tuberculin test first observed that the reaction was lost during measles; von Pirquet himself a year later published his own observations. He found that the reaction was lost during the first week, reappearing usually on the 6th day after the appearance of the rash. His observations have been confirmed by various workers using the scarification test, notably by Téssier and Léon-Kindberg (1911), Moltschanoff (1912) and more recently Lesné and Coffin (1926), Debré and Papp (1926), and Lereboullet and Baize (1931).

The less popular intra-dermal test has not been used so commonly in investigating the phenomenon, although by its precision and accuracy of dosage it lends itself to such a study. Mantoux with Harvier (1910), in 32 cases of measles found negative reactions. No details of the duration of the negative period are given.

Mitchell (1929) found a definite increase in the percentage of positive reactors in convalescence, using the Mantoux test, but he offers no data as to the duration of the negative period.

(2). **Review.** The majority of workers have used the scarification test in the study of the tuberculin
reaction in measles. Von Pirquet (1908) found that all his cases lost their reaction in the four days following the appearance of the rash. Moltschanoff (1912) in a group of 31 cases found that all were negative in the eruptive period, whereas 17 reacted in convalescence, and accordingly agreed with von Pirquet that measles suppressed the reaction in 100% of cases.

Debré and Papp (1926), in a larger series (229 cases) found that some patients did not lose their sensitivity completely; in 3 out of 37 sensitive subjects the reaction remained positive throughout and they found them to have mild rashes such as is usual in cases modified by convalescent serum. These observations were confirmed by Nobécourt (1930); in 23 cases he found 6 persisting positive in the eruptive period. Similarly Lesné and Coffin (1926) in 16 positive reactors found 2 which did not lose their reaction.

**Duration of the period of energy.**

Von Pirquet found that the reaction was lost in the four days following the appearance of the rash, but he also considered that the reactions became weaker as the eruptive period approached. Lereboullet and Baize (1931) found that the reaction was actually lost 24 to 36 hours before the rash appeared - i.e. on the
13th day of the incubation period. This is contrary to the usual observations. Debré found the loss of the reaction precise and abrupt - on the 2nd day of the rash, an observation which I have confirmed with the intra-dermal test.

The usual period of "anergy" is found to be the first 7 days, but some workers have found that occasionally the positive response is not regained until a later date. Klein (1927) found cases persisting negative for as long as 17 days; Kollar (1926) obtained negative reactions as late as the 20th day. Debré similarly found that the effect could persist into the third week and where active tuberculosis was present the sensitivity appeared slower in returning. He observed two cases remaining negative for as long as 2 to 4 months. Nobecourt and Liegè (1930) reported 2 cases negative as late as the 25th and 30th days, but these cases had active tuberculosis and it is probable that the von Pirquet test was not sufficiently sensitive for these cases.

**Intra-dermal tuberculin test in measles.**

Those workers using the intra-dermal test do not give details; Mantoux with Harvier (1910) noted a loss of the reaction in 32 cases of measles. Mitchell (1928) and his co-workers, using the Mantoux method find that in 200 cases of measles 7 reacted in the
acute stage, while 30 reacted in convalescence, an increase from 3.5% to 15%. They did not attempt to define the duration of the hypo-allergic phase.

(3). Observations on 900 cases of measles.

Von Pirquet in his original study performed tests daily; this would stimulate the subjects' sensitivity and probably cause a positive response to return sooner. If his cases are analysed, one finds that positive reactions returned earliest in those cases subjected to daily tests in the incubation period, as compared with those in which tests were begun in the prodromal stage or later.

1. 3 cases tested daily in the last 8 days of the incubation period showed a return of the positive response on the 5th, 6th and 7th day after the rash appeared.

2. In 9 cases in which daily tests were begun on the second day of the rash, a positive result first occurred on the 6th day in only 4.

3. Four cases tested only from the third day of the rash were all negative on the 6th day, 2 being positive on the 7th. By thus stimulating allergy von Pirquet would find the negative phase perhaps shorter or alternatively would render his test more sensitive than if used on one occasion only, as it would be in routine practice.
Value of serial dilutions.

Although the purpose of the investigation was to determine the effect of measles on tuberculin allergy as judged by testing the standard dilution of 1-100 O.T., a small series were tested with a higher concentration to ascertain if this would counterbalance the effect of the measles. As there is a depression of the sensitivity, it would be unnecessary to start with a dilution higher than 1-1000.

In 182 consecutive cases a negative result to 1-1000 dilution was checked by a second test usually 2 to 4 days later, using 1-100 dilution. Five cases in the series reacted positively to 1-1000 dilution; in 2 of the 177 patients negative to 1-1000 O.T. a reaction occurred with 1-100 dilution, but in these two cases the test with 1-1000 was done within the first week - the period of maximum "anergy", while the 1-100 test was done after this period had passed, so that one cannot be certain that the reaction would have been negative to 1-1000 on the second occasion; in the other 175 cases the result was negative to 1-100 as well as to 1-1000 dilution.

I have found the 1-100 dilution more a hindrance than a help, as it gives rise to pseudo-reactions despite the precautions of freshness and sterility by
which I have been able to exclude pseudo-results in the 1-1000 dilution. The pseudo-reaction to 1-100 C.T. persists for 48 hours, often with a definite infiltration, but fades without leaving the definite stain, although an indefinite area like an old bruise may remain. In contrast to the true reaction, although there may be infiltration there is no oedema; in colour it is of a darker hue and its margin is not so well defined; also its size varies, more often exceeding the 20 mm. maximum diameter of the infiltrated zone in a true reaction.

In 177 tests with 1-100 dilution such reactions occurred on 12 occasions, and owing to the difficulty or interpretation the method was discontinued in favour of repeating the 1-1000 test, knowing that the stimulation of a previous test is a factor of more importance in increasing sensitivity.

During the years 1930-32 I have performed routine intra-dermal tuberculin tests on the cases of measles admitted to the Park Hospital, Hither Green, London; for the purpose of investigation only cases where the diagnosis was definite were included, i.e. cases with a uniform morbilliform rash accompanied either by Köplik's spots and/or catarrh with or without temperature and leaving the typical morbilliform staining. For example, in infants morbilliform rashes
frequently occur; in the absence of other clinical evidence such cases were excluded. In mild attacks such as those modified by convalescent serum there may be very little catarrh and little or no temperature but the history of contact, the duration of the incubation period and character of the rash assist diagnosis.

A total of 900 cases were studied, but of these some were tested only in the acute phase and others only in convalescence. The majority, however, were tested both in the eruptive period and at subsequent intervals in convalescence.

As the purpose of the investigation was to determine the effect of measles on the sensitivity of the intradermal test in the standard dilutions of 1-1000 C.T., the cases were tested relatively infrequently in contrast to von Pirquet's daily testing, thus avoiding to some extent the stimulation of repeated injections of tuberculin.

An endeavour was made to test each case once in each week of the disease, the initial test being made usually on the day after admission, when the rash was at its height. The results may be summarised in the following table:-
Table I.

<table>
<thead>
<tr>
<th>No. tested in first week only</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only in 3rd week or later</td>
<td>6</td>
<td>114</td>
<td>120</td>
</tr>
<tr>
<td>Both in 1st and 2nd week</td>
<td>1</td>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>Both in 1st week and 3rd week or later</td>
<td>11</td>
<td>249</td>
<td>260</td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>457</td>
<td>489</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>850</td>
<td>900</td>
</tr>
</tbody>
</table>

It is only those cases tested both in their eruptive period and also in convalescence that will provide an accurate estimate of the effect on allergy. From the above table, however, can be calculated the percentage incidence of positive reactions in the acute period compared with those tested in convalescence, and it indicates in a rough way that there is an effect on tuberculin allergy; 24% reacted in eruptive period while 8.25% were found positive in the third week or later. This would suggest that about 75% of tuberculin sensitive subjects lose their reaction during measles.
Table II.

<table>
<thead>
<tr>
<th></th>
<th>Eruptive period</th>
<th>3rd week or later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number tested</td>
<td>831</td>
<td>520</td>
</tr>
<tr>
<td>No. found positive</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>Percentage</td>
<td>2.40%</td>
<td>8.25%</td>
</tr>
</tbody>
</table>

This indication of a depression of sensitivity is in itself of little value. What is more important is the duration of this anergic period. For how long can a measles rash suppress the tuberculin reaction? As each case was not tested daily, one cannot determine but exactly when sensitivity returned/with a large number of cases the incidence of negative reactions among them will determine the approximate duration of this hypo-allergic period.

Duration of the Anergic Period in Measles.

Nineteen tuberculin-sensitive subjects gave a negative result to the intra-dermal test during their attack of measles. The following table shows the incidence of positive and negative reactions classified according to the day of disease, counting the date on which the true measles rash appeared as the first day. The delayed reactions are excluded and will be
considered separately.

**Table III.**

Incidence of positive and negative tuberculin reactions in tuberculin-sensitive subjects during measles.

<table>
<thead>
<tr>
<th>Day of disease</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive reactions:</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Negative reactions:</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Percentage negative</td>
<td>60</td>
<td>25</td>
<td>75</td>
<td>66</td>
<td>50</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Combined positive reactions.</td>
<td>2</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>16</td>
<td>20</td>
<td>22</td>
<td>24</td>
<td>25</td>
<td>27</td>
<td>29</td>
</tr>
<tr>
<td>Combined negative reactions.</td>
<td>19</td>
<td>16</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Expected percentage negative</td>
<td>90</td>
<td>66.6</td>
<td>66.423</td>
<td>23</td>
<td>9.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Reference to this table shows that the negative results occurred only in the first week, except in one instance. The positive results given include both initial positive reactions and also the results in cases previously having given a negative or a delayed response. If it is assumed that cases negative on a certain day would have been negative the preceding day, and, conversely, that a case positive on one day would also be positive on subsequent days, the figures may
MEASLES.

PROPORTION OF NEGATIVE REACTIONS IN TUBERCULIN-SENSITIVE SUBJECTS.

PERCENTAGE OF NEGATIVE REACTIONS.

100% 90% 80% 70% 60% 50% 40% 30% 20% 10%
the second week. This effect appears to be at its maximum not with the appearance of the rash but when the eruption is fully developed and suppresses the reaction at least temporarily in about 60% to 75% of cases.

**Effect of the rash of measles on tuberculin allergy.**

If the depression of the individual's reactivity be due to the effect of the eruption on the skin, one would expect that the more intense the rash, the more marked would be the effect on allergy with a greater proportion of negative results. Accordingly the rashes were classified by the following standards:

- **Mild:** a rash beginning to fade on its second day and leaving little or no staining;
- **Moderate:** a rash still bright on the second day beginning to fade on the third day and leaving definite staining;
- **Intense:** a rash still bright on the third day and leaving marked and prolonged staining.

The following table shows the distribution of the results in each category. Only the results obtained in the first five days are included.
Table IV.

Results classified according to the character of the rash.

<table>
<thead>
<tr>
<th></th>
<th>Mild No.</th>
<th>%</th>
<th>Moderate No.</th>
<th>%</th>
<th>Intense No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive reactions</td>
<td>9</td>
<td>56.26</td>
<td>8</td>
<td>34.78</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Delayed positive</td>
<td>1</td>
<td>6.24</td>
<td>5</td>
<td>21.75</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>reactions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative reactions</td>
<td>6</td>
<td>37.50</td>
<td>10</td>
<td>45.47</td>
<td>3</td>
<td>75</td>
</tr>
</tbody>
</table>

The table shows a definite correlation between the incidence of negative reactions and the character of the rash; the more intense the rash, the greater proportion of negative results were obtained.

It is also seen that the delayed reaction represents a balance between sensitivity and the rash, the proportion being highest when the exanthem is moderate. When the results are classified according to the degree of allergy, delayed reactions are found associated with the moderate or highly allergic cases.
Reactions of Allergic Subjects

Classified According to the Type of Rash.

Positive Reactions (Immediate)

Delayed Positive Reactions

Proportion of Negative Reactions

Mild

Moderate

Intense
Effect of the Degree of Allergy.

It has been shown that the effect on tuberculin sensitivity has a direct relation to the character of the rash. What relation has the patient's own allergic state to the result of a tuberculin test in Measles?

One can gauge the degree of sensitivity from the response obtained to a tuberculin test in convalescence. For this purpose one has classified the patients into the 4 categories of allergy: 

+; ++; +++; and ++++; the proportion of positive, delayed and negative results have been calculated in each class including only those reactions obtained during the period of maximum energy - the first week. From the table and graph it is seen that the higher the degree of sensitivity the more likely is a reaction to remain positive; the greatest proportion of negative results irrespective of the type of rash occurred in those cases with the lowest degree of allergy; there is a progressive decline in the incidence of negative reactions as sensitivity increases.

If the delayed reactions are grouped with the straight positive results the curve of the increase in positive reactions becomes almost a straight line showing the close relation between the degree of sensitivity present and the
probable result of a tuberculin test during Measles.

TABLE V.
RESULTS CLASSIFIED ACCORDING TO THE DEGREE OF TUBERCULIN ALLERGY.

<table>
<thead>
<tr>
<th>DEGREE OF ALLERGY</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative Result</td>
<td>+</td>
<td>60</td>
<td>+</td>
<td>46.16</td>
<td>+</td>
<td>33.33</td>
<td>+</td>
<td>25%</td>
</tr>
<tr>
<td>Delayed Positive</td>
<td>0</td>
<td>-</td>
<td>3</td>
<td>23.08</td>
<td>3</td>
<td>16.67</td>
<td>1</td>
<td>25%</td>
</tr>
<tr>
<td>Immediate Positive</td>
<td>2</td>
<td>40%</td>
<td>4</td>
<td>30.76</td>
<td>9</td>
<td>50%</td>
<td>2</td>
<td>50%</td>
</tr>
<tr>
<td>Totals</td>
<td>5</td>
<td>100%</td>
<td>13</td>
<td>100</td>
<td>18</td>
<td>100</td>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>

CASES POSITIVE THROUGHOUT THE COURSE OF MEASLES.

Of the 50 cases observed 17 gave a positive response on the initial test performed in the acute stage: of these 10 were tested at a later date and as is to be expected even in ordinary circumstances the second tests produced more marked reactions but the increase although somewhat greater than occurred in other infections is not sufficient to be accepted as evidence of some weakening effect on the initial test.
Reactions classified according to the degree of allergy.

- Positive reactions (immediate)
- Delayed positive reactions

Proportion of negative reactions:
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%

Proportion of positive reactions:
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%

Degree of allergy:
- +
- ++
- +++
- ++++
- ++++

Ex. B. L. Univ. Edinburgh
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day of Rash</th>
<th>Reaction</th>
<th>Day of Rash</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>8</td>
<td>+ + 10mm</td>
<td>16</td>
<td>+ + : 25 mm. E10</td>
</tr>
<tr>
<td>28</td>
<td>2</td>
<td>+ + 15mm</td>
<td>17</td>
<td>+ + : 20 mm. E15</td>
</tr>
<tr>
<td>31</td>
<td>2</td>
<td>+ + 15mm</td>
<td>17</td>
<td>+ + : 15mm</td>
</tr>
<tr>
<td>33</td>
<td>5</td>
<td>+ + 10mm</td>
<td>19</td>
<td>+ + + : 18 mm. E20</td>
</tr>
<tr>
<td>34</td>
<td>2</td>
<td>+ 15mm</td>
<td>11</td>
<td>+ + + : 20 mm. E20</td>
</tr>
<tr>
<td>#35</td>
<td>2</td>
<td>+ 10mm</td>
<td>5</td>
<td>+ 15 mm</td>
</tr>
<tr>
<td>39</td>
<td>5</td>
<td>+ 10mm</td>
<td>18</td>
<td>+ + 15</td>
</tr>
<tr>
<td>40</td>
<td>4</td>
<td>+ 10mm</td>
<td>19</td>
<td>+ + + : 16</td>
</tr>
<tr>
<td>49</td>
<td>1</td>
<td>+ 15mm</td>
<td>18</td>
<td>+ + + : 23 E17</td>
</tr>
<tr>
<td>#50</td>
<td>1</td>
<td>+ 13mm</td>
<td>4</td>
<td>+ 18 mm</td>
</tr>
</tbody>
</table>

For cases 7, 12, 16, and 18 not tested in convalescence.

*Cases 35 and 50 can be excluded as the second test was performed also in the acute phase. The others show that there was always an increase in the reaction in the test made in convalescence. It is known that in normal subjects allergy is enhanced by repeated tests at short intervals so that a difference must be marked to indicate that there was some temporary influence depressing the first reaction.

**Degree.**

In 8 cases - 1 case showed no increase in degree

4 cases " an " of 1 "

3 " " " 2 "

1 " " " 3 "
Size In 8 cases - 1 case showed no change in size
7 others all showed an increase in size

Surrounding Erythema - as is to be expected the erythema accompanying more intense reactions found only in 1 test in the acute stage accompanied 5 reactions in convalescence.

7 other cases are quoted when only one test was made towards the end of the first week of disease; 5 of those were reactions of +++ intensity ten with erythema suggesting that a high degree of allergy present initially had been little impaired by the exanthem.

**TABLE VII.**

**CASES WHOSE TUBERCULIN SENSITIVITY WAS KNOWN PRIOR TO MEASLES.**

A more accurate estimate of the effect of the exanthem can be ascertained if the allergic response of the patient be known prior to the onset. The following cases founded such an illustration.

<table>
<thead>
<tr>
<th>Case</th>
<th>Days before Rash</th>
<th>Reaction before Rash</th>
<th>Days of Reaction</th>
<th>Reaction in Convalescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>13</td>
<td>+12</td>
<td>1</td>
<td>Neg</td>
</tr>
<tr>
<td>49</td>
<td>22</td>
<td>++++20</td>
<td>1</td>
<td>+15</td>
</tr>
<tr>
<td>50</td>
<td>2</td>
<td>++++20</td>
<td>1</td>
<td>+13</td>
</tr>
<tr>
<td>17</td>
<td>12</td>
<td>+16</td>
<td>1 (Delayed)</td>
<td>+12</td>
</tr>
<tr>
<td>25</td>
<td>48</td>
<td>+12</td>
<td>1</td>
<td>+15</td>
</tr>
<tr>
<td>19</td>
<td>6</td>
<td>++++20mmE5</td>
<td>2</td>
<td>Neg</td>
</tr>
</tbody>
</table>

*Note: The reactions are denoted as follows: *

- **-** for no reaction
- **+** for slight reaction
- **++** for moderate reaction
- **+++** for intense reaction

*(Values in parentheses indicate dilutions)*
Those 6 cases show (1) that there is a definite depression of the allergic response during the acute phase (2) that despite this the enhancing effect of serial tests is apparent if the reactions performed prior to measles are compared with those obtained in the convalescent period; in cases 49 and 25 an increase of one degree in the 10,000 dil. reaction as intense with a dilution on the last test as compared with the dil. on initial test.

If these cases are considered in detail the period of maximum "anergy" can be determined.
### Table VIII.

<table>
<thead>
<tr>
<th>Case</th>
<th>Pre-measles Test</th>
<th>Days before Reaction</th>
<th>Rash appears</th>
<th>Day of Rash</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reaction</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>13</td>
<td>+12</td>
<td>Test</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td>19</td>
<td>6</td>
<td>+12</td>
<td>T (4)(13)</td>
<td>(4)(10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T neg.</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(8)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(8)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)(6)(4)</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>12</td>
<td>+16</td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(10)</td>
<td>+12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(10)</td>
<td>+10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(8)</td>
<td>(4)(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4)(8)</td>
<td>(4)(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td>25</td>
<td>48</td>
<td>+12</td>
<td>T (4)</td>
<td>+15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td>(4)</td>
</tr>
<tr>
<td>49</td>
<td>22</td>
<td>+12</td>
<td>T (4)</td>
<td>+15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td>50</td>
<td>2</td>
<td>+12</td>
<td>T (4)</td>
<td>+15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T (4)</td>
<td>(4)</td>
</tr>
</tbody>
</table>
It will be seen that if the test is performed before the rash appears it will give a reaction; a test is only negative if the rash is present before the test is performed. In case 19 the test performed the day before the rash appeared was positive although faint while the test performed two days after the rash had appeared was negative on the 3rd day; this is in agreement with the general results.

In case 17 the test performed 24 hrs. after the rash appeared was negative but in case 25 when a test was also done 24 hrs. after the rash appeared there was a reaction in the first 24 hours but fading on the 3rd day of the rash to reappear on the 7th day suggesting that the 2nd to the 6th day is the period of maximum energy.

Pirquet quotes two cases which illustrates the period of energy accurately.

Day of Rash

<table>
<thead>
<tr>
<th>Day</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4 5 3 mm.</td>
</tr>
<tr>
<td>2</td>
<td>3 4 5</td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3 3</td>
</tr>
<tr>
<td>7</td>
<td>5 8 8 5</td>
</tr>
<tr>
<td>8</td>
<td>5 7 7</td>
</tr>
<tr>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>
Day of Rash

0 1 2 3 4 5 6 7 8
T - - - 18 11 11
T - - - 12 7 7
T - - - - -
T 12 9 9
T 9 9 9
T 11 11

Also illustrating the maximum period of energy it is seen that the test performed in Pirquet's cases on the 2nd and 3rd days were completely negative in contrast to the delayed responses of the 1st 4th and 5th days confirming the conclusion previously formed that it is the rash which causes this phenomenon. The eruption on the first day is usually confined to the face and trunk and it is only on the 2nd and 3rd days that it becomes established on the arms - the site of these tests. If a test has been done at a site not yet affected by the rash the cells of the skin will have begun to react to the tuberculin and probably are then refractory to the measles toxin; the converse occurs when the rash is established before the tuberculin is introduced. After the 6th day the epidermis has recovered sufficiently to react to tuberculin whether introduced one or as long as five days previously.
### Case Illustrating That the Sensitivity is Not Lost Until the Rash is Established

**Date** | Prodromal stage | Int. der.- dermal test | Pre-exanthem 1 | 24 hrs. | Koplik spots & temp. of 100.5
---|---|---|---|---|---
21/2/32 | of measles recog. by | 10.00

22/2/32

| Bright measles rash on face, neck, trunk | (+) 13 mm. | (see photograph) |

23/2/32

| Rash still bright; now generalised | (+) 10 mm. | I.D. test 1 |

24

| Rash beginning to fade on trunk | (+) 10 mm. | negative |

25

| Rash fading generally | Negative | negative | I.D. test 1 |

26

| | | | 10,000 |

27

| Morbilliform staining moderate | | | very faint |

28

| With staining still present on the 7th day of the rash there was a reactivation of all three reactions on the abdomen appearing as 5 mm: Intra dermal test 1 |

29

| All these reactivated tests faded again | (+) 15 mm |

1/3

| Photograph taken | ++ 15 mm |
CASE 19.

22/2/32 - Photograph of the abdomen showing the immediate response to a tuberculin test performed 24 hours previously with the measles rash in its first day.
Case 19. Photograph on the 9th day of the Rash

Morphilliform staining still obvious, the two reactions performed on the 2nd and 4th days have faded again (left side of umbilicus) while the reaction on the 7th day is still bright and the stain of the test performed before the rash appeared can be seen below the umbilicus on the right side. This case illustrates that the tuberculin introduced before the rash appeared gives a response persisting even when the rash has come out whilst the test done with the rash established 48 hrs. was completely negative.

On the 7th day of the rash there was slight activation of the three previous tests again limiting the maximal effect to the first 6 days.
Delayed Reactions.

The usual response on the skin to tuberculin is a reaction appearing in 24 hours usually at its maximum in 48 hours and always persisting over that period at least. It has been found, however, in routine work that occasionally delayed reactions occur the response not appearing within 24 hrs; it may not make its appearance for 2, 3 or even 10 days. This is regarded as exceptional and being infrequent its meaning has been difficult to interpret.

In this investigation I have found delayed reactions not unusual and particularly in Measles. Furthermore the delay in the appearance of the reaction has exceeded the usual maximum of 10 days some not appearing until 12 days afterwards.

Possible results of a tuberculin test.

There are 5 possible results to a tuberculin test:

(1) a negative result
(2) an immediate positive response
(3) a delayed positive response the reaction appearing only after an interval of 48 hours or more
(4) An immediate positive response fading and later re-activated by a subsequent test.
(5) A test hitherto negative activated by a subsequent test.

(1) and (2) are the common results obtained. In measles I have found examples of (3) (4) and (5), particularly 3.
Table IX.

Day of rash.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Delayed</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>11</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

% Delayed: 16.6%, 18.2%, 27.7%, 20%
Incidence of Delayed Reactions.

Reference to Table IX shows that the delayed results were obtained from tests performed during the period of maximum energy - the 1st, 2nd, 3rd and 4th days of the rash. They were most common in the third day when they occurred in 27% of the tests done on that day; this suggests that they occur when the rash is at its height; it is at this period that one expects that the negative results will be at their maximum. Thus it was found that the greatest proportion (75%) of negative results occurred on the third day also.

Therefore whatever may be the cause of delayed reactions in routine practice it would appear that in measles it is due to the effect of the acute infection on sensitivity; it probably indicates an effect not quite powerful enough to abolish the reaction completely.

Significance of the Delayed Reactions.

The fact that the period of delay does not correspond with the period of energy determined by the negative results would not preclude it from indicating the period of hypo-sensitivity yet the marked immediate reactions obtained from tests performed on the day the delayed response appeared indicated that an immediate response could certainly have been obtained if the patient had been tested earlier.
Where a second test was done during the latent period the stimulation of this test although it shortened the interval it could not bring the delayed response within the first 5 days, the phase of maximum energy. I am inclined to believe that the delayed response indicates a balance between the two factors - exanthem and allergic state. When the rash outweighs the tuberculin sensitivity a negative response is obtained; when a mild rash occurs in the highly allergic individual a straight positive response is to be expected. It is in the intermediate stages between those two extremes that the delayed response may occur. (See Charts of reactions classified according to allergy.)

As regard the mechanism of the reaction it appears that the cells of the skin sensitized by the injection of tuberculin in the energeic period respond later at the time that the patient's returning allergy reaches its height; it has been shown that the sensitivity is stimulated even higher than before the attack of measles by the tuberculin injected during the energeic period. (See Section on cases whose tuberculin allergy was known prior to measles).
POSSIBLE MAXIMUM DURATION OF ANERGY IN MEASLES.

Although my results have indicated that a false negative result may be obtained up till the 10th day other workers record longer periods. (Klein 1927) found that negative results might occur as late as the 17th day; Kollar (1926) obtained negative results up to the 20th day.

Debré and Pepp (1926) record two cases found positive prior to the onset of measles but continuing negative for 4 months after. They were using the Von Firquet test which is more difficult to interpret and more liable to trauma reactions; and cannot imagine that this persistent negative result could be due to the attack of measles. Lere-Bouillet and Baize (1931) using the same technique quote a case which persisted negative for 2 months and then died of tubercular meningitis. In this case probably the scarification method was not sufficiently sensitive to show the weak sensitivity associated with the terminal stage of tuberculosis.

Nobécourt and Liége (1930) observed 2 cases continuing negative for 25 and 30 days after measles.

The results I have given so far concern the reactions observed while the patients were in hospital. The majority of the patients were discharged on the
3rd and 4th week so that on the average the last tuberculin test in the 850 negative cases was done in the third week.

In order to ensure that the total period of weakened sensitivity had been covered and that no tuberculin sensitive subjects were passing out of hospital wrongly classed as negative, I re-tested a group at an interval of 2 to 4 months. After their attack with the following results:

<table>
<thead>
<tr>
<th>Cases reacting negative up to 3 weeks from onset</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result of test 2 to 4 months after attack.</td>
<td>1</td>
<td>127</td>
<td>128</td>
</tr>
</tbody>
</table>

Only one case gave a positive result; a boy of 6 years, he was admitted on the 21st Feb. 1932; he was tested on the first day of the rash and later on the 10th day; both results were negative. This boy was again tested on 11th July, 1932 — fully 4 months after and he gave a positive response of +15 mm. He therefore had regained or acquired sensitivity between the 10th day and the 5th month. His case was exceptional forming only 0.7% of those late tests.
Further in over 400 cases tests were performed as late as the third week and the only other case negative in the second week regained his sensitivity in the third so that it is highly probable that the case also would have reacted positively had he been tested in the third week.

**SUMMARY.**

(1) Using the intradermal tuberculin test on the standard dilution of $1 - 1000$ OT it is found that 60 to 75% of tuberculin sensitive subjects do not react at the height of the eruption.

(2) The effect is short-lived usually passing off quickly at the end of the first week; exceptionally it may persist into the second week.

(3) To exclude the chance of a negative response in a normally sensitive subject tuberculin tests should be deferred till the third week.

(4) The effect on tuberculin allergy is due to the action of the rash on the skin and varies with the character of the rash, and the degree of allergy pre-existing.
THE RELATION OF MEASLES TO TUBERCLE INFECTION

III.

(1) Review When tubercle infection was more widespread it may be that measles deserved its reputation as "la maladie tuberculissante". It is not till the end of the 19th century that any doubt on the matter appears to have arisen.

In 1898 Frenkel published a study in which he questioned the hitherto accepted view.

He found that the severe and complicated cases of measles arose when there had already been a bronchitis or enteritis or if an added infection such as lobar pneumonia, scarlet fever, typhoid fever or diphtheria was present. And in the same category he places tuberculosis; active tuberculosis already present would result usually in an exacerbation.

However, he pointed out the fallacy of assuming that when any tubercular lesions were found in fatal cases of measles the cause of death was necessarily the tubercle bacillus; a child infected with tubercle may succumb to an ordinary broncho-pneumonia without pre-existing infection necessarily contributing to the fatal issue. Frenkel found that tubercular children withstood secondary infection extremely well but could succumb when their resistance had been lowered by an illness such as measles.
This careful discrimination by Frenkel is notable; he definitely refutes the idea that there is a special relation between the two diseases. In America Landis (1906) found tuberculosis an infrequent complication of measles occurring in only 0.45% of 457 cases. Copeland (1909) similarly found no instance of tuberculosis arising in 75 cases.

In France, however, the older view was favoured by Gazeau (1910); one finds, however, that in 4 of the 7 cases he classes as deaths from tuberculosis the reports of the autopsies suggest that the children died from an ordinary broncho-pneumonia the tubercle lesions being localised in the glands.

Recent work is more or less consistently suggestive of the negative view, namely that there is no direct relation between the two infections. Koeggerath and Eckstein (1924) observe no increase in tuberculosis after a severe epidemic of measles and whooping cough among school children; Klein (1927) in the same age period likewise found no evidence of activation of tubercle after measles.

Nobecourt (1929) however maintains that catarrhal inflammation of measles may activate tuberculosis; his studies were made in younger children. Choffé (1929) in 137 cases found that of 6 with active tuberculosis only one developed fresh manifestation after measles. In 10 cases with e
previous tuberculous lesion there was no re-activation after measles

Lereboullet and Beize (1931) in 16 cases with positive tuberculin tests of whom 2 had active tuberculosis found no instance of a fresh manifestation occurring.

There is therefore an increasing body of evidence refuting the old idea of some particular relation between measles and tuberculosis.
(2) OBSERVATIONS on 901 cases of MEASLES.

EFFECT OF MEASLES ON THE TUBERCULOUS CHILD.

All cases giving a positive tuberculin reaction are accepted as cases which are infected with tubercle whether it be latent or active; those cases will be referred to as "tuberculoid" or "tuberculæur" without necessarily implying clinical activity.

850 cases gave negative reactions while 51 tuberculous subjects were observed. It must be accepted that of the 850 negative patients a proportion of the 120 cases tested only in acute stage may actually have been tuberculous - probably 6%; of the 260 cases tested only up to the end of the second week, 1% may have been missed being still negative in the second week. It is likely then that about 8 tubercular subjects are erroneously included in the 850 negative cases.

CASE MORTALITY.

The first 500 cases found negative were tested consecutively including all cases admitted to hospital irrespective of the character of their attack and therefore these gave a true estimate of the mortality; the subsequent 250 cases did not include some of the fatal ones as later in the investigation tests were deferred when a child seemed too ill to warrant a procedure of no therapeutic value. There-
fore a few died in the acute stage without being tested, so that the mortality figure over the whole series would not be accurate. Also cases complicated by whooping cough are excluded as this has considerable effect on mortality (See Chapter on Whooping Cough).

**CASE MORTALITY, TABLE X.**

<table>
<thead>
<tr>
<th>No. Died</th>
<th>Case Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 consecutive negative cases</td>
<td>35</td>
</tr>
<tr>
<td>51 positive or tubercular cases</td>
<td>4</td>
</tr>
</tbody>
</table>

The slight increase in mortality in the tubercular group is probably a real difference as the cases are necessarily of a higher age period and should have a better prognosis.

If the cases are subdivided at the age of 2 years the following results are obtained.

**TABLE XI.**

<table>
<thead>
<tr>
<th></th>
<th>0 - 2 years</th>
<th>2 years and over</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total No. Died</td>
<td>Case Mortality</td>
</tr>
<tr>
<td>Negative Group</td>
<td>176</td>
<td>25</td>
</tr>
<tr>
<td>Positive &quot;</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>excluding deaths from Tuberculosis</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>
The number of tubercular cases is rather small to provide an adequate comparison; age is so important, however, in the prognosis that such a classification is necessary. In the non-tubercular group, there is the usual high mortality under 2 years (14.2%) while over 2 years the prognosis is very much better (mortality of 2.4%). In the tubercular group, however, the mortality is appreciably higher at both age periods. One must in this respect exclude deaths due to tuberculosis as the prognosis to an uncomplicated case of tubercle infection is grave in itself, figures of 40 to 60% being usually given as the mortality in tuberculin-positive children under 2 years.

Both the deaths under 2 years were due to tuberculosis so that the mortality from causes similar to those of the non-tubercular children was nil. This is rather surprising. The contrary holds in the tubercular subjects over 2 years; 3 died from causes other than tuberculosis and the mortality is higher than in the control series suggestive of an increased susceptibility to complications.

The 11 tubercular children under 2 years escaped fatal complications from secondary invaders and favours Frenkel's opinion that they withstand pyogenic infection remarkably well; the
converse is suggested in the older tubercular subject.

If these fatal cases are analysed it is striking that the deaths in tubercular children are not from pulmonary complications in contrast to the negative group.

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>Total deaths in control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broncho-pneumonia</td>
<td>36</td>
</tr>
<tr>
<td>Enteritis</td>
<td>4</td>
</tr>
<tr>
<td>Acute Septicaemia</td>
<td>1</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>2</td>
</tr>
<tr>
<td>Diphtheritic Group</td>
<td>2</td>
</tr>
</tbody>
</table>

| Total deaths in 51 tubercular children | 45 |

Causes of Death

Acute streptococcal septicaemia

"""" "" and pneumococcal meningitis

Tubercular Enteritis - miliary spread complicated by Whooping Cough

Tubercular Meningitis

It is rather striking that although bronchopneumonia is by far the commonest cause of death in measles not one of the tubercular children succumbed to this complication although 6 actually had this complication.
SUMMARY of 4 FATAL CASES IN TUBERCULAR GROUP

(See Appendix)

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>f.</td>
<td>2yrs. This child died within 48 hours of the onset of measles - an unusually rapid illness. At autopsy she was found to have extensive glandular tuberculosis principally in the abdomen; at the root of the mesentery the spine was plastered by a solid caseous mass of glands; the thoracic glands were not so markedly affected. There were no focal lesions in the lungs or intestines. The actual cause of death was an acute septicemia; a haemolytic streptococcus being isolated from the spleen post-mortem; there was also an early acute inflammation in the lung from which a predominating growth of streptococci were obtained.</td>
</tr>
<tr>
<td>35</td>
<td>M.</td>
<td>17 yrs. This boy had no clinical evidence of tuberculosis prior to measles, although he had been suspect. He developed a pneumococcal meningitis (Type IV infection) on the 11th day of measles which was further complicated by an</td>
</tr>
</tbody>
</table>
Otitis media in the third week from which arose a streptococcal septicaemia (blood culture - pure growth of haemolytic streptococci), he succumbed 35 days from the onset of measles. At autopsy he was found to have tubercular foci in the hilar glands; on the left side they were lesions with some calcification. There was no trace of a focus in the lungs and no evidence of any recent activity or spread. The causes of death - pneumococcal meningitis and streptococcal septicaemia were confirmed.

Case 47 (13 in whooping cough series), 1 yr. 10 mths.
Female.
This child had pre-existing active focal tuberculosis in the form of tubercular enteritis; in the 7th week of whooping cough she developed a mild attack of measles and died of Miliary tuberculosis in the 9th week. At autopsy she was found to have a primary focus in the lung and a chronic tubercular ulcer of the ileum; cause of death was from a miliary spread.

Case 40, 6 months, female: In her first 4 months this baby was in close contact with open
phthisis, her mother developing activity after the child was born. The child had a mild attack of measles with no complication. She had signs of primary infiltration of the left lung confirmed by X-ray. She was isolated and kept under observation. She continued fairly well for 3 months and then died of tubercular meningitis.

Discussion. Under two years the fatal cases succumbed to tuberculosis; in one whooping cough was an added complication and the measles was very mild having been mitigated by convalescent serum so that it is doubtful if it had any considerable influence on the miliary spread. The other child only 6 months old survived its attack for 3 months so that considering the child's age there is no reason to ascribe the meningeal metastasis to the measles. In both cases then the measles infection played no great part.

The other two cases both died of streptococcal septicemia. The child of 2 had no clinical evidence of tuberculosis; prior to the attack of measles she looked and behaved like a perfectly healthy child and seemed to belie the positive tubercular result.
This made the rapid dissolution following the onset of measles all the more surprising. It is difficult not to conceive some relation between the rapid success of the haemolytic streptococcus and the extensive lymphatic tuberculosis found at autopsy. This case is similar to those fatal "malignant" cases of scarlet fever described by Millien and others in which pre-existing tubercular foci were suggestively common.

In the same category could be placed the youth of 17 who died from a streptococcal infection superimposed on the low-grade pneumococcal meningitis but the tubercular lesions in his case were not extensive and his case on its own merits could not be said to show a relation between the streptococcus and the tubercle bacillus.
COMPPLICATIONS.

The incidence of complications varies with age, enteritis and pneumonia being more common under two years. Sub-dividing the 901 cases, observed in this way the tubercular groups are again rather small to provide reliable figures.

**TABLE XII.**

<table>
<thead>
<tr>
<th>Tuberculin Negative</th>
<th>Tuberculin Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 yrs. 2 yrs. &amp; over</td>
<td>0-2 yrs. 2 yrs. &amp; over</td>
</tr>
<tr>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Total</td>
<td>598</td>
</tr>
<tr>
<td>Broncho- pneumonia</td>
<td>60 16.1%</td>
</tr>
<tr>
<td>Lobar Pneumonia</td>
<td>6 1.3%</td>
</tr>
<tr>
<td>Enteritis</td>
<td>20 5.1%</td>
</tr>
<tr>
<td>Otitis Media</td>
<td>52 129%</td>
</tr>
<tr>
<td>Adenitis; Abscesses</td>
<td>10 2.5%</td>
</tr>
<tr>
<td>Furunculosis, Impetigo etc.</td>
<td>3 6.7%</td>
</tr>
</tbody>
</table>

Broncho pneumonia in the negative group is common under 2 years; the reverse is true of the tubercular children the incidence over 2 being higher than below that age; one would have expected that the tubercular children would have been more liable to pulmonary com-
Complications but there is certainly no evidence that this is so in the most dangerous period - under 2 years.

ENTERITIS - the complication to be dreaded in infants - was definitely higher in the tubercular group.

OTITIS MEDIA, was more frequent in tubercular subjects at all ages and the tubercular child does seem more liable to those septic complications as I have found similar results in the other acute infectious diseases.

ADENITIS - a less frequent complication, shows no appreciable difference in incidence in the two groups.
SEQUELAE OF MEASLES in TUBERCULAR and NON-TUBERCULAR SUBJECTS.

It may well be argued that to observe cases simply in the acute and immediate convalescence does not cover the whole period during which an obvious legacy of the illness may be observed. Accordingly an endeavour has been made to follow out the cases after their leaving the hospital; this has not been done so completely as might be desired as the cases admitted to the hospital were drawn from a wide area of London and therefore made it difficult to arrange for re-attendance. Where cases were from the Eastern district of London arrangements were made for them to attend Dr. Leonard Findlay's clinic at the East London Children's Hospital.

In other areas by the courtesy of the local tuberculosis Officer I was able to examine cases at the Tuberculosis dispensary. A group of non-tubercular children were re-examined 3 to 6 months after the attack; the majority were re-tested with tuberculin to confirm the previous result.

NON-TUBERCULAR GROUP (Tuberculin test negative while in Hospital).

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases personally re-examined and negative test confirmed by re-test</td>
<td>115</td>
</tr>
<tr>
<td>&quot; but not re-tested</td>
<td>30</td>
</tr>
<tr>
<td>attending East London Children's Hos. and found tubercular negative 3-6 months after attack</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>158</td>
</tr>
</tbody>
</table>
Of these 158 cases not one provided an instance of tuberculosis arising as a sequel of measles; the enquiry revealed that one case died 14 days after leaving hospital following an operation for hernia, so that 1 out of 159 cases died 3-6 months after the attack and that death was in no way related to measles.

**TUBERCULAR CHILDREN.**

I have included in the mortality table a baby of 9 months which died of tubercular meningitis 3 months after the attack of measles; although included as a death from measles the interval is rather long to ascribe the fatal end to the effect of the acute infection 3 months before. In the first year meningitis must be regarded as a likely development in the tubercular subject under the best of circumstances.

Apart from this case I have traced 31 other children for periods ranging from 2 to 14 months after their attack and in no instance did a tubercular manifestation arise.

In 5 cases whooping cough was a complication or sequel and those cases shared the same satisfactory end result as the others.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age Period of Observation</th>
<th>Case No.</th>
<th>Age Period of Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8yrs. 14 months</td>
<td>26</td>
<td>2 yrs. 8 mos.</td>
</tr>
<tr>
<td>3</td>
<td>20 yrs. 6 mos.</td>
<td>27</td>
<td>2 yrs. 14 mos.</td>
</tr>
<tr>
<td>6</td>
<td>4 yrs. 11 mos.</td>
<td>29</td>
<td>4 yrs. 4 mos.</td>
</tr>
<tr>
<td>7</td>
<td>3 yrs. 14 mos.</td>
<td>30</td>
<td>3 yrs. 16 mos.</td>
</tr>
<tr>
<td>8</td>
<td>4 yrs. 2 mos.</td>
<td>31</td>
<td>4 yrs. 6 mos.</td>
</tr>
<tr>
<td>10</td>
<td>2 yrs. 7 mos.</td>
<td>36</td>
<td>10 mos. 6 mos.</td>
</tr>
<tr>
<td>11</td>
<td>3 yrs. 12 mos.</td>
<td>37</td>
<td>3 yrs. 6 mos.</td>
</tr>
<tr>
<td>13</td>
<td>5 yrs. 4 mos.</td>
<td>39</td>
<td>5 yrs. 6 mos.</td>
</tr>
<tr>
<td>14</td>
<td>6 yrs. 7 mos.</td>
<td>41</td>
<td>6 yrs. 11 mos.</td>
</tr>
<tr>
<td>15</td>
<td>6 yrs. 8 mos.</td>
<td>42</td>
<td>6 mos. 6 mos.</td>
</tr>
<tr>
<td>16</td>
<td>7 yrs. 4 mos.</td>
<td>43</td>
<td>15 mos. 5 mos.</td>
</tr>
<tr>
<td>17</td>
<td>6 yrs. 10 mos.</td>
<td>45</td>
<td>15 mos. 5 mos.</td>
</tr>
<tr>
<td>20</td>
<td>4 yrs. 11 mos.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>3 yrs. 7 mos.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>6 yrs. 6 mos.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>2 yrs. 6 mos.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>3 yrs. 8 mos.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It will be seen that 6 of the cases were under 2 years, an age at which an active tubercular manifestation would be expected. Yet all were alive and well 8-11 months after. This certainly is evidence against any particular actuating effect from the attack of measles.

Of course contact with tubercle infection after leaving hospital would be important to those cases, and I endeavoured to exclude the possibility. The procedure I adopted was to explain to the parents that the child had been in contact with tuberculosi at some time prior to the attack of measles and that
it was important to prevent further exposure. I was thus able to ensure that none of the cases after their attack were in contact with "open" tuberculosis.

Cases of recovered phthisis although sputum negative are not necessarily non-infective and two of the cases returned home to live with their parents who had had pulmonary tuberculosis. Both these patients did well.

9 of the cases had been in intimate contact with human infection prior to the attack of measles; one died of tubercular meningitis (case 40) the others survived without evidence of any tubercular activation.

Measles complicated by whooping cough (See Chap. V, p. 121).
THE INCIDENCE OF TUBERCULOSIS
IN MEASLES.

It is difficult to compare figures of various series of cases as the class and age of the patients alter both the proportion of tuberculin reactions and the incidence of clinical tuberculosis. Also there is no unanimity in the definition of "tuberculosis" in children. For example some include in this term cases with X-ray evidence of hilar infection but the older the child the less is this evidence deserving of recognition as active disease.

Furthermore in the younger children just as active lymphatic lesions may be localised in the abdomen, yet not clinically ascertained. Accordingly statistics vary with the individual ideas of what is and what is not "tuberculosis" in children.

I prefer to accept the positive tuberculin test as indicating tubercle infection past or present; the younger the child the more likely is the infection to be active. In only one case did I find clinically active focal disease - a tubercular enteritis in a girl of 1,10/12 years, and this child succumbed to miliary tuberculosis after measles and whooping cough. In the children under a year there were signs of primary infiltration or epituberculosis of the lungs but
again this lesion requires X-ray confirmation.

The only reliable comparative figure would be the incidence of tuberculin reactions but even that varies a great deal with class and age grouping.

I quote the following statistics of various authors without attempting to compare them. My own results for London indicate the incidence of fatal tuberculosiss in measles among patients of the "hospital" class.

<table>
<thead>
<tr>
<th>INCIDENCE OF TUBERCULOSIS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cases</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Rilliet &amp; Barthez (1854) 314</td>
</tr>
<tr>
<td>Niessinger (1894) 650</td>
</tr>
<tr>
<td>Landis (1909) 457</td>
</tr>
<tr>
<td>Copeland &quot; 75</td>
</tr>
<tr>
<td>Robecourt (1930) 459</td>
</tr>
<tr>
<td>Berebouillet &amp; Beize (1931) 75</td>
</tr>
<tr>
<td>Klein (1927) 172 (over 5yrs.)</td>
</tr>
<tr>
<td>Bushnell (1915) 5,943 adults</td>
</tr>
<tr>
<td>Choffé (1929) 157</td>
</tr>
<tr>
<td>Park Hosp. 1930-32 901</td>
</tr>
</tbody>
</table>
SUMMARY.

(1) The mortality from tuberculosis in measles is not considerable and in relation to age is no higher than would be expected in the ordinary course of childhood tuberculosis.

(2) Tubercular children appear to have less susceptibility to pulmonary complications in measles.

(3) On the other hand they are more liable to pyogenic infection.

(4) There is no evidence that activation of tubercle infection follows after measles.
IV. Conclusion.

Tuberculin Allergy.

The earlier results of von Pirquet and others suggesting that all cases lost their reaction during measles have not been borne out by subsequent studies. The majority of cases do lose their reaction in the first week, in exceptional cases not regaining their sensitivity till after the second week.

Cases have been reported where the test initially positive continued negative for months after measles, but in such instances the less sensitive von Pirquet test was used and occurred in cases with active tuberculosi s such as tubercular meningitis. Adopting the improved technique and criteria of interpretation suggested by McNeil or by the intra-dermal method, it is probable that a positive result could have been obtained.

Von Pirquet tested his cases daily. This would tend to stimulate and enhance allergy, and therefore possibly cause the positive response to re-appear earlier than if only one test had been made previously. Accordingly, the relatively infrequent tests done in this series of cases show more accurately the duration of the anergic period in measles.

It would seem, however, that the increased sensitivity or facility of reading of the intra-dermal
test has counterbalanced the effect of infrequent tests as the period of anergy is found to be the first 5 days in the majority of cases; Von Pirquet found a similar period of hypo-sensitivity, using the scarification test at infrequent intervals.

**Relation of tubercle infection to measles.**

The incidence of fatal tuberculosis in measles does not suggest any increased susceptibility following this acute infection; only 0.2% of 901 cases succumbed. The two individual cases themselves, when examined critically, do not indicate that the measles had any specific effect on the fatal dissemination of the tubercle infection. Further, both were under 2 years, and in this age period a total of 11 children with positive tuberculin reactions were observed, and the mortality of 18.18% for this group is not above the average.

Apart from these fatal cases, I did not observe any tubercular manifestation arising during or subsequent to the attack of measles, cases being observed for a period of 3 to 14 months subsequently.

It might be expected that the tubercular child would be more liable to pulmonary complications in measles, but my results suggest the contrary.

Pyogenic complications such as otitis media, however, are more common in those children with a
positive tuberculin reaction, and in this respect tuberculosis might be said to bear a relation to measles.
V. WHOOPING COUGH.

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II. Tuberculin Allergy in Whooping Cough. 93.
   (1). Review of the literature........ 93
   (2). Personal observations.......... 98.
   (3). Summary.......................... 112.

III. Relation of Tuberculosis to Whooping Cough. 113.
   (1). Review of the literature...... 113.
   (2). Personal observations........ 117.
   (3). Summary......................... 129.

IV. Conclusion............................ 129.
I. Introduction.

Whooping cough ranks with measles as one of the dread diseases of infancy and childhood. Unlike measles, it can attack the infant under 6 months, but although it has lower age incidence it has usually a mortality slightly less than measles. The reason of this is that the fatalities ensue from pulmonary or gastro-intestinal complications, and the pulmonary complications are more frequent in measles, essentially a catarrhal infection, whereas in pertussis the initial catarrh is slight if present at all, and the disease itself is more a lymphatic infection, as the blood picture indicates. Also, the state of the hilar glands found at autopsy - always intensely congested and often haemorrhagic - suggest that this is the seat of the disease.

Whooping cough is an acute infection without an exanthem; nevertheless there has been recorded evidence of a temporary effect on tuberculin allergy, and of course the danger of tubercular sequelae has been regarded as almost as imminent as in measles.

II. Tuberculin Allergy in Whooping Cough.

(1). Review. As in measles, so in whooping cough, the explanation of the liability to active tubercular
infection has been sought in the allergic state of the patient. It was assumed that tuberculin allergy signified a measure of resistance both from the evidence of the Koch phenomenon and the observations on the diminution and apparent loss of allergy in severe and fatal cases of tuberculosis. Also in measles, "la maladie tuberculissante", there was the definite energy or depression of allergy. It would therefore be expected that in whooping cough - regarded as a close rival of measles in the liability to tubercular complication - there would be a similar effect on allergy.

The investigations that have been made are few and some are unconvincing. The more extensive studies favour the view that tuberculin allergy is not affected in whooping cough.

Cozzolino (1913), using the von Pirquet test with undiluted tuberculin (0.1T.) made a study of 227 cases of whooping cough ranging in age from a few months to 12 years; 67 were positive (29.5%). When his results were tabulated according to age he found little or no difference between the percentage of positive reactors as compared with similar groupings of normal children. 41 cases negative on their first test gave a similar result after an interval of at least 14 days, except in one instance, in which the second test was positive. It occurred in an uncomplicated case of moderate
intensity; there was no apparent cause for the first test being negative. There being no corroborative evidence, Cozzolino does not ascribe the fallacy to the pertussis infection. He found also that grouping his cases according to the stage of the disease in which the test was performed, there was no difference in the proportion of positive tests obtained. He therefore concludes that whooping cough does not influence the tuberculin reaction.

Schlemmer (1914) took a similar view to Cozzolino; he found 28.5% of cases of whooping cough under 5 years reacting positive to the von Pirquet test, a figure not much less than usual for that age period. But Nobécourt and Forgeron (1922) in 37 cases ranging from a few months to 9 years found only two positive; these were in the age period 2 to 4 years, of which 20 had been tested - a percentage of 10% as compared with the usual 13% to 51%. This is rather slender evidence of a decreased allergy. However, they further record two cases which were known to be positive to the von Pirquet test and subsequently became negative during whooping cough. But these were cases with complications; one became negative when acute broncho-pneumonia developed; the other with a moderate attack gave a negative response on the 9th day of the spasmodic stage while febrile.
Although not mentioned, some complication was probably present, as uncomplicated pertussis is afebrile in the spasmodic stage.

These two instances of negative responses can therefore be ascribed to causes other than whooping cough.

The same authors also record that in 13 cases with negative von Pirquet tests, two at autopsy showed tubercular lesions: one had acute miliary tuberculosis. It is of course recognised that the von Pirquet test may fail in the acute type of tuberculosis. The other was tested only during a terminal broncho-pneumonia. Again, other causes can explain the failure of the test, although Nobécourt and Forgeron considered the effect due to the whooping cough.

Galli (1923), using both the von Pirquet and intradermal tests, came to a similar conclusion, but while Nobécourt and Forgeron thought it could completely suppress the reaction, Galli considered there was merely a weakening of the allergy. He based this on his observation that some cases negative to the scarification test gave a positive test with the intradermal method. The intradermal test is, however, is admittedly more sensitive than the von Pirquet test, and in any case a previous tuberculin test enhances allergy, so that Galli's deduction is not really admissible. He further records that in 8 cases
previously positive he observed to become negative both to the von Pirquet and intra-dermal tests; or these he cites one which developed tubercular meningitis twenty days after the whooping cough had subsided; another 14 years old (an unusual age for pertussis) became negative and persisted negative even after recovery. (No dates are given). One case then was suffering from acute tuberculosis, making a frank positive tuberculin result unlikely; in the second there is no explanation of the persistence of the negative response after recovery, although whooping cough is claimed to have a relatively slight effect on tuberculin allergy. It is possible that this case may have given a pseudo response prior to the onset of the disease.

Lesné and Coffin (1926) in 45 cases observed that in 14 positive cases the initial result was negative in two instances, but there was no evidence that this was due to the whooping cough and they favour the view that the tuberculin sensitivity is unaffected.

Dumans (1932) in 14 tubercular cases found that some of the reactions appeared weaker than usual, but in no instance was a negative result obtained.

There is therefore no conclusive evidence that in whooping cough there is any effect on tuberculin sensitivity; complications arising in the course of
the illness may do so. Also, actual tubercular complications co-existent with the whooping cough may influence the allergy, but pertussis of itself does not appear to have an influence such as to give rise to fallacious negative results in tubercle-infected subjects.

(2). Observations on 386 cases of whooping cough.

Whooping cough is a disease in which the actual date of onset is difficult to determine; from the history of the case the catarrh at the onset is not always present and is usually so mild that it passes unnoticed by the parents. It is only when the typical spasmodic cough develops or a preliminary complication ensues that the doctor is called upon. For this reason one has been unable to study many cases from the actual onset of the disease.

Being a protracted illness, the patients were submitted to tuberculin tests on admission and thereafter at intervals of a fortnight to a month, the majority having at least two tests. For convenience the tests are indicated not by the day of the disease, but by the week in which they were performed.

Incidence of positive reactors.

A proportion of the cases were tested only on one occasion, including those positive reactors whose
response was rather marked; such cases were not tested again, to avoid severe reaction of a stimulated sensitivity. 126 cases were tested on one occasion; if classified into two groups - those tested in the first week and those tested after the first week - the percentage of positive reactors is almost identical. Age grouping being similar, this suggests that there is little or no effect on tuberculin sensitivity, although of course the numbers are rather small to be conclusive.

Table I.

<table>
<thead>
<tr>
<th>Cases tested on one occasion only.</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
<th>Percentage positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tested in first week.</td>
<td>22</td>
<td>5</td>
<td>27</td>
<td>18.5%</td>
</tr>
<tr>
<td>&quot; after first week.</td>
<td>80</td>
<td>19</td>
<td>99</td>
<td>19.0%</td>
</tr>
</tbody>
</table>

If these cases are grouped with those tested on more than one occasion so that all are included, the incidence of positive reactions in those tested in the first week is 8.47%, compared with 9.6% in those tested in the second week or later. There is a slight difference of just over 1% in favour of an increased incidence in the later stages of the disease, but it is too small to suggest any effect on allergy.
Table II.

All cases grouped according to period of initial test.

<table>
<thead>
<tr>
<th></th>
<th>Tested in first week</th>
<th>Tested in second week or later.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. tested once only.</td>
<td>27</td>
<td>99</td>
</tr>
<tr>
<td>No. tested twice or oftener.</td>
<td>79</td>
<td>181</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>280</td>
</tr>
<tr>
<td>Total positive</td>
<td>9</td>
<td>27</td>
</tr>
<tr>
<td>Percentage positive</td>
<td>8.47%</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

Results of positive reactions at various stages of whooping cough.

36 cases out of 386 were found giving positive reactions at some period of the disease. The results are tabulated below according to the week in which each test was performed, showing the response obtained.
<table>
<thead>
<tr>
<th>Case</th>
<th>INITIAL TEST.</th>
<th>SECOND TEST.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week of disease</td>
<td>Result.</td>
</tr>
<tr>
<td>10</td>
<td>1st</td>
<td>+18</td>
</tr>
<tr>
<td>11</td>
<td>&quot;</td>
<td>++18</td>
</tr>
<tr>
<td>12</td>
<td>&quot;</td>
<td>++15</td>
</tr>
<tr>
<td>14</td>
<td>&quot;</td>
<td>+++10 E10</td>
</tr>
<tr>
<td>27</td>
<td>&quot;</td>
<td>+++20 E5</td>
</tr>
<tr>
<td>29</td>
<td>&quot;</td>
<td>+10(delayed)</td>
</tr>
<tr>
<td>32</td>
<td>&quot;</td>
<td>+20 E5</td>
</tr>
<tr>
<td>5</td>
<td>2nd</td>
<td>Negative</td>
</tr>
<tr>
<td>6</td>
<td>&quot;</td>
<td>++12</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>++20</td>
</tr>
<tr>
<td>8</td>
<td>&quot;</td>
<td>+++20</td>
</tr>
<tr>
<td>9</td>
<td>&quot;</td>
<td>+++15</td>
</tr>
<tr>
<td>17</td>
<td>&quot;</td>
<td>+++15</td>
</tr>
<tr>
<td>20</td>
<td>&quot;</td>
<td>+++20 E20</td>
</tr>
<tr>
<td>21</td>
<td>&quot;</td>
<td>+++17 E20</td>
</tr>
<tr>
<td>24</td>
<td>&quot;</td>
<td>+++15</td>
</tr>
<tr>
<td>25</td>
<td>&quot;</td>
<td>+15</td>
</tr>
<tr>
<td>26</td>
<td>&quot;</td>
<td>Negative</td>
</tr>
<tr>
<td>30</td>
<td>&quot;</td>
<td>+++26 E5</td>
</tr>
<tr>
<td>34</td>
<td>&quot;</td>
<td>+15</td>
</tr>
<tr>
<td>1</td>
<td>3rd</td>
<td>+15</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>+++20 E18</td>
</tr>
<tr>
<td>4</td>
<td>&quot;</td>
<td>+++18</td>
</tr>
<tr>
<td>31</td>
<td>&quot;</td>
<td>+20</td>
</tr>
<tr>
<td>33</td>
<td>&quot;</td>
<td>+++20 E15</td>
</tr>
<tr>
<td>35</td>
<td>&quot;</td>
<td>+11 E25</td>
</tr>
<tr>
<td>22</td>
<td>4th</td>
<td>Negative</td>
</tr>
<tr>
<td>36</td>
<td>&quot;</td>
<td>++++16 E10</td>
</tr>
<tr>
<td>3</td>
<td>5th</td>
<td>Negative</td>
</tr>
<tr>
<td>15</td>
<td>&quot;</td>
<td>+++20</td>
</tr>
<tr>
<td>28</td>
<td>&quot;</td>
<td>+++20 E10</td>
</tr>
<tr>
<td>13</td>
<td>6th</td>
<td>+++18</td>
</tr>
<tr>
<td>18</td>
<td>&quot;</td>
<td>+10</td>
</tr>
<tr>
<td>23</td>
<td>&quot;</td>
<td>(+)4</td>
</tr>
<tr>
<td>16</td>
<td>9th</td>
<td>++++20</td>
</tr>
</tbody>
</table>
Only 4 cases were found negative on their first test - a percentage of 11.11%. This appreciable error bore no relation to the stage of the disease; two were obtained in the second week, one in the fourth and another in the fifth week. This suggests that these negative reactions were not related to the whooping cough infection. The actual cases will be described in detail later.

In only one instance (Case No. 29) was a delayed response obtained. The reaction in the first week was delayed three days; a subsequent test in the 4th week gave an immediate response of ++ 20.

The other 31 cases all gave immediate positive reactions in their first test. Those which were tested on a subsequent date showed an increase in allergy from the stimulation or the initial test. The increase was not as great as in measles and scarlet fever patients, so that it cannot be said to indicate anything more than the stimulating effect or the previous injection of tuberculin.

Table IV.

Results of cases tested on two or more occasions.

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Week of first test</th>
<th>Usual week of last test</th>
<th>No. of positive reactions who were negative on first test.</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>1st 6th week</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>61</td>
<td>2nd 6th &quot;</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>55</td>
<td>3rd 7th &quot;</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>65</td>
<td>4th week or 10th &quot;</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>260</td>
<td></td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>
The above table shows that 260 cases were tested on two or more occasions, covering all stages of the disease. Only 4 of those with a tuberculin sensitivity gave a negative response to the first test. The important feature is that the incidence of this fallacy bears no relation to the stage of the disease; it was as frequent in the 4th and 5th week as in the first three weeks. If this had been due to the acute pertussis infection one would expect it to be more marked at the onset, yet in 79 cases tested in the first week of the disease none of the tubercular group gave a negative result.

In measles and scarlet fever the period of depressed sensitivity coincides with the initial acute phase of the disease, but in whooping cough the occurrence of these negative results is not related to the stage of the disease. Do these cases in themselves show any reason for the fallacious result? The clinical history of the cases may reveal the cause of the phenomenon.

Four cases which gave an initial negative response.

Case No.3. R.F., a girl of 4 years was admitted to hospital on 29/10/31 with a history of a spasmodic cough accompanied by a whoop for 10 days. On admission her spasms were severe and frequent,
accompanied by occasional vomiting. There was some bronchitis but the temperature was normal; pulse 116; resps. 29. She continued afebrile throughout.

After the first week the spasms, which had averaged 7 daily, became less frequent.

On 17/11/31 the bronchitis had subsided; the spasms occurred 2 to 5 daily. The child was now allowed up.

13/12/31 Tuberculin test (5th week) was negative.
23/12/31 " (7th week) " positive.
29/12/31 ++ 20 mm.
30/12/31 ++ 12 mm. Erythema 23 mm.

On this date the child was discharged.

Results of tests performed 11 months later.

23/11/32 A Tuberculin test was done, using 1/1000 Human O.T. The result was negative.

On 28/11/32 a Tuberculin test, using equal parts of human and bovine O.T.- 1/1000 was positive. Reaction + 12 mm. (48 hrs.)

Summary. This case had a moderate attack; she was afebrile throughout; the tuberculin test negative in the 5th week cannot be attributed to any special feature of the attack of whooping cough. The second test 15 days later gave an immediate response of moderate degree.

The tuberculin tests performed 11 months later gave almost a similar result; the first test was
negative: a week later a further response was obtained.
It might be said that the negative response to the
human tuberculin alone was because of an allergy
specific to the bovine protein, hence the response to
the second test, using equal parts of human and
bovine O.T.

Accepting the view that an allergic subject will
react to either tuberculin, then in this case the
results obtained during the whooping cough become
comparable with those obtained a year later. Each
time the first test was negative and the second positive
so that the results were not dependent on the presence
of an acute infection like whooping cough, as the child
was in good health on the second occasion.

I consider the phenomenon was due each time to a
degree of allergy so weak that it required the stimula-
tion of a small dose of tuberculin before the character-
istic local response could be elicited. There is no
evidence that the whooping cough played any part.

Case 5, a boy of 10 years was admitted to hospital on
10/12/31 afebrile, without any pulmonary complication,
with a typical cough of one week's duration.
Spasms occurring about 7 daily accompanied by a whoop.

10/12/31 Tuberculin test (2nd week) - negative.
14/1/32 Tuberculin test (5th week) - positive.

++ 15 mm; erythema 5 mm. (24 hrs.)
++ 20 (48 hrs.)
The cough had now gone and the patient was convalescent. He left hospital on 23/1/32.

Summary. This was a case with an afebrile mild attack; there is no evidence that the whooping cough had any influence on the tuberculin allergy.

Case No. 22. E.B., a boy of 5 years.

When 2 years old, he had a tubercular arthritis of the right knee, which was cured after a year of sanatorium treatment. One therefore would expect this child to be allergic at the onset of the whooping cough.

On admission on 14/6/32 he had had a spasmodic cough for three weeks; on 11th June he started to whoop. On examination one found a few basal crepitations in the lungs; he had a moderate spasmodic cough accompanied by a whoop. He was afebrile and continued so throughout his stay in hospital.

On 19/6/32 Tuberculin test (4th week) was negative.

On 24/6/32 he developed otorrhoea (left) without any premonitory symptoms.

On 3/7/32 Tuberculin test (6th week) - positive.

+ 16 mm; erythema 9 mm. (24 hrs.)

+++ 20 mm; erythema 44 mm. (48 hrs.)

On 16/7/32 there was still induration with desquamation at the site of the test. It was therefore a well-marked reaction. The erythema, a feature of the higher degree of allergy, was extensive. The
whooping cough was moderate in character and the first test was made in the fourth week of the disease.

Had this child a tuberculin allergy which had waned to a minimum degree to be stimulated by the first intra-dermal test? The marked response to the second test is rather surprising if representing a low degree of allergy stimulated by .01 mgm. of O.T. intra-dermally. When 3 years old the child had had an attack of conjunctivitis 5 weeks after measles. The conjunctivitis was apparently severe, as he was four weeks in hospital; it may have been phlyctenular, indicative of a high degree of tuberculin allergy.

In this case there is therefore the history of a tubercular infection previously, which was followed by a possible para-tubercular condition - conjunctivitis, which would indicate a high degree of allergy. There was no feature in his attack of whooping cough to suggest an explanation of the initially negative result. It would seem that even a high degree of sensitivity can fade sufficiently so that a tuberculin test may be completely negative although a subsequent test may show a marked reaction.

Case 26 (No. 34 in diphtheria series). B.B., age 5 yrs.
On 12 June, 1932 the boy was admitted to Guy's Hospital as a case of pneumonia.
On 17/6/32 he was transferred to the Park Hospital,
having developed a typical cough with whoop.

On admission there were no signs of consolidation, there being numerous fine crepitations with vesicular breathing at each base indicative of a resolving bronchopneumonia. The child had three convulsions on the evening of admission; they were of the type associated with severe and frequent spasms.

Temperature on admission was 99.2° Pulse 144. Resps. 60

18/6/32  Tuberculin test (2nd week) - was negative.

The child continued febrile with severe and frequent spasms (10 to 12 daily) till the 30th June; thereafter the temperature continued normal with a gradual improvement in the symptoms, the chest signs having now gone.

On 24/7/32  Tuberculin test (7th week) was positive.
   ++ 12 mm.; erythema 18 mm. (24 hrs.)
   ++ 12 mm. (48 hrs.)

The child had now a moderate cough; there was no febrile reaction to the test.
On 18/8/32 his convalescence was interrupted by an attack of faucial diphtheria. His temperature rose to 102°; there was a follicular deposit on the right tonsil, the fauces were congested and submaxillary glands on the right side enlarged. A culture from the throat found positive.

Next day (19/8/32) there was a definite plaque of membrane on the right tonsil, spreading to the anterior faucial pillar; temperature, 101.5°; Diph. antitoxin, 24,000 units, given intra-muscularly.

Tuberculin test (10th week: 2nd day of diphtheria) - positive. ++ 20 mm. (24 hrs.)
21/8/32 ++ 20 mm. (48 hrs.); the membrane had now separated; the throat clean; the adenitis subsided.

Apart from a transitory albuminuria on the 28th Aug., his recovery was uninterrupted.

**Summary**

This case is one of a severe type of whooping cough associated with convulsions on admission. The initial test was negative. Why? It cannot be due to the temperature, as it was only 99°, rising to
the evening following the test and resuming the level of 99° the next day, whereas the third test made during the attack of diphtheria was positive although the temperature was round 101°.

In this case the negative test occurred as a broncho-pneumonia was subsiding.

It is recognised that the response to tuberculin may be lost during broncho-pneumonia, as well as in lobar pneumonia, and can explain the fallacious result in this case.

Discussion. The four cases in which the initial test was negative show no feature common to their pertussis infection to suggest a cause for the failure to react. In two cases other factors can explain the phenomenon; in case 26 an acute pneumonia at the onset probably caused the negative result, as a failure to respond to tuberculin has been observed both in lobar and broncho-pneumonia (McNeil, 1909; Rolly, 1926).

Case No. 3 is of particular interest; the same results were repeated a year after the attack of whooping cough, suggesting that the cause of the initial negative result was due to the sensitivity having raded below a level at which a response to the standard dilution of 1/1000 O.T. would occur, always presuming that the child would react similarly to human and bovine O.T., as the initial test a year after was to
human O.T. only, whereas the subsequent test was made with equal parts of human and bovine tuberculin.

The other two cases were uncomplicated afebrile attacks, and I believe that the initial negative result probably was due to the reason just put forward, that their sensitivity had regressed below the reaction level.

**Average degree of sensitivity in groups tested at varying stages of whooping cough.**

If a study of these individual cases has not revealed that the whooping cough accounted for the fallacious result, do the other positive reactors indicate any temporary weakening of sensitivity?

Cases vary in their individual degree of allergy but if whooping cough had any depressing effect one would expect that the average response from primary tests would increase the later the tests were performed. Second tests must be excluded, as they represent an enhanced allergy from the previous injection. The following table shows that there is no striking increase in the average degree of allergy the later the tuberculin test is performed.

**Table V.**

<table>
<thead>
<tr>
<th>Week of primary tuberculin test.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4th et seq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>5</td>
<td>12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Average degree of tuberculin allergy</td>
<td>2+</td>
<td>2.5+</td>
<td>2.3+</td>
<td>2.4+</td>
</tr>
</tbody>
</table>
The average response in the first week is somewhat lower than that of any later period, but there is no apparent progressive rise in the average degree of allergy the later in the disease the tests were performed. The results are too uniform to indicate definitely any effect from the pertussis.

Summary.

(1). The incidence of positive reactors in the acute period of whooping cough is not appreciably less than that found in convalescence.

(2). The average degree of sensitivity was similar in all stages of the disease.

(3). A failure to respond to the initial intra-dermal test was observed in 9% of the allergic subjects, but there was no evidence that this had any relation to the whooping cough.

(4). An increase in sensitivity was noted in second tests not sufficiently marked to indicate more than the expected stimulation from the initial test.

(5). There is no evidence that whooping cough has any effect on tuberculin sensitivity, although the complications of the disease may do so.
III. Relations of Tuberculosis and Whooping Cough.

(1). Review. The question of the activation of tubercular infection by whooping cough has always excited more interest than the relation to tuberculin sensitivity. As would be expected, the earlier studies made when tuberculosis was much more frequent in childhood seemed to indicate a definite relation between the two diseases. On the other hand, the more recent investigations produce no evidence of any such specific relation. For example, Rolly (1906) records a mortality from tuberculosis of 8% in 198 cases, and concludes that whooping cough has a marked effect on tubercle infection. Leger (1909) finds tuberculosis occurring as a complication in 8% of 170 cases and stated that whooping cough could either activate a quiescent infection or predispose to an infection following.

Gottlieb and Müller (1922) agreed that there was a danger to the child with a pre-existing tubercular infection. In 8 known tubercular cases—all young children—3 died of meningitis following a miliary spread and the hilar glands appeared to be the focus from which the miliary dissemination arose.

On the other hand, Koenigsburger and Fuerst (1924) in an extensive study, found no evidence of a specific relation between the two diseases. In 900 cases they
found that of 13 cases under 2 years with latent infection 9 became active and all died, a mortality of 70%; and of 55 cases aged 2-14 years 6 became active (10%). The 70% mortality under 2 years is a little higher than is to be expected normally and might suggest a specific effect from the whooping cough, but Koenigsberger and Fuerst considered that the effect, if any, was not considerable; they thought a more frequent cause of activation of the tubercle infection.

Meyer and Burghard (1925) in a statistical study definitely contradict the other view; they reviewed 1064 cases of whooping cough treated at Dusseldorf from 1907 to 1925, and they could find no evidence that there was any harmful effect to the tubercle infected patient. In 220 deaths, only 2 were due to tuberculosis - under 1%.

Noegerath and Eckstein (1924) observed that in a severe combined epidemic of measles and whooping cough among school children there was no increase in the mortality from tuberculosis, nor was there any evidence of activation or latent tubercle infection in children of school age.

Mausset (1926) likewise finds that there is no danger in latent infection; 12 cases were observed and no complication ensued. He does not specify the ages.

Moses (1927) recorded that in extra-pulmonary tuberculosis there was no exacerbation, so that the general resistance to the infection was apparently
unaffected.
In 53 cases with Pott's disease, got worse due to the mechanical effect of the coughing. Choffé (1929) in 99 cases with evidence of tubercle infection only found one to develop a fresh manifestation during whooping cough. Dumas (1932) in 14 children under 2 years found no effect from the pertussis: 10 gave a positive tuberculin test but had no evidence all of focal activity; they did well; 4 others had definite hilar and/or lung changes; one died 6 months after.

Statistical: Only one death in 14 children under 2 years with positive tuberculin reactions is really a favourable result and Dumas therefore suggests that even under 2 years there is no specific effect on the primary lymphatic tubercle infection detected by the tuberculin test. This primary infection in infants is not to be described as "latent" as such cases coming to autopsy show evidence of activity in the lesions (MacGregor, 1930).

Where statistics have been drawn from a large series of cases there is agreement that whooping cough has no specific effect in the activation of tuberculosis. Even under 2 years of age the mortality of tuberculosis differs little from that found
in straightforward uncomplicated tubercle infection at that age.
Observations on 383 cases.

Whooping cough is a specific infection usually ascribed to the Bacillus or Bordet and Gengou, although it has been suggested by Rich that the disease behaves more like an infection due to a filterable virus. The cases can be diagnosed clinically on the recurrent paroxysms of coughing followed by the typical whoop or, in infants, vomiting. Before this stage develops the high lymphocytosis is a valuable guide.

Other conditions are said to give rise to confusion such as enlarged tubercular hilar glands. Cases such as these can be differentiated from whooping cough by the fact that, although they have a short, dry cough, it is not paroxysmal and is not followed by a whoop.

In this study I have only included cases in which the clinical diagnosis was definitely established.

Effect of tuberculosis on whooping cough.

In discussing these two diseases the interest has always centred on the question of the activation of the tubercle infection. If there had been any striking effect on the character of the whooping cough in tubercular subjects, it would no doubt have been recognised. In the 36 cases I have observed there was no evidence that they suffered from a more severe and prolonged attack.
Duration of Illness. Calculating the average duration of the cough, which is a measure of the duration of the illness, there is no difference between the tubercular subjects and the controls - 7 weeks in each case.

Severity of the Illness. The severity of the illness measured by the average number of spasms during the week of maximum frequency shows a greater severity in the control group, in which the average number of spasms was 7 daily, compared with 4 in the tubercular group. This difference is to be expected, as the control group has a much greater proportion of younger children in whom the disease is more severe.

Incidence of complications.

Although there is no appreciable difference in the duration of the illness, there might be a greater tendency to complications such as enteritis and bronchopneumonia are so much more common in the younger child that it is necessary to subdivide the groups. Unfortunately this makes the figures of the tubercular children too small from which to draw any definite conclusions.
Table VI.

Complications of whooping cough.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Negative Tuberculin test</th>
<th>Positive Tuberculin test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-2 yrs.</td>
<td>Over 2 yrs.</td>
</tr>
<tr>
<td>Acute enteritis</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>Broncho-pneumonia</td>
<td>19</td>
<td>13.2</td>
</tr>
<tr>
<td>Lobar pneumonia</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Bronchietasis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>6</td>
<td>4.1</td>
</tr>
<tr>
<td>&quot;Convulsions&quot;</td>
<td>8</td>
<td>5.6</td>
</tr>
<tr>
<td>Adenitis, abscesses</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Otitis media</td>
<td>13</td>
<td>9.0</td>
</tr>
<tr>
<td>Ophthalmia</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Furunculosis, impetigo</td>
<td>11</td>
<td>7.6</td>
</tr>
<tr>
<td>Total cases</td>
<td>143</td>
<td>204</td>
</tr>
</tbody>
</table>

The cases of bronchitis classed as complications are only those which were of acute and persistent character, accompanied by fever. I have excluded the slight pulmonary catarrh which may occur at the onset of whooping cough. The table shows that in the larger control group there is the usual high incidence of enteritis in the younger children; pneumonia also frequent in infancy is still a common complication over two years, whereas enteritis is not
Complications in tubercular children.

Acute enteritis. The fact that in the 7 positive cases under two acute enteritis did not occur as a complication, is probably explained by the fact that the 11 cases were all in the second year, and it is under a year that acute enteritis is common.

Broncho-pneumonia. This complication - the most common of all, only occurred in one instance in the tubercular group - in a boy of 5 years with a favourable result. Under 2 years broncho-pneumonia did not occur in any of the 7 tubercular children.

Convulsions may occur occasionally associated with cerebral haemorrhage or meningitis, but usually it is a manifestation of severe and frequent spasms in the children under a year. Their exact nature is not yet satisfactorily explained. One case of the tubercular group died following such convulsions, autopsy revealing early lymphatic tubercle but no evidence of tubercular meningitis.

Otitis media, as in the other acute infections, was more frequent in tubercular children.

As far as can be judged from such a small series, it appears that the tubercle-infected child is not more liable to pulmonary complications; in this study they were strikingly immune.
Mortality from whooping cough in tubercular and non-tubercular children.

During the period from December, 1931 to March, 1932, every case of whooping cough admitted to the Park Hospital was subjected to a tuberculin test. After that period, when a child was acutely ill on admission the test was deferred, and some of these cases died without a tuberculin test being performed. Accordingly, the mortality in the control group of negative reactors has been calculated only from the cases studied in the period December to March. As measles increases the gravity of the prognosis in whooping cough, cases thus complicated are excluded, and their mortality calculated separately.

The following table shows the mortality in each group:

<table>
<thead>
<tr>
<th>Case Type</th>
<th>Total</th>
<th>Deaths</th>
<th>Case Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Cases with a negative tuberculin reaction (Dec. 1931 to Mar. 1932 only)</td>
<td>100</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>ii. Cases with a positive tuberculin reaction</td>
<td>36</td>
<td>4</td>
<td>11.11%</td>
</tr>
<tr>
<td>iii. Cases with a negative tuberculin reaction complicated by measles</td>
<td>41</td>
<td>5</td>
<td>12.19%</td>
</tr>
</tbody>
</table>
Age is an important factor in the prognosis of whooping cough; the younger the child, the more fatal it is. Groups (i) and (iii) are closely comparable in regard to age grouping except that measles, unlike whooping cough, is not a disease of the first six months. Accordingly, the measles cases will have a higher age grouping and should have a slightly better prognosis. Therefore the high mortality of 12.19% is probably relatively under-estimated, so that measles complicating whooping cough greatly imperils the child's chances of recovery.

In group (ii) the tubercular children show a mortality of 11.11%; again there is a higher age grouping, so that this figure of 11.11% is also under-estimated and shows a definite increased risk for the tubercular child. This increased risk, however, is not due to those fatal complications accounting for the mortality in the control series, as 3 of the 4 deaths in the tubercular children were due to tuberculosis. It would be necessary to show that those deaths from tuberculosis were not just coincidence, but actually the result of the pertussis before this high mortality becomes comparable. Consideration of the age of those fatal tubercular cases shows that the fatality is little more than would be expected had the tuberculosis been uncomplicated.
Effect of whooping cough on Tuberculosis.

In the 36 cases with a positive tuberculin test, there was no instance of an active form of tuberculosis arising in the course of the illness, apart from the cases which proved fatal.

Mortality from Tuberculosis in whooping cough.

Of the 4 fatal cases in the 36 positive reactors, 3 actually died from tuberculosis; in the group of 367 cases with a negative tuberculin test there were 20 deaths, none of which were due to tuberculosis; the absence of tubercle infection was excluded at autopsy in 7 of these (see appendix).

The total number observed was 403, giving a case mortality from tuberculosis of 0.74%. The case mortality from whooping cough at the present time varies from 9% to 11% (Annual Reports of M.A.B., 1925-29) so that the contribution of tuberculosis to the mortality is not great.

The figure 0.74% is apparently lower than most workers have found; Goebel (1929) gives the following figures:

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84%</td>
<td>Monraisse (1901)</td>
</tr>
<tr>
<td>1.76%</td>
<td>Boulade (1907)</td>
</tr>
<tr>
<td>1.23%</td>
<td>Deschamps (1904)</td>
</tr>
<tr>
<td>2.46%</td>
<td>Lehlemmes (1914)</td>
</tr>
<tr>
<td>2.17%</td>
<td>D'Espine (1914)</td>
</tr>
<tr>
<td>2.38%</td>
<td>Wall (1921)</td>
</tr>
</tbody>
</table>

To these may be added the following:
Most of these results are obtained at a period when the tuberculosis mortality was much higher than it is now.

Koenigsberger and Fuerst (1924), in 900 cases, had 9 deaths from tuberculosis, a mortality of 1%. Incidentally, they found that tubercular complications which did not prove fatal occurred in 6 cases - 0.66%, so that this is also an uncommon feature. Meyer and Burghard (1935), analysing results in 1064 cases occurring from 1907 to 1925, found only 2 deaths due to tuberculosis, a case mortality of less than 0.2%. Therefore in these two extensive studies the results are similar to my own - 1% and 0.2% compared with 0.74%.

Age of fatal cases.

Age is an important factor in the prognosis of the tubercular child. It is necessary, then, to analyse the results from this point of view.

The 3 deaths from tuberculosis occurred in the group reacting to tuberculin, and they were all in the age period 1-2 years; there were a total of 7 cases of this age, so that the mortality was 42.8%. This figure does not exceed the usual mortality in uncomplicated tubercular infection, so that these 3 deaths in whooping cough might well be coincidence.
It must be remembered, however, that these children, during their attack of whooping cough were not in contact with tubercle infection, which makes a considerable difference in the mortality. Under two years the mortality in tubercular children is 82% if left in contact, whereas if the children are segregated from the source of infection, the mortality is only 7.5% (Bemard, Debré and Lelong, 1925). From this point of view, then, the mortality of 42% is high and probably indicates that the whooping cough influenced the final efflorescence of the tubercle infection.

### Table VIII.

Age incidence of deaths in 36 tuberculin-positive cases.

<table>
<thead>
<tr>
<th>Age</th>
<th>0-1 yr.</th>
<th>1-2 yrs.</th>
<th>2-3</th>
<th>3-4</th>
<th>4-5</th>
<th>5 &amp; over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td></td>
<td>7</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Deaths from Tb.</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths from other causes.</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Summary of fatal cases in tuberculin-positive group.

**Case 13.** A girl of 1 10/12 yrs. On admission in the fifth week of whooping cough had active tuberculous in the form of tubercular enteritis (faeces Tb +;
palpable abdominal glands) but no clinical evidence of a focus in the lungs; measles ensued in the 7th week and she died of **miliary tuberculosis** in the 10th week; at autopsy a primary focus was found in the lung; there was also tubercular ulceration of the intestine and recent miliary spread; cause of death - miliary tuberculosis complicated by whooping cough and measles.

**Case 23.** A girl of 1 4/12 yrs., admitted in the 5th week of whooping cough with no clinical evidence of active tubercle; died of tubercular meningitis in the 6th week; at autopsy primary focus found in the lung with no evidence of recent spread; the hilar glands were caseous and may have been origin of spread to the meninges; cause of death - tubercular meningitis.

**Case 13.** A girl of 1 3/12 yrs., admitted in the 4th week of a moderate attack of whooping cough; died in 11th week, following a very modified attack of measles; at autopsy extensive primary lymphatic tubercle principally in thorax and evidence of early miliary spread. Cause of death - early miliary tuberculosis, possibly accelerated by modified measles.

**Case 34.** A girl of 3 1/2 yrs. admitted in first week of a severe attack; died in the second week following convulsions; at autopsy small tubercular focus found in the right submaxillary gland; the child did not die from tuberculosis, the convulsions evidently being of the type associated with severe whooping cough.
Discussion.

The four fatal cases just described show that there is no direct evidence that the whooping cough activated the pre-existing tuberculosis. Case No 13 died of miliary tuberculosis in the 8th week of whooping cough; this miliary spread may have been due to the acute inflammation in the hilar glands, but in any case the older tubercular lesions were extensive, representative of a massive infection which at that age - 1, 10/12 years - was found to have a grave prognosis. Case No 18 likewise died of miliary tuberculosis associated with a massive lung infection: the child died in the 10th week of whooping cough and, as was probable in the previous case, there was a super-added infection - an attack of measles, although modified, preceding death. Again the age - 1 3/12 years - was within the danger period.

Case 20, again in the same age period - 1, 4/12 years - died of a tubercular meningitis in the 6th week of whooping cough; the primary lesion in the lung was quiescent and it is probable that the spread to the meninges originated from the acutely inflamed hilar glands which were caseous, so that in this instance whooping cough might be classed as an exciting factor.

Case 34 - 3 1/2 years old - did not die of tuberculosis; the tubercle infection was slight and did not appear to contribute to death.
It will be noted that the children died in the 6th, 8th and 10th weeks of their attack; this suggests that if the pertussis infection had any effect it was by the lowering of the general resistance from the exhaustion of the illness; a specific effect from the acute inflammation of the hilar glands would be expected earlier in the course of the illness.

_Tuberculosis as a sequel to whooping cough._

Whooping cough is a prolonged illness, and most cases are under observation in hospital over 7 weeks. However, it might be that tubercular sequelae would arise even later. I have endeavoured to trace the tuberculin-positive cases subsequent to their leaving hospital; 14 were traced for periods ranging from 5 to 14 months after and in no instance did a tubercular manifestation arise, and all were alive and well. The following table indicates the age of these cases and the period of observation:

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Period of observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6 yrs.</td>
<td>5 months.</td>
</tr>
<tr>
<td>3</td>
<td>4 &quot;</td>
<td>13 &quot;</td>
</tr>
<tr>
<td>8</td>
<td>2 &quot;</td>
<td>8 &quot;</td>
</tr>
<tr>
<td>9</td>
<td>3 &quot;</td>
<td>14 &quot;</td>
</tr>
<tr>
<td>10</td>
<td>5 &quot;</td>
<td>5 &quot;</td>
</tr>
<tr>
<td>11</td>
<td>4 &quot;</td>
<td>9 &quot;</td>
</tr>
<tr>
<td>12</td>
<td>3 &quot;</td>
<td>6 &quot;</td>
</tr>
<tr>
<td>13</td>
<td>3 1/2 &quot;</td>
<td>6 &quot;</td>
</tr>
<tr>
<td>16</td>
<td>4 &quot;</td>
<td>10 &quot;</td>
</tr>
<tr>
<td>17</td>
<td>3 &quot;</td>
<td>8 &quot; (Complicated by measles)</td>
</tr>
<tr>
<td>19</td>
<td>2 1/2 &quot;</td>
<td>9 &quot;</td>
</tr>
<tr>
<td>21</td>
<td>3 &quot;</td>
<td>8 &quot;</td>
</tr>
<tr>
<td>26</td>
<td>5 &quot;</td>
<td>9 &quot;</td>
</tr>
</tbody>
</table>
All but one child were 2 years or over and they are examples of what is usually called "latent" infection, as none had clinically active lesions; in no instance did a tubercular manifestation arise following the whooping cough. The only case under 2 years shared the same favourable convalescence as the others.

Summary.

(1). There is no evidence of a specific relation between whooping cough and tuberculosis; the mortality from tuberculosis in children suffering from whooping cough is little higher than that occurring in similar age groups of uncomplicated cases.

(2). Tubercular sequelae were not found to ensue for as long as 5-14 months after in children with "latent" infection, so that there appears to be no danger of activation of the quiescent focus.

IV. Conclusion.

Tuberculin Allergy in Whooping cough.

There is no conclusive evidence of any effect on tuberculin sensitivity in uncomplicated whooping cough. There was, however, an error in the intra-dermal test; in 3 uncomplicated cases later proved positive the first test was negative: this is an error of 9%.
I suggest that these were cases whose allergy was too low to react to the dilution used (1-1000); all three reacted two to three weeks later to this same dilution.

Where a loss of allergy has been reported, the cases were usually complicated. It must be remembered that a pneumonia can affect tuberculin sensitivity; also in others active acute tuberculosis was present, and using the von Pirquet test on such cases, interpretation is often difficult. Pertussis by itself does not appear to have an appreciable effect on tubercular allergy.

The idea that whooping cough has some particular influence on tubercle infection is not warranted; it is often that the two infections must coincide, but there is no evidence that the one activates the other. It is probable that the lowering of resistance associated with a prolonged and often exhausting illness such as whooping cough leads in time to that terminal miliary spread or meningeal localisation which proves fatal, but it only occurs in cases of an age whose prognosis, even in the most favourable circumstances must be guarded.
VI. SCARLET FEVER.

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I. Introduction.

Since the original descriptions of Sennert and Sydenham in the 17th century, scarlet fever has been recognised as a clinical entity, but, unlike measles and whooping cough, it has not acquired a reputation as a "phthisogenic" disease. In fact it has even been regarded as an infection antagonistic to tuberculosis (Rilliet and Bartet, 1854). The probable explanation is that scarlet fever, is not a disease of infancy but of later childhood, and as the active and fatal forms of tuberculosis occur in the earlier years, there cannot be the same coincidence with scarlet fever as with measles and whooping cough.

II. Tuberculin Allergy in Scarlet Fever.

(a) Review. The interest stimulated by the studies of the tuberculin reaction in measles led to similar investigations in scarlet fever. Rolly (1910), using von Pirquet's test, found that most cases gave a negative response in the eruptive period; in 46 cases he found 8 who were positive in the acute stage as well as in convalescence, and 26 who gave a negative reaction in the acute period but a positive result in convalescence. Moltschanooff (1910) also using the scarification test, obtained similar results; in 43 cases 3
reacted positively throughout, while 17 negative in the acute period were positive in convalescence. He concluded that 85% of positive reactors lost their sensitivity in the acute phase of the disease.

Mitchell (1928), using the intra-dermal technique, records 31 cases, of which 3 reacted both in the rebrile period and in convalescence, while 4 reacted in the convalescent period only. So that with the intra-dermal test 57% of the tuberculin sensitive cases failed to react in the acute stage.

Lereboullet and Baize (1931) mention that in 5 cases of scarlet fever, using the von Pirquet test, they observed no effect on tuberculin reactions.

Those studies so far made have been on small series of cases and although there is evidence of some effect on the tuberculin allergy, no attempt has been made to assess accurately the effect particularly in regard to the possible duration or the period of "anergy". It is of value to know what are the chances of a negative test occurring in scarlet fever, but it is more important to determine for how long after the eruption fallacious results may be obtained.

(b). Personal observations.

Character of the rash of scarlet fever.

The reaction of the susceptible subject to the exo-toxin of the haemolytic streptococcus is character-
The rash itself is an acute inflammation of the skin follicles, showing as minute, bright red, raised punctate papules; the more intense rashes show in addition an erythema between the papules, so that the whole body is covered with the rash and, to quote Sennert's description, "appears as on fire." The rash at its height then is not discrete but confluent; it has a brilliant scarlet colour, in contrast to the red hue of measles. It is relatively short-lived; spreading all over the body within 24 hours, it is often fading in the trunk as it is appearing in the limbs. The most intense rash may persist 4 or 5 days and leave a light yellow staining. It is unusual for a scarlatiniform rash to be haemorrhagic, although with the severe rash there may be

The exanthem of scarlet fever is milder in comparison with that of measles. It is only the most intense scarlet rashes that leave a faint yellow staining, which is to be expected after the milder measles rashes, while the well-marked morbilliform rash commonly leaves petechial staining; a haemorrhagic rash in scarlet fever is unusual, although a few petechiae in the flexures may be found in the more intense types. If the effect in the tuberculin
reaction in measles is due to the action of the rash itself on the skin, one would expect in scarlet fever a milder exanthem, a less marked effect, and the occurrence of negative reactions less frequent.

Observation on 318 cases of Scarlet Fever.

A group of scarlet fever patients of ages varying from 0 - 7 years were investigated during 1931-32, the method adopted being to test the patients in the eruptive stage and thereafter at weekly intervals, during convalescence usually until the fourth week. The results may be tabulated as follows:-

Table I.

<table>
<thead>
<tr>
<th></th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. tested both in acute stage (1st seven days) and in convalescence (2nd week or later)</td>
<td>185</td>
<td>19</td>
<td>204</td>
</tr>
<tr>
<td>No. tested in acute stage only</td>
<td>29</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>&quot; &quot; &quot; convalescent stage only</td>
<td>70</td>
<td>11</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>284</td>
<td>34</td>
<td>318</td>
</tr>
</tbody>
</table>

As a crude indication of some effect on the tuberculin response, one can calculate the percentage of positive reactors in the acute period and in convalescence; in this series 6.5% gave positive tests in the acute stage, while 11.7% reacted in convalescence. This would suggest that probably 44% of the tuberculin-sensitive subjects gave a negative response in the
initial test.

Table II.

Incidence of positive reactions in the acute and convalescent periods.

<table>
<thead>
<tr>
<th>Total No. tested.</th>
<th>Acute period</th>
<th>Convalescence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>214</td>
<td>255</td>
</tr>
<tr>
<td>No. of positive reactions</td>
<td>14</td>
<td>30</td>
</tr>
<tr>
<td>Percentage &quot; &quot;</td>
<td>6.5%</td>
<td>11.7%</td>
</tr>
</tbody>
</table>

Duration of anergic phase in scarlet fever.

9 cases among 23 tuberculin-sensitive subjects gave a negative response when tested during the acute period. The scarlet rash is therefore capable of completely abolishing the response to a tuberculin test using the standard dilution of 1/1000. The distribution of these negative results will indicate the duration of the effect. The following table shows the results classified according to the day of disease on which tests were performed; the actual response in each case is indicated. It will be seen that negative results occurred up to the 10th day, counting the day of the appearance of the rash as the first day of the disease. "R" signifies that the rash was present at the time the test was performed.
Assuming that any case negative on a given day would have negative if tested the previous day, and any case positive on a given day would have reacted positive on subsequent days, the total results can be added together omitting the two delayed reactions and also allowing for identical results in the same patient (whether negative or positive). This summation of the results will then indicate the expected proportion of positive and negative results to be obtained on each day of the disease.

**Table IV.**

<table>
<thead>
<tr>
<th>Day of rash</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total negative.</td>
<td>-</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total positive.</td>
<td>-</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Summation of negative results</td>
<td>-</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Summation of positive results</td>
<td>-</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Expected % negative in each day of the disease</td>
<td>56%</td>
<td>42%</td>
<td>35%</td>
<td>21%</td>
<td>14%</td>
<td>7%</td>
<td>6%</td>
<td>6%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

From this table then it appears that just over 50% of positive reactors would be expected to be
negative on the second day of a scarlet fever rash; the effect is greatest in the first four days, and, like measles, persists well-marked for the first six days. Thereafter the effect passes quickly off. The latest negative test was obtained on the 10th day; the same case on the 19th day gave a ++ 20 mm. response. This marked increase suggests that the initial negative was probably not due to a natural low sensitivity, but rather to the temporary effect of the exanthem. To be certain, then, of excluding a fallacious negative result in scarlet fever the test should be done after the second week.

The effect of the Rash in the occurrence of a Negative Response.

In order to assess the effect of the rash the cases have been classified into two groups - those with mild rashes and those with moderate or intense rashes.

Mild rashes were those not becoming generalised, or, if generalised, faded on the third day. Moderate or intense rashes were those generalised and persisting to the third day or longer.

At the same time it is to be expected that the degree of allergy of the patient will influence the result of a tuberculin test in the eruptive phase. Accordingly, the allergy has been estimated from the response to the test in convalescence. The following table illustrates the distribution of the results when so classified:-
Table V.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Initial test</th>
<th>Allergy</th>
<th>Day of test</th>
<th>Case No.</th>
<th>Initial test</th>
<th>Allergy</th>
<th>Day of test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>+++</td>
<td>25</td>
<td>2</td>
<td>++</td>
<td>+++</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>+++</td>
<td>27</td>
<td>11</td>
<td>+</td>
<td>+++</td>
<td>27</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>++</td>
<td>19</td>
<td>12</td>
<td>+</td>
<td>+++</td>
<td>21</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>+</td>
<td>12</td>
<td>13</td>
<td>(+)</td>
<td>+</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>-</td>
<td>?</td>
<td>13</td>
<td>14</td>
<td>(+)</td>
<td>++</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>(+)</td>
<td>++</td>
<td>10</td>
<td>9</td>
<td>-</td>
<td>+</td>
<td>37</td>
</tr>
<tr>
<td>11</td>
<td>+15</td>
<td>+++</td>
<td>9</td>
<td>23</td>
<td>-</td>
<td>+</td>
<td>37</td>
</tr>
<tr>
<td>18</td>
<td>(+)</td>
<td>?</td>
<td>65</td>
<td>14</td>
<td>+</td>
<td>+++</td>
<td>21</td>
</tr>
<tr>
<td>22</td>
<td>+</td>
<td>++</td>
<td>12</td>
<td>16</td>
<td>+</td>
<td>+++</td>
<td>21</td>
</tr>
</tbody>
</table>

Table VI.

<table>
<thead>
<tr>
<th>Moderate or intense rash.</th>
<th>Mild rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>% Allergy</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
<tr>
<td>Negative</td>
<td>7</td>
</tr>
<tr>
<td>Positive</td>
<td>5</td>
</tr>
</tbody>
</table>

Classified thus according to the character of the rash, 58.3% of the results are negative in the acute phase when the rash is moderate or intense, as compared with only 25% found negative initially when the rash is
a mild one. It might be argued that it had happened that the cases with mild rashes were more highly allergic, but the average degree of allergy as estimated from those cases tested later in the diseases shows practically no difference; in 10 cases in which the rash was moderate or intense, the average degree of allergy was 1.9+; in 5 cases with mild rashes the average was 1.8+, so that the two groups are comparable and therefore the higher incidence of negative results with the more severe rashes can be assumed as due to the different character of the rash; the more intense it is, the more likely is the result to be negative.

**Effect of the Degree of Allergy in the Occurrence of a Negative Response.**

Reference to the tables again show that in both groups the negative results occurred in cases with a lower tuberculin sensitivity than those that gave a positive reaction. This is similar to the results obtained in measles. There are always two factors, the intensity of the rash and the degree of allergy of the patient. Illustrating both factors, the only two negative results in the group with mild rashes had a low degree of allergy - 1+, whereas the intense rashes rendered negative patients with an average sensitivity of 1.8+. 
Delayed Reactions.

One case showed a delay of 48 hours, but has been regarded as an immediate response. Two others showed a delay of 6 days. The tests were made during the maximum period of anergy - the 2nd and 3rd day. In one the delayed response occurred spontaneously, while the other may have been activated by the subsequent test.

Case 19. P.L. act. 6 yrs. was admitted on 7/10/32, having developed a scarlatiniform rash the previous day. The rash was moderate and generalised. On 8/10/32 the rash was still bright and an intradermal test was performed on the right forearm, the rash being present at the site of injection.

Mantoux (rash present - 3rd day), negative till 14/10/32 Erythema of 15 mm. (+) red Mantou (9th day)

(6 days delay)

15/10/32 Stain only + 20
16/10/32 - +++ 15 mm.

In this case the rash was of moderate intensity and the allergy as indicated by the test on the 9th day well marked (++++). This suggests that the association of a rash severe enough to prevent an immediate positive response in a case with a sufficient degree of allergy results in a delayed response at the time the effect of the rash is waning.
Case 20. A boy of 5 years, was admitted to hospital on 7/10/32, having that day developed a scarlet fever rash, following upon the typical symptoms of headache, vomiting and sore throat the previous day. Again the rash was of moderate intensity and was still bright the next day when the first test was performed.

8/10/32 Mantoux test (Rash present: 2nd day) negative.

12/10/32 " Mantoux (6th day)
13/10/32 " + 15 mm.
14/10/32 + 5 mm (6 days delayed) ++ 15 mm.

This case corresponds to the previous one; a moderate rash in a case with less marked allergy caused the initial test on the 2nd day to persist negative; probably because the allergy was less intense a spontaneous reaction on the 6th day failed to appear. However, a second test on the 6th day was followed after 48 hours by an activation of the initial test. Did this second test just sufficiently stimulate the sensitivity to produce the delayed response? The allergy, as indicated by the second test was ++ 15, compared with the +++ 15 of case 19.
c. Conclusions.

There is a definite effect on the tuberculin sensitivity during scarlet fever. Although not so marked as in measles, the scarlet fever rash can completely abolish the positive response in about 50% of cases at the height of the eruption. The effect persists into the second week, and to be certain or avoiding this chance of a false negative result, a tuberculin test should be deferred till the third week.

As in measles, the mechanism of the reaction seems to be due to action of the rash on the skin itself. The individual's own allergic state is an important factor; the greater the sensitivity, the less likely is a negative result to occur.
III. Relation of Tuberculosis to Scarlet Fever.

(a). Review. Choffé (1929), in a study of 178 cases, has found among 66, who were known to have been in contact with tubercle infection, two instances of actual disease ensuing after scarlet fever; one case—a boy of 14 years—developed a tuberculous epididymitis 2½ months after; the other—a child of 6 years—developed a tubercular arthritis of the right knee four months after. The interval in each case is rather long to ascribe the activity as due definitely to the scarlet fever.

Choffé also noted 8 patients with definite tubercular lesions prior to the onset; in 4 the lesions were active. In no instance was any effect noticed following the streptococcal infection. These results are therefore equivocal.

Some recent work on the continent, however, has indicated a relation between the hyper-toxic or malignant type of scarlet fever and tuberculosis. Dumitrescu-Baldowin (1922) quotes 4 cases dying on the 5th to the 8th day, and post-mortem found to have miliary tuberculosis, all the viscera being affected; in addition there were old tubercular foci such as apical cavities in the lungs. These were cases clinically suggesting toxic scarlet fever, yet actually
instances of the streptococcal infection precipitating a miliary tuberculosis.

Millian (1932) in Bucharest, made similar observations. Nine cases aged 2-16 years, all of the toxic type dying on the 3rd-4th day came to autopsy; 6 had miliary tuberculosis: the other 3, although without miliary spread, showed caseous tubercular lymph nodes. Millian finds that over 50% of the fatal cases of scarlet fever have tuberculous foci and such cases provide the early deaths in the "toxic" stage, whereas the cases dying of the complications, such as nephritis and carditis, do not show tubercular foci. Also he finds that in similar age groups the other infectious diseases, such as diphtheria, do not show as high an incidence of tubercular lesions among the fatal cases.

Millian suggests that both the tubercular and the streptococcal toxins have a specific influence on the supra-renal and the liver. When both infections occur together the hypertoxic picture is likely to occur.

(b). Personal Observations.

Effect of tuberculosis on scarlet fever.

Scarlet fever is at present a mild infection in this country; toxic cases are very rare and in the present series, although some of the cases observed had severe attacks, none were actually of the
fatal malignant type. Although the toxic features of the acute phase are mild, the incidence of complications is appreciable. In comparing the incidence of complications it must be remembered that in scarlet fever the disease presents a clinical picture differing according to age. The younger the patient, the more common are the septic complications such as otitis media and late adenitis; they are most common up to 5 years. From 5 to 10 years is the period that nephritis is more liable to ensue, septic complication still occurring, but less commonly, while over 10 rheumatism and carditis are the characteristic complications. The present series of cases tested were chosen from those of 7 years of age or less. This will alter the incidence of complications with a greater frequency of the septic ones.

The following table indicates the incidence of complications in 255 cases not infected by tuberculosis (proved by a tuberculin test performed after the acute stage), and 34 cases with primary tubercle infection:
Table VII.
Complications in Scarlet Fever.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Non-tubercular group</th>
<th>Tubercular group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Total</td>
<td>255</td>
<td>100</td>
</tr>
<tr>
<td>Cervical Adenitis &amp; abscess</td>
<td>22</td>
<td>7.26</td>
</tr>
<tr>
<td>Otitis media</td>
<td>38</td>
<td>13.15</td>
</tr>
<tr>
<td>Mastoiditis</td>
<td>2</td>
<td>0.69</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>46</td>
<td>2.07</td>
</tr>
<tr>
<td>Nephritis</td>
<td>46</td>
<td>2.07</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>6</td>
<td>2.07</td>
</tr>
<tr>
<td>Skin sepsis</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>(impetigo furuncles; onychia)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The high incidence of otitis media in the negative group can be explained on the larger proportion of younger children. The positive cases are necessarily of an average age higher than their controls as the percentage of positive reactors increases with age, so that the 34 positive cases selected from the total 289 children of 7 years or less must have a greater number say over 4 years than under 4 years. On this assumption, the incidence of adenitis should also be less in the older group — the tuberculin reactors —
but actually the proportion is greater, suggesting that this complication is more likely to occur in the tubercular subject. Similarly, although otitis media was not so frequent in the positive cases, mastoiditis was more common - 5.88%, compared with 0.69%; this suggests that, should otitis media arise in scarlet fever, mastoiditis is more likely to ensue in the subject with a previous tubercle infection.

The minor complications such as rhinitis, impetigo furuncles, and onychia show a greater frequency in the tubercular group.

Apart from these septic manifestations, the more serious though less frequent complication of nephritis was only observed in the negative group. There was no mortality in the whole series.

As regards the toxic factor, I obtained no impression that the positive reactors tended to show more toxicity than the controls.

**Effect of scarlet fever on tuberculosis.**

The 34 cases observed were all "latent"; none had focal lesions pre-existing. One case had had a tubercular cervical abscess drained a month prior to her attack; she developed a typical "cold" abscess on the opposite side of the neck in her 6th week but
following closely on the additional complication of measles in the 4th week. In this instance there was more than the streptococcal factor present; there had been activity not long before, and in addition measles complicated her illness at a period when late adenitis is most likely to arise in scarlet fever.

Conclusion.

There is evidence of some relation between scarlet fever and tuberculosis. The tubercle infection appears to favour the invasive properties of the streptococcus suggested by the greater frequency of such complications as late adenitis and mastoiditis. It would seem also from the observations of others that the toxic factor is enhanced when tuberculosis is already existent as cases weakened by tubercle infection have been observed to succumb to scarlet fever with all the features of "malignancy."

Conversely, when there is active focal tuberculosis an acute streptococcal infection may precipitate a miliary spread. The cases I have observed were all "latent", in that they had no clinical evidence of activity and there was no definite evidence of a tendency to activation by the streptococcus scarlatinae.
IV. Summary.

1. In scarlet fever the exanthem has an effect on tuberculin sensitivity sufficient to give rise to a complete negative response in a normally sensitive subject.

2. This "anergy" is most marked in the first week and may persist until the end of the second week, so that if a tuberculin test is to be accepted as reliable in a case with scarlet fever, it should be deferred to the third week.

3. There appears to be a relation between tuberculosis and scarlet fever, both the toxic and septic manifestations being more liable to arise in tubercular subjects.

4. Also in active tuberculosis miliary dissemination may follow quickly after the acute streptococcal infection, but in "latent" infection there is no evidence of activation.
VII. DIPHTHERIA.

I. Introduction............................... 152
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Addendum: Effect of a serum rash on
tuberculin allergy............. 166

III. Relations of Tuberculosis and Diphtheria. 168

IV. Summary. ................................. 169
I. Introduction.

Diphtheria is an acute infectious disease without an exanthem; accepting the deduction made in the study of measles that it is the rash that gives rise to the temporary "anergy" to tuberculin, one would not expect the phenomenon to occur in diphtheria. Nevertheless one finds it stated that the same fallacy exists in diphtheria as in the other acute infections.

IIa. Review. Rolly (1910), using the von Pirquet test on 23 cases found 15 positive in the acute stage; of 8 negative at this period, 2 out of 5 retested in convalescence were positive. The two cases positive only in convalescence Rolly accepted as illustrative of the effect of the diphtheria infection. Moltschanoff (1912) records that of 15 cases negative in the acute stage, two were positive in convalescence; he does not give details of these cases nor suggest any special feature that might correlate the observations with the character of the diphtheria infection. In 14 cases which were positive both in the initial stage and in convalescence, 6 gave stronger reactions, 6 similar reactions and 2 weaker reactions on the second test. This does not suggest any effect on the tuberculin sensivity during diphtheria, although it is apparent that an initial negative response may be
obtained in allergic subjects in an appreciable proportion of cases. Did they occur in the severe cases? Were they associated with severe rashes? Neither author suggests such a cause; Moltschanozoff found one reaction delayed 4 days (the positive response) appearing as an intense serum rash was waning.

Mitchell and his co-workers (1928) in 58 cases of diphtheria found that 8 reacted positive in the febrile period, while 4 more reacted in convalescence - a total of 12, representing an increase from 13.7% to 25%. Again, details of the cases are not given nor any suggestion made to explain the 4 cases negative in the first test. They are assumed to be due to the diphtheria infection.

IIb. Observations on 218 cases of Diphtheria.

A group of cases of diphtheria have been studied in the age period 0-7 years; tuberculin tests were made in the acute stage and in convalescence. When a strong response was obtained in the acute stage, the test was not repeated to avoid unnecessary stains on the patients' skin, as the important fact to determine was whether an actual negative result might occur in tubercular subject during diphtheria.

The following table summarises the cases tested:-
I find no appreciable difference between the percentage of reactions in the acute period and in convalescence. The cases tested on one occasion only have been divided into two groups - those tested in the first two weeks and those tested after the second week. The following table shows that there is a difference of less than 1%; age groups being comparable, this excludes any gross effect on tuberculin sensitivity in the acute period of diphtheria.

Table II.

<table>
<thead>
<tr>
<th></th>
<th>Acute period</th>
<th>Convalescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases tested</td>
<td>188</td>
<td>152</td>
</tr>
<tr>
<td>Number of positive reactions</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>Percentage of positive reactions</td>
<td>14.3%</td>
<td>13.8%</td>
</tr>
</tbody>
</table>
The above table includes the cases tested on one occasion only; only those patients who were tested both in the acute stage and convalescence will demonstrate whether a negative response may be obtained in the patient normally sensitive to tuberculin. Table I shows that 122 patients were so tested of whom 18 were found to give a positive reaction; in only one case was the test in the acute stage negative. This is an error of 5.5% and seems considerable enough. As it was the exception it will be of value to describe this case in detail to discover if it shows any unusual features.

One case (of 18 positive reactions) which gave an initial negative response.

Case No. 6. C.B., a boy aet. 8 yrs.

**History.** - On 9/12/31 he complained of a sore throat and headache. On 11/12/31 vomiting occurred. On admission on 14/12/31 he showed small deposits of membrane on the upper pole of each tonsil; a culture from the tonsils yielded diphtheria bacilli. There was no adenitis; no nasal discharge; as a mild case of diphtheria he was given 16,000 units of serum. He was afebrile throughout and no complications arose.

On 15/12/31 a tuberculin test was performed. (6th day from the onset of symptoms) - negative.
On 20/12/31 a generalised serum rash of urticarial type appeared; it faded in 24 hrs.

On 14/1/32 tuberculin test (36th day) - was negative until 25/1/32, when a delayed response of + 10 mm appeared - 11 days delayed.

On 25/1/32 Third test performed (47th day) immediate positive response ++ 17 mm (24 hrs).

The boy was afebrile throughout; the attack of diphtheria was mild; he had had no rash immediately prior to the initial test on the 6th day which was completely negative. He had a serum rash subsequently, but the second test was performed 25 days after, so that the delayed response cannot be ascribed to this rash as Gase 34 shows that a serum rash has a very slight effect on the tuberculin test. Was this child in the process of acquiring a tuberculin sensitivity, or did it require the stimulation of two injections to raise his allergy to the reaction threshold? If it had been due to the diphtheria one would expect it to have been a severe attack instead of a mild one; in contrast, severe cases of diphtheria gave a frank positive result in the acute stage.

The second test on the 36th day of the disease was markedly delayed (11 days); in measles - the disease with most effect on the tuberculin sensitivity - I found delayed reactions commonly occurred, but usually
when performed in the first week - the period of maximum "anergy". Yet in this case of diphtheria the delayed reaction was obtained in the 6th week of the disease - long after one would expect any effect even in measles.

As the other cases of diphtheria studied showed no great alteration in tuberculin sensitivity, this case must be regarded as one in which the initial negative response and, later, the delayed positive result were due to factors other than the diphtheria infection. This was probably a case whose tuberculin sensitivity had waned below the reaction threshold, and it required the stimulation of two tuberculin tests before an immediate response was obtained.

If the boy had been in the process of acquiring sensitivity for the first time, one would have expected a history of recent contact with tubercle infection, but on careful enquiry there was no knowledge of his having been in contact either just preceding his illness or in his earlier years. There was no tuberculosis in the family, so that probably he had acquired a slight incidental tubercle infection from milk or temporary human contact.

The other 17 cases gave a positive result to the first test; in one - a case of nasal diptheria - it was a delayed response. The clinical history of the case was as follows:-
Case 26. A boy of 4 yrs. was noted to have a nasal discharge on 14/3/32.

On 17/3/32 he was admitted to hospital with a characteristic rhinitis - thin watery nasal discharge exuding the nares; there was no faucial inflammation; the submaxillary glands were slightly enlarged. There was no toxaemia, the boy being quite comfortable and bright, without symptoms or fever. Diphtheria bacilli were isolated from the nasal swab.

On 18/3/32 the nasal discharge had ceased.

Tuberculin test (5th day) showed no response till 6/4/32, when a papule of 10 mm. appeared + 10 mm. (19 days delay). Tuberculin test on this date - 24th day - gave an immediate response of +++ 18 mm.; erythema 27 mm. (24 hrs.)

The nasal infection was so mild that one cannot suppose it could have any effect on the production of a delayed response. I class this case as one in which the stimulation of the injection of a minute amount of tuberculin was necessary before the response appeared; 19 days later the sensitized cells at the site of injection reacted in the usual characteristic way.
Comparison of the degree of response in cases tested in the acute and convalescent stages of diphtheria.

If there were any great effect on the tuberculin sensitivity during the acute period, one would expect that on the average the degree of response obtained at this stage would be less than that found in convalescence. To make this comparison we must exclude all but initial tests, so that the fallacy of a stimulated sensitivity from a previous test is excluded. In the following table cases which were tested on one occasion only are classified according to whether the test was performed in the first week or later.

Table III.

Cases tested only in the acute stage.

<table>
<thead>
<tr>
<th>Case</th>
<th>Day of disease</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>3</td>
<td>+++ 20 mm</td>
</tr>
<tr>
<td>17</td>
<td>3</td>
<td>++ 20 E 30</td>
</tr>
<tr>
<td>18</td>
<td>5</td>
<td>+ 15</td>
</tr>
<tr>
<td>23</td>
<td>7</td>
<td>+ 15 E 30</td>
</tr>
<tr>
<td>24</td>
<td>6</td>
<td>+++ 18 E 35</td>
</tr>
<tr>
<td>27</td>
<td>7</td>
<td>+++ 20</td>
</tr>
<tr>
<td>29</td>
<td>7</td>
<td>++ 20 mm</td>
</tr>
</tbody>
</table>

Cases tested only after the acute stage.

<table>
<thead>
<tr>
<th>Case</th>
<th>Day of disease</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>47</td>
<td>+++ 18 E 17</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>+++ 20 E 20</td>
</tr>
<tr>
<td>13</td>
<td>9</td>
<td>++ 15</td>
</tr>
<tr>
<td>14</td>
<td>18</td>
<td>+ 15</td>
</tr>
<tr>
<td>21</td>
<td>32</td>
<td>+ 10</td>
</tr>
<tr>
<td>22</td>
<td>32</td>
<td>++ 15 E 25</td>
</tr>
<tr>
<td>26</td>
<td>35</td>
<td>+++ 15 E 35</td>
</tr>
<tr>
<td>28</td>
<td>14</td>
<td>+++ 18 mm. E 22</td>
</tr>
</tbody>
</table>
Comparison of the two groups shows that there is no difference in the degree of allergy; those in the acute group show no tendency to a lower degree of sensitivity than the convalescent group.

The distribution of allergy is practically identical

<table>
<thead>
<tr>
<th>Table IV.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy</td>
</tr>
<tr>
<td>Numbers in &quot;acute&quot; group</td>
</tr>
<tr>
<td>&quot;convalescent&quot; group</td>
</tr>
</tbody>
</table>

These cases then, although rather few in number, are strictly comparable in regard to the degree of tubercular sensitivity, and suggest no depressing effect during the acute period of diphtheria.

The other cases, which were tested both in the first week and also later in the disease, show an increased response to the second test in almost all cases - a result to be expected normally. There is no suggestion in this series that the increase in response to the second test was greater than usual.
### Table V.

Comparison of degree of response in cases tested both in the acute and convalescent stages of diphtheria.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day of disease</th>
<th>Response</th>
<th>Day of disease</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>++15</td>
<td>21</td>
<td>++15 E 30</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>+++15 E 7</td>
<td>20</td>
<td>++15 E 10</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>++15</td>
<td>30</td>
<td>++15 E 10</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>+15</td>
<td>12</td>
<td>+15 E 10</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>+++20 E 10</td>
<td>46</td>
<td>++20 E 10</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>++16</td>
<td>25</td>
<td>++16</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>++17</td>
<td>34</td>
<td>++20 E 10</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td>+12</td>
<td>72</td>
<td>++16 E 14</td>
</tr>
<tr>
<td>15</td>
<td>6</td>
<td>+20</td>
<td>49</td>
<td>++20</td>
</tr>
<tr>
<td>16</td>
<td>3</td>
<td>++15</td>
<td>20</td>
<td>++18 E 12</td>
</tr>
<tr>
<td>19</td>
<td>4</td>
<td>++18 E 17</td>
<td>32</td>
<td>++20 E 25</td>
</tr>
<tr>
<td>20</td>
<td>3</td>
<td>+17</td>
<td>32</td>
<td>++15 E 45</td>
</tr>
<tr>
<td>26</td>
<td>5</td>
<td>+10 (delayed 19 days)</td>
<td>25</td>
<td>++18 E 27</td>
</tr>
<tr>
<td>30</td>
<td>5</td>
<td>+14</td>
<td>58</td>
<td>+++14</td>
</tr>
<tr>
<td>31</td>
<td>5</td>
<td>+12</td>
<td>8</td>
<td>+10</td>
</tr>
<tr>
<td>32</td>
<td>6</td>
<td>+15</td>
<td>33</td>
<td>+10</td>
</tr>
<tr>
<td>33</td>
<td>4</td>
<td>+15</td>
<td>27</td>
<td>++15 E 17</td>
</tr>
</tbody>
</table>

Case 31 was one of tubercular meningitis complicated by nasal diphtheria; it can be excluded as some decline in sensitivity is recognised in this form of tubercular infection.
OBservations on cases whose tuberculin sensitivity was known prior to the onset of diphtheria.

So far one has been unable to demonstrate from the statistical results any effect on tuberculin sensitivity. The most accurate estimate of such an effect would be obtained by observing the reactions during diphtheria in a case whose degree of reactivity was already known. I have been able to observe two cases in this way.

(1) Case 33 (No. 15 in measles series) A.C. a girl of 6 years admitted on 9/1/32 suffering from measles, developed a severe attack of faucal diphtheria in the third week just following an acute cervical abscess.

11/1/32 Tuberculin test (3rd day of measles) - negative.

20/1/32. Tuberculin test (12th day of measles)
   + 15 mm. (24 hrs.)
   + 15 mm. (48 hrs.)

21/1/32 Onset of submaxillary adenitis (left) which suppurated.

29/1/32 The abscess was incised and drained; on this date the child had no evidence of diphtheria infection.

2/2/32. Having had no symptoms she was found to have extensive membrane covering the tonsils and faucal pillars extending on to the soft palate; a culture of the throat was positive. Presuming that the diphtheria infection was in its third day a tuberculin test on 3/2/33 would be the 4th day of disease.
3/2/32 Tuberculin test (26th day of measles; 4th day of diphtheria) + 15 mm. (24 hrs.)
+ 15 mm (48 hrs.)

25/2/32 Tuberculin test (26th day of diphtheria) + + 13 mm; erythema 17 mm. (24 hrs.)
+ + 13 mm; (48 hrs.)

The unusual feature in this case is that the expected increase in the response to the test made on 3/2/32 did not occur; the reaction was identical with the previous one. The test was made on the 4th day of a severe attack of faucial diphtheria. A subsequent test made three weeks later showed an increase in the degree of response. This case therefore suggests that severe diphtheritic infection there is a slight depressing influence on the tuberculin sensitivity.

(2) Case 34; B.B. a boy of 5 years.

17/6/32. Admitted suffering from whooping cough complicated by broncho-pneumonia.
18/6/32 Tuberculin test. Temp. 102.
19/6/32 Negative; Temp. 99.
20/6/32 " " 99.
24/7/32. **Tuberculin test - positive**

- ++12 mm; erythema 18 mm.  
- ++12 mm.

(24 hrs.)

(48 " ")

18/8/32 he complained of sore throat; his temperature was 102°; the tonsils and faucæ were congested and there was follicular deposit on the right side and the regional glands enlarged.

On 19/8/32 there was a definite plaque of membrane covering the right tonsil encroaching on the anterior faucial pillar; the submaxillary glands on that side were enlarged; the throat culture was positive.

**Tuberculin test. (2nd day of diphtheria)**

- ++ 20 mm. (24 hrs.)
- ++ 20 mm. (48 hrs.)

Temp. 102°

" 98

" 97.8

Recovery was straightforward.

**DISCUSSION.** The initial negative response in this case was probably due to the pneumonia. A straight positive result was obtained five weeks later, there being a 24 hrs. response of ++ 12 mm.

Four weeks after he developed a moderate attack of faucial diphtheria; on the second day of the diphtheria infection a tuberculin test gave a positive
result; in 24 hours it was +20mm. less intense but of greater size than the previous one; in 48 hrs. however it was ++20 mm. equal in intensity to the former one. The expected result would have been one of greater intensity; instead it was of the same intensity but 24 hours slower in reaching its maximum. There was therefore a slight depressing effect during the attack of diphtheria.

II. CONCLUSION.

Although the statistical results in this series do not suggest any effect on the tuberculin sensitivity the observation made on two individual cases whose degree of response to tuberculin was already known prior to the onset of diphtheria demonstrate that in moderate or severe infection there is a slight effect. The influence on the test is so small that it is unlikely to create the fallacy of a negative test in the sensitised subject.

Out of 18 patients proved tuberculin sensitive only one gave a negative result initially but critical examination of this case reveals no evidence that this was due to the diphtheria. It is probable that the similar cases quoted by Rolly and Moltschenoff were examples of what I regard as subjects whose tuberculin allergy has diminished and fallen below the reaction level.
**ADDENDUM.**

**EFFECT OF A SERUM RASH ON TUBERCULIN ALLERGY.**

The usual serum rash is urticarial and transient only lasting 24 hours as a rule; it does not leave staining like a measles rash or a severe scarlet fever eruption. It is therefore unlikely to have a great effect on the tuberculin reaction.

I tested one case at the height of an intense serum rash of punctate erythematous type.

**CASE 32.**

25/2/32 Tuberculin test (right arm): Control (left arm)

<table>
<thead>
<tr>
<th>Time</th>
<th>Right Thigh</th>
<th>Right Arm</th>
<th>Control (Left Arm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 hrs.</td>
<td>11mm.</td>
<td>+ 15mm.</td>
<td>nil</td>
</tr>
</tbody>
</table>

4/5/32. Serum rash of scarlatiniform type; punctate on trunk but an intense erythema on right thigh - the site of the serum injection; also there was a 20mm. erythema at the site of the previous tuberculin test, but none at the control.

<table>
<thead>
<tr>
<th>Test Date</th>
<th>Right Thigh</th>
<th>Right Arm</th>
<th>Control (Left Arm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/5/32</td>
<td>10mm.</td>
<td>+ 20mm.</td>
<td>&quot;</td>
</tr>
<tr>
<td></td>
<td>(24 hrs.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/5/32</td>
<td>+ 11mm.</td>
<td>++ 15mm.</td>
<td>&quot;</td>
</tr>
<tr>
<td>(48 hrs.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17/5/32</td>
<td>+ 16mm.</td>
<td>4mm.</td>
<td>(24 hrs.)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Date</th>
<th>Right Thigh (Same Site)</th>
<th>Left Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/5/32</td>
<td>+ 18mm. erythema 4mm.</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION. This case showed a slight weakening of the tuberculin reaction during the serum rash which was of intense character. The reaction on the thigh is best compared with the subsequent test also made on the thigh at the same site. The 24 hour readings show a difference in degree and size but not sufficiently marked to suggest any great effect. The test on the right arm during the rash was slower in achieving the same intensity as the previous test on the arm. This definitely signifies some depressing effect on the reaction; usually it would be certainly as intense in 24 hours if not more marked.

This case therefore suggests that a serum rash has only a slight effect on tuberculin sensitivity not sufficient to give rise to an appreciable fallacy.
III. RELATION OF TUBERCULOSIS TO DIPHTHERIA.

It is not usually claimed that there is any specific relation between the two diseases. The diphtheria bacillus is not an invasive organism like the streptococcus and septic complications are not common.

In 188 cases found negative to tuberculin Otitis Media was the commonest septic complication occurring in 15 cases, in 6 of whom it was bilateral. In the 32 cases found with positive tuberculin reaction there were 3 cases of Otitis Media; all were bilateral, whereas less than half the negative group were bilateral. The incidence was similar in both groups.

Late cervical adenitis occurred in 5 of the 188 negative subjects; none occurred in the 32 positive reactions. In the whole series there was no instance of an active tubercular manifestation during the acute stage or immediate convalescence of diphtheria.

**TABLE VI. INCIDENCE OF SEPTIC COMPLICATIONS.**

<table>
<thead>
<tr>
<th></th>
<th>Negative cases</th>
<th>Positive cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Total</td>
<td>188</td>
<td>-</td>
</tr>
<tr>
<td>Otitis Media</td>
<td>15</td>
<td>7.9%</td>
</tr>
<tr>
<td>Late adenitis</td>
<td>5</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

Although it is suggested that tubercle infection can play a part in the production of the toxic fea-
features of scarlet fever (Millien, 1932) there is no evidence that the tubercular child is more susceptible to the toxin of diphtheria. I obtained no impression of any greater toxicity in the tubercular Group.

IV.

DIPHTHERIA SUMMARY.

1. In only one case out of 18 tuberculin sensitive subjects was an initial tuberculin test found negative; that case was exceptional and the negative test could not be ascribed to the diphtheria infection.
2. Although diphtheria does not entirely suppress tubercular allergy there is evidence that it has a slight but negligible weakening effect. It is not sufficient to render the test fallacious.
3. A serum rash has only a slight influence on the tuberculin reaction.
4. In the 34 cases of tubercular infection all "latent" in that there was no clinical evidence of active visceral lesions, diphtheria did not give rise to any immediate activation.
5. In the incidence of the septic complications of diphtheria such as Otitis media there was no appreciable difference between infected and non-infected children.
CHAPTER VIII.

GENERAL CONCLUSIONS AND SUMMARY.

I. Tubercular Allergy in Acute Infectious Diseases. 171
   Mechanism of Temporary Anergy. ............... 175
   The value of Repeated Tests. ................. 176

II. Tuberculosis in Relation to Acute Infectious Diseases. .................. 178

III. Summary and Conclusions. ................. 185
This investigation concerns the relation of tuberculosis to the common acute infectious diseases: Measles, Whooping Cough, Scarlet fever and diphtheria. During the period from November 1930 to January 1933 over 1800 cases admitted to the Park Hospital, London, have been studied, using the intra-dermal tuberculin test.

As the positive tuberculin reaction is only of real significance in the younger child the cases were selected from the age period 0 to 7 years, but including the few exceptions over that age in measles and whooping cough.

I. TUBERCULIN ALLERGY IN ACUTE INFECTIONOUS DISEASES.

In addition to the four diseases I have investigated some effect on tuberculin sensitivity has been recorded in most of the acute infections including typhoid fever, lobar and broncho-pneumonia (McNeil, 1909; Feisseu and Tixier, 1909; Rolly, 1910; Cavel, 1912; Jousset, 1926); erysepeles (Rolly, 1910; ) and Chickenpox (Schonfield, 1924; Cozzlino, 1925). Although it has been found that in these diseases there may be an effect sufficient to suppress the reaction to tuberculin it is a feature of the acute stage only not persisting long enough to constitute a serious fallacy.
In 901 cases of measles I was able to observe the effect on allergy in 50 tuberculin-sensitive patients. There is a depression of sensitivity beginning as the rash appears and at its maximum from the second to the fourth day; 60 to 75% of the allergic subjects lose their reaction completely during the period. Sensitivity returns in all but exceptional cases by the 7th day.

The longest period during which a patient remained completely insensitive was 10 days. Therefore to be certain of avoiding a fallacious negative result in measles a tuberculin test should be deferred till the third week.
SCARLET FEVER.

In scarlet fever there is a similar but less marked effect on tuberculin allergy. In 34 cases with a sensitivity to tuberculin there was evidence of temporary depression of allergy during the eruptive period but no more than 50% would be expected to fail to react to the intra-dermal test when the rash was at its height. As in measles the effect is of short duration sensitivity being regained as a rule by the end of the first week.

In only one case which had an average sensitivity the reaction persisted negative into the second week, therefore to be certain of a reliable response in scarlet fever a tuberculin test should be postponed until the third week.

DIPHTHERIA. In 50 cases of diphtheris sensitive to tuberculin I was unable to demonstrate an effect on allergy sufficient to suppress the reaction completely. In one severe case there was a slight weakening manifest only by the fact that the usual increased response to a second test failed to occur, when the patient was in the acute stage of the diphtheria infection.
WHOOPING COUGH  In whooping cough there is no appreciable effect on tuberculin allergy. I was unable to observe the effect on a child whose degree of sensitivity was already known but in 32 cases tested among their attack there was no evidence of any effect analyzing the results from various points of view; (1) comparing the percentage incidence in the acute stage with that found in convalescence; (2) the average degree of allergy found at various stages of the illness; and (3) the increase in the reaction to second tests. A complication such as pneumonia may affect the reaction. Using the Von Pirquet test an effect on sensitivity has been observed but usually a secondary infection has been present or there has been acute tuberculosis as well in which case the scarification test with the ordinary technique may fail.
MECHANISM OF THE TEMPORARY AENERGY.

In the four diseases studied only those with an exanthem - measles and scarlet fever had an appreciable effect on tuberculin allergy. The evidence of this investigation favours the view of Rolly (1910) Cozzolino (1918) and Debré (1927), that the depression of sensitivity is due to the action of the rash itself on the skin. For example in measles the reaction is not lost until the rash is established although the disease is then in its 4th or 5th day. If it were a systemic effect one would expect it to be manifest from the onset. It may be said that whichever reaches the skin first - the tuberculin or the measles toxin - will produce its characteristic response. Once the rash has appeared the result of a tuberculin test then depends on two opposing factors - the intensity of the rash and the degree of sensitivity. The more intense the rash the more likely is the test to be negative and conversely the greater the sensitivity the more probable is the reaction to be positive. A delayed reaction represents a balance between the two factors - rash and allergy.
THE VALUE OF REPEATED TESTS

There is a source of error in the tuberculin test probably more important than the effect of the exanthemata especially as there is no indication when this fallacy is present. In Whooping Cough and diphtheria I found cases negative to the first test yet subsequently positive when the test was repeated in the same dilution a week or a fortnight later. In those cases there was no evidence that the acute infection was responsible for the initial failure to react.

It is recognized that the injection of the small amount of tuberculin of a first test stimulates sensitivity and that second tests repeated within a few weeks are always more intense. Debret (1927) considered the maximum period of enhanced allergy was 7 to 12 days after. Hart (1932) found that sensitivity decreased for the few days just after the first test followed by an increase or supersensitization. This effect lasts for 3 to 4 weeks at least. In those negative to the initial test it is probable that this sensitivity had faded below the reaction threshold and the stimulation of the first test was sufficient to give a positive result to the second. To be certain therefore of
excluding tuberculosis the test should be repeated at an interval of a week or a fortnight. I prefer to use the same dilution – 1.10° rather than a stronger solution thus avoiding the chance of a pseudo-reaction. (See Chapter III.)
The original intention in starting this investigation was to determine the duration of the active phase if any in each disease after which the tuberculin test would be applied after this period had passed and the "bad risks" - the tuberculin positive reactions discovered.

### MEASLES

<table>
<thead>
<tr>
<th>CASE</th>
<th>MORTALITY.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All ages</td>
</tr>
<tr>
<td></td>
<td>All causes only</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>901</td>
</tr>
<tr>
<td>Positive reactions</td>
<td>51</td>
</tr>
</tbody>
</table>

In 901 cases of measles 51 had positive tuberculin reactions and there was no instance of an active manifestation ensuing except in those two which proved fatal. The two children that died of tuberculosis were both under 2 years; one had whooping cough prior to the onset of a modified attack of measles; the other died 3 months after at the age of 9 months from tubercular meningitis. In both cases therefore there was no evidence that the measles had any particular effect on the ultimate fatal
issue. Eleven children under 2 had positive reactions; the mortality for this group of 16.18% below the average of 55% (see Chap. II). Those cases however were not in contact with infection at the time of their attack so that the figure might be regarded as high compared with that of 8% and 4.5% quoted by Walquist and Myers (1926) and Lemaire (1925) respectively for tubercular infants segregated from infection.

**TUBERCULOSIS AS A SEQUEL OF MEASLES.** Apart from the case of tubercular meningitis already mentioned I found no instance of a tubercular manifestation arising subsequent to measles over a period of 3 to 14 months in 189 cases of whom 31 had positive tuberculin reactions.

The tubercular child is apparently not greatly jeopardised as regards the danger of activation of the tubercle infection. Is there a greater danger of secondary complications?

My results suggest the converse in the younger child with measles: it appears less susceptible to pulmonary complications. On the other hand the older patients appear more liable to pyogenic infection both focal and systemic, analogous to the re-
results of Millikan (1932) and Dunitrescu-Baldwin (1922) in scarlet fever.

WHOOPING COUGH

<table>
<thead>
<tr>
<th>CASE MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>All ages</td>
</tr>
<tr>
<td>0 - 2 years</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Total All causes</td>
</tr>
<tr>
<td>T.B. only</td>
</tr>
<tr>
<td>All causes</td>
</tr>
<tr>
<td>T.B. only</td>
</tr>
</tbody>
</table>

The case mortality from tuberculosis was 0.74%, a figure comparable to the results in the larger series of Koenigsberger and Fuerst and Meyer and Burgard. It does not suggest that tuberculosis is a serious factor in mortality from whooping cough. In regard to the age incidence, the three deaths from tuberculosis were in children aged 1 - 2 years, of whom a total of 7 with positive reactions were observed - a mortality of 42.8% which is higher than that in measles.

Koenigsberger and Fuerst found a mortality of 7.0% in 13 cases in this age period. This figure is higher than the average in uncomplicated tubercle-infection and much higher than the figure of 8% and 4.5% in segregated cases of tubercle infection.

COMPLICATIONS. Apart from the three fatal cases
there was no instance of a tubercular manifestation arising during or subsequent to the whooping cough. The tubercular children showed a greater susceptibility to the minor secondary complications such as Otitis Media but there was no evidence of an increased liability to pulmonary complications.

**SCARLET FEVER.**

In 289 cases 34 with positive reactions were observed. The positive reactors showed a greater susceptibility to the later septic complications particularly adenitis; in one case a "cold" abscess developed the only actual tubercular manifestation observed.

Although Otitis Media was not more common in the tubercular children, mastoiditis was a more frequent complication.

The minor complications such as rhinitis impetigo; etc. were more frequent in tubercular children.

In diphtheria I found no evidence of any relation between the two infected.
DISCUSSION. The belief in the specific relation of tuberculosis to measles and whooping cough appears to have arisen in the period when tuberculosis was a clinical syndrome - "phthisis" - a prolonged pneumonia accompanied by wasting, hectic fever, cough and expectoration. This picture of tuberculosis in adults also describes the protracted type of broncho-pneumonia in infants so common in measles and whooping cough and without a knowledge of the pathology this condition was probably diagnosed as "phthisis".

The term applied to measles and whooping cough was "phthisogenic" and in the description of tuberculosis following measles or whooping cough - the earlier physicians did not describe meningitis - the usual active form in infants - but a pneumonia (vide introduction to Chap. IV.).

As tubercular meningitis is the usual manifestation of active tuberculosis in children under 5 accounting for at least 50% of the deaths it is a reliable index of the incidence. One method of demonstrating the alleged effect of measles and whooping cough in causing an exacerbation of tubercle infection would be to show that the active manifestations increase after an epidemic of measles and
whooping cough.

Analysing the incidence of tubercular meningitis it has been found to bear no relation to epidemics of measles (Beisen 1925) nor does tubercular meningitis precede measles and whooping cough in such frequency to suggest a specific relation between the infections. (Noeggerath and Eckstein - 1924; Cremieu-Alcan, 1926)

The sum of the evidence is in favour of the view that measles is not really "la maladie tuberculissante"; it is to be realised that the disease is the commonest of acute infections; very few children escape it and it attacks the child usually in the first 3 years the period when tubercle infection is active and liable to prove fatal so that the coincidence must be no unusual. Whooping cough, however, by its general effect as a prolonged exhausting illness appears to have an unfavourable effect.
POLICY.

It was originally thought that one might select positive reactors as suitable cases for convalescent treatment to obviate the tendency to activation of the latent T.B. infection but the investigation has shown rather surprisingly that the majority of cases make straightforward recoveries even when returning to home surroundings straight from the hospital. Such cases as did develop active tuberculosis were cases to be suspect of activity either by age or clinical evidence and the result was what might be expected even without the added complications of an acute infection.

It would seem therefore that a policy of selecting positive reactors for special convalescent care is unnecessary provided that it is ascertained that the child is returning to a non-infected atmosphere.

The ultimate hope is that tuberculin tests will rank with the Schick and Dick tests as a routine procedure in the Child Welfare and School Clinic; the positive reactor when found can then be put in a position of safety under the special care of the tuberculosis clinic.
In conclusion the findings of this study may be summarised by answering the four questions set out in the introduction:

(1) **To what extent may the intradermal tuberculin test be fallacious in acute infectious diseases?**

The intradermal tuberculin test in the standard dilution of 1-1,000 C.T. is fallacious to a small extent in those diseases with an exanthem - measles and scarlet fever.

The effect is of short duration only rarely persisting into the second week. Any possibility of a false negative result can be avoided by testing patients after the second week.

(2) **What is the value of the test in these diseases?**

As there is no particular danger to the tubercular subject with an acute infectious disease the routine use of the test is not warranted. In children under 2 years will be of value in diagnosis and prognosis particularly in whooping cough when a “fetal” efflorescence of the infection may occur.

What is the prognosis for the tubercular child suffering from an acute infectious disease?

The tubercular child has as good a prognosis as the non-infected subject in regard to the acute
infection itself.

Of course, the infected child under 2 years still has the grave prognosis associated with the tuberculosis: in measles and whooping cough there is no evidence that there is a special tendency to activation.

Whooping cough the more prolonged disease by affecting the general condition has probably a greater effect than measles, but in both diseases there is no evidence of any specific effect.

Is special after care necessary for such children? No. Any child under 5 with a positive tuberculin reaction requires at least observation to ensure it is not in further contact. Such a child if it develop measles or whooping cough should have hospital treatment and be nursed though its illness in non-infected hygienic surroundings. Afterwards there is no need for that child to have any special after care as long as it continues protected from further contact with tuberculosis.
I began this investigation a disciple of the faith that the "energising" diseases particularly measles were an especial danger to the tubercular child; I complete the study a sceptic.

FINIS.
APPENDIX I.

Delayed Reactions.
Examples of Delayed Positive Reactions.

Case No. 20. D.B.

7/12/31 morbilliform rash appeared on trunk.
8/12/31 now generalised, bright, or moderate intensity.

<table>
<thead>
<tr>
<th>Day of rash</th>
<th>Tuberculin test (rash at site of injection)</th>
<th>Tuberculin test (+)</th>
<th>Tuberculin test (++)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>nil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-20</td>
<td>15 mm+ (17th day after test)</td>
<td></td>
<td>++ 20 mm.</td>
</tr>
<tr>
<td>21</td>
<td>positive response. 15 mm+ (17th day after test)</td>
<td></td>
<td>++ 20 mm.</td>
</tr>
<tr>
<td>22</td>
<td>14 mm+ (18th day after test)</td>
<td></td>
<td>++ 20 mm.</td>
</tr>
<tr>
<td>23</td>
<td>photographed</td>
<td>++ 20 mm.</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>stain or 12 mm.</td>
<td>++ 20 mm.</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>15 mm+ (+)</td>
<td>++ 20 mm.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erythema 15 mm.</td>
<td>++ 20 mm.</td>
<td></td>
</tr>
</tbody>
</table>

In this case, the initial test performed on the 4th day of the rash with the exanthem still bright at the site of injection did not show a positive response until 17 days later; an immediate response was obtained from the second test on the 23rd day of the rash.
Case No. 20. D.B. Photograph taken on 29/12/31 - 23rd day of measles rash. Right arm shows delayed positive response 19th day after test (now 72 hours old). Left arm shows immediate positive response 24 hours after test.

Case No. 22. D.C.
On 12/2/32 appeared a bright morbilliform rash on the face and trunk. Temperature 101.5°
13/2/32 - the rash now generalised and intense; Temperature 102°
14/2/32 - the rash still intense and generalised.
Day of rash.

3 Tuberculin test - rash at site.

4 Erythema only - 7 mm. (+)

5 Faint erythema just - Tuberculin test staining present 7 mm (+) Temp. normal et seq.

6 nil. -------------- Faint erythema 10 mm. (+)

7 nil. -------------- 11 mm. ++

8-9-10 nil. ---------- Fading.

10 14 mm. ++ - a 24 ---- 11 mm. +-- Tuberculin test hrs. appearance.

12 10 mm. + 48-56 hrs. appearance. ---- 5 mm. pink stain ----- ++15 mm.

13 ___________________ ++15 mm.

14-15-16-17

18 8 mm. + --------- 8 mm. + -- 10 mm. purple stain. Looks oldest test.

25 7 mm. purple stain. 8 mm. seal- 10 mm. seal- ing stain. ing stain.

In this case there was an immediate response to the test on the third day but so weak as to be classed for practical purposes as negative; a true response was delayed for 8 days. On the 5th day, when the rash had faded leaving marked but not petechial staining, the second test gave a true response in 48
hours but did not activate the primary test as might be expected.

The second test also revived to a slight extent on the 11th day, showing that this phenomenon depends on some change in the patient not related to the date of the tuberculin test; i.e. that any test performed in the first 5 days of the disease would have shown its maximum response or a re-activation on the 11th day. The temperature was normal on the 5th day. The rash then appears to be the factor determining the phenomenon. On the 18th day the most recent test appeared, the oldest, being a stain only, while the others retained some infiltration.

Case No. 26. B.A.

7/11/31 - morbilliform rash appeared on face and trunk.
8/11/31 - rash became generalised.
9/11/31 - rash still bright. Temp. 100°. Tuberculin test (1/100 dilution).

Day of disease

<table>
<thead>
<tr>
<th>Date</th>
<th>Tuberculin test (rash at site)</th>
<th>Temp.</th>
<th>Tuberculin test (1/1000 dilution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>nil.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-12</td>
<td>nil.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>15 mm + (red)</td>
<td></td>
<td>15 mm + (red)</td>
</tr>
<tr>
<td>14</td>
<td>15 mm. (fading purplish)</td>
<td></td>
<td>15 mm. (fading purplish)</td>
</tr>
<tr>
<td>15</td>
<td>no change</td>
<td></td>
<td>no change</td>
</tr>
<tr>
<td>16</td>
<td>dull red stain</td>
<td></td>
<td>dull red stain</td>
</tr>
<tr>
<td>18</td>
<td>fading stain</td>
<td></td>
<td>fading stain</td>
</tr>
</tbody>
</table>

Still a red papule = +
In this case the initial test was delayed 10 days. The rash was of moderate intensity and the degree of allergy as indicated by the immediate response to the second test was also moderate. There was no relation to the temperature.
Case No. 26. B.A. Photograph taken on 22/11/31 showing:

(1) on left arm delayed response (now 13 days from date of test and itself in its 4th day);

(2) on right arm the normal immediate response of the test performed three days previously.

The morbilliform staining on the skin is just visible. The oedema of the immediate response on the right arm can be discerned in contrast with the dull dark papule of the delayed response on the left.
APPENDIX 11.

Summary of 51 cases of measles with a positive Tuberculin Reaction.
Definitions and Abbreviations.

P.H. - Previous history.

T.E. Content = definite contact with human tubercle infection.

Clinical T.E. = any evidence of tubercle infection whether "latent" or active and focal.

Adenopaty: any appreciable changes in the lymphatic glands clinically, whether it be the typical micro-adenitis of tubercle the glands being small, rounded and "shotty" or a more gross enlargement not necessarily tubercular; impetigo of the scalp or chronic Otitis media may give rise to a enlargement of the cervical glands.

Duration of Cough - refers to the total duration of the cough including the terminal simple cough of convalescence.

Spasms: the average number of spasms occurring during the week of maximum frequency is indicated.
APPENDIX II

No. 1. T. R. male; 6 years.

P. H. Otitis Media (3 weeks ago).

T. B. Contact No.

Clinical T. B. Nil.

Tuberculin tests: 5th day negative
14th " positive (not measured)

Clinical Summary: Mild attack; febrile 1 day
no complications, recovery

After history 14 months later alive and well; no
clinical evidence of tubercle infection; occasional
bronchitis as sequel.

Case No. 2. L. P. female 23 years.

P. H. Whooping cough at 10 years; influenza at 20 years.

T. B. contact No.

Clinical T. B. Nil.

Tuberculin tests: 3rd day Negative
11th " 15mm. erythema 23mm.
(48 hrs)

Clinical Summary: Moderate attack; febrile 3 days;
no complications, recovery.

Case No. 3. J. S. Male; 1 8/12 years.

P. H. Rubella.

T. B. contact. No.
Clinical T.B. Nil

Tuberculin tests. 8th day --- 10mm. erythems 25mm. (48hrs.)
16th day ----20mm. " 15mm. (48hrs.)

Clinical Summary: Moderate attack, febrile 3 days, no complication; recovery.

After history: 8 months later alive and well; no sequelae; no signs of tubercle infection.

No. 4. J. S. male; 4 years.
P.H.: Nephritis
T.B. Contact ?

Clinical T.B. Nil

Tuberculin test. 11th day --- 15mm. (48 hrs.)

Clinical Summary: Mild attack: febrile 3 days; no complications; recovery

No. 5. H. T. male; 5 years.
P.H.: Nephritis
T.B. Contact. No.

Clinical T.B. Nil

Tuberculin tests: 4th day - negative
27th " ----15mm. (48 hours)

Clinical Summary: Moderate attack with mild rash, febrile 3 days; no complications; recovery.

No. 6. F. D. Male: 4 8/12 years.
T.B. Contact: - Yes.

Clinical T.B. history of "consumptive bowels" as a baby of 7 months, Sanatorium treatment for 1 year; no evidence of active disease on admission.
Tuberculin tests: 3rd day negative

Clinical Summary: severe attack with marked catarrh; febrile for 6 days: bronchitis; recovery.

After History: 11 months later alive and well; no sequelae; no clinical evidence of tuberculosis.

No. 7. E. J. female, 3 4/12 years.

P. H. Nil.

T. B. contact Yes; mother a recovered case of phthisis now home 2 years.

Clinical T.B. Nil.

Tuberculin tests: 4th day - negative

Clinical Summary: Moderate attack; febrile 4 days; complication: rhinitis, recovery.

After History: 14 months later re-examined and found well with no sequelae; no tubercular manifestation.

No. 8: L. C. female: 4 5/12 years.

P. H. nil.

T. B. Contact: No.

Clinical T. B. Cervical and mesenteric adenopathy.

Tuberculin tests: 3rd day negative

16th day --- 20 mm. erythema 20mm.
Clinical Summary: Severe attacks; febrile 6 days; complication - right otitis media (30th day); recovery.

After history: sequelae - bilateral otitis media 2 months from onset; no tubercular manifestations

No. 9. R. G. female; 14 years.

T. B. Contact - ?.

Clinical T. B. - nil

Tuberculin tests - 3rd day - negative.

41st " -- 20mm; erythema 10mm
(48 hrs.)

Clinical Summary: Moderate attack with intense rash; febrile for 7 days; complication - styes; recovery

No. 10 S. M. female. 2 years.

T. B. Contact. ?

Clinical T. B. Nil

Tuberculin tests; 4th day - negative

17th " - 11mm. (3rd day)
50th " --- 15mm. (48 hrs.)

(N.B. complicated by scarlet fever on 19th day so that - 11mm. response of 17th day test probably modified by the exanthem of scarlet fever.)

Clinical Summary. Severe attack with intense confluent rash; febrile 6 days; complications - broncho-pneumonia (4th day); scarlet fever (19th day) followed by left otitis media (29th day) and
and right otitis media (37th day) probably from the streptococcal infection.

After History: 7 months later alive and well.

No. 11 D. L. female, 3 3/12 years.
P. H. Nil.
T. B. Contact: No.
Clinical T. B. - cervical adenopathy (left side)
Tuberculin tests: 5th day - negative.
18th " --- 17 mm. erythema 6mm
5th month -- 15 mm.

Clinical Summary: Moderate attack with mild rash febrile for 4 days; complications - right otitis media (2nd day) recovery.

After History: Examined at 5 months and a year afterward and found to have no tubercular symptoms of any kind.

P. H. bilateral otitis media 3 months ago.
T. B. Contact: No.
Clinical T. B. - Cervical adenopathy (left)
Tuberculin Test: 1st day - negative
16th " --- 10 mm. erythema 10mm. (24 hrs.)
Clinical Summary: Moderate attack; febrile 5 days; no complications: recovery.

No. 13. J. T. Male, 6 years
F. H. Nil.
T. B. Contact: No.
Clinical T.B. Nil.
Tuberculin tests: 5th negative
18th "
27th -- 15 mm. erythema 15mm. (24hrs.)

Clinical Summary: Mild attack with moderate rash, febrile 3 days: no complications: recovery.
After History: 4 months later alive and well: no symptoms: no tubercular manifestations: suffering from a chronic diphtheritic rhinitis.

F. H. bronchitis at 2 years.
T. B. Contact: Nil.
Clinical T.B. Cervical adenopathy (bilateral)
Tuberculin tests. 5th Negative.
27th day - 10 mm. (24 hrs.)

Clinical Summary: Moderate attack with mild rash; febrile 7 days; complication - acute bronchitis from the onset subsiding in the second week; recovery.
After History: 7 months later alive and well; no tubercular manifestations.
No. 15. C. C. Female; 6 years.

P.H., Whooping cough at 3 years; cervical adenitis 1 year ago.

T.B. Contact: No.

Clinical T. B. Nil.

Tuberculin Tests: 3rd day negative

12th " - 15 mm. (48 hrs.)

4th day of diphtheria 28" - 15 mm. (48 hrs.)

26th " " " 48" - 13 mm; erythema 17 mm.

Clinical Summary: Mild attack with a moderate rash febrile 4 days; complications: cervical adenitis (left sub-maxillary) 13th day; abscess found and drained 8 days later; severe faucial diphtheria on 22nd day; with palatal and late diaphragmatic and facial paralysis; ultimate recovery.

After History: 8 months after alive and well.

No sequelae; no tubercular manifestation.

Case 16. D. R. Male; 7 years

P.H. Nil.

T.B. Contact: No.

Clinical T.B. Nil.

Tuberculin Tests: 3rd day negative.

\[ \frac{1}{4} \text{th} \ " (100) - 20 \text{ mm.} (48 \text{ hrs.}) \]

Clinical Summary: Mild attack and slight rash; febrile one day after admission; No complications; recovery.
After History: 8 months after alive and well.

Case 17: R. A. male; 7 years
P.H. Acute rheumatism at 4 years.
T.E. Contact: No.
Clinical T.B. Nil.

Tuberculin tests: 1st day - 12 (delayed till 4 days after)
3rd " - 10 m.m. (72 hrs.)
8th " - 12 m.m. (24 hrs.)
16th " - 12m. m. (24 hrs.)

Clinical Summary: Mild attack with moderate rash:
febrile 2 days: no complications; recovery.
After History: 4 months later alive and well:
No sequelae: no tubercular manifestations.

No. 18. (23. in scarlet fever series) P.W. male
3 years.
P.H. Tonsillitis.
T.E. Contact: No.
Clinical T.B. Cervical edenopathy (bilateral)
Tuberculin tests: 6 days before onset - + 10 mm.
1st, 3rd and 7th negative.
12th (+) 5 m.m. (48 hrs.)
23rd (+) 5 m.m. (48 hrs.)

Clinical Summary: (admitted to hospital with scarlet fever 50 days before;) No complications; recovery.
Case 19. J. A. female - 6 years.

F. H. vide infra.

T.B. No.

Clinical T.B. previously had had enlarged cervical glands and "cold abscess" drained (rt. side.)

Tuberculin tests: 5 days before (1000) + 2 Cmm. e: 5 m.m. (24 hrs.)

24 hrs. before onset of rash

(10,000) (1) 13 m.m. (24 hrs.)

2nd day of rash

10,000 - negative

4th " " " " (4) 6 m. (24 hrs.)

7th " " " " +1 15 mm. "

Clinical Summary: (Admitted to hospital with scarlet fever 17 days before:) Moderate attack with bright rash; febrile 4 days; complications: cervical adenitis (right submaxillary gland) on 7th day. Typically tubercular: a painless swelling as large as a hen's egg developed and ultimately broke down to form a "cold" abscess; drained by a small incision after 18 days; the sinus closed in 4 days; a diphtheritic rhinitis in the 5th week (with a persistent positive nasal swab) delayed her discharge from hospital for 3 months during which time no further complications arose.
After History: 10 months later alive and well no tubercular manifestations.

No. 20. D. B. female: 4 years

P.H. Bronchitis 1 year ago: chicken pox 6 months ago.

T.B. Contact: Father died of phthisis 14 months previously.

Clinical T.B. Typical microadenopathy of left cervical chains particularly in supra-clavicular region.

Lungs: An impaired note over the whole of the left side with diminished expansion: vesicular breathing: no accompaniments; vocal resonance unchanged.

X-ray examination: increased hilar shadows on right side; upper lobe of left lung showed increased density compatible with consolidations or tubercular lymphatic infiltration.

The child apparently had a primary lymphatic infiltration on the left lung at the time of the attack of measles.

Tuberculin tests: 4th day - Delayed positive x 15mm. (17 days)

22nd " ++ 20 mm. erythema 15mm. (48 hrs.)

Clinical Summary: Severe attack with confluent rash; initial bronchitis persisted into 3rd week; febrile 9 days; at no time any signs of consolidation in lungs; signs in left upper lobe persisted unchanged.
After History: 11 months later alive and well. No symptoms cervical adenopathy unchanged; physical signs in lungs gone.

No. 21. C.S. Male 3 3/12 yrs.
P.H. Bronchitis when 1 year old
T.B. Contact Yes.
Clinical T.B. Nil.
Tuberculin tests - 2nd day Delayed positive - 11mm. (17 days)
25th ---- 15mm. (48 hrs.)

Clinical Summary: Moderate attack; febrile for 7 days Complicated by a broncho-pneumonia at onset; nephritis on the 10th day (blood and casts in the urine) recovery.

After History: This child was subsequently under observation at the East London Children's Hospital during which time no tubercular manifestations occurred; there was no recurrence of the haematuria to suggest tubercle infection of the kidneys.

7 months after I again examined him and found him fit and well with no clinical evidence of tubercle infection.

Case 22. D. C. Male; 6 years.
P.H. Enteritis when 6 months old.
T.B. Contact: No.
Clinical T.B. Cervical micro-adenopathy principally left side
Tuberculin Tests: 3rd day -- 14mm. (re-activated; 6th day after)

5th " -- 11mm. (48 hrs.)

11th " -- 15 mm. (48 hrs.)

Clinical Summary. Moderate attack with intense rash; febrile for 4 days: no complications; Recovery.

After History: Whooping cough: developed one month after; the cough lasted 4 months but no complications arose; examined 7 months after the attack of measles and found fit and well; no tubercular manifestations.

No. 23. K. H. Female: 2 2/12 yrs.

F.H. always subject to cough.

T.B. Contact: No.

Clinical T.B. - a few shotty cervical glands on right side principally.

Tuberculin tests: 3rd day. Delayed positive - 11 mm. (6 days)

11th " -- 15 mm. erythema 20 mm. (48 hrs.)

Clinical Summary: Mild attack with rash of moderate intensity; febrile 3 days; complications: left Otitis media at onset.

After history: re-examined 6 months later and found sound and well with no clinical evidence of tubercle infection; X-ray examination of the chest had shown no pulmonary or glandular lesions (St. Thomas's Hospital)
Case 24. L. S. female; 3 years.

P.H. Nil.

T.B. Contact. No.

Clinical T.B. Nil.

Tuberculin tests: 12th day -- 15 m.m. (48 hrs.)

23rd " --- 20 m.m. erythema (24 hrs.)

Clinical Summary: acute stage of measles not observed; admitted with typical morbilliform staining; complicated by whooping cough and bronchitis at onset; no sequelae: recovery.

After History: - 8 months later re-examined and found fit and well with no tubercular manifestations.

No. 25. L. M. Male: 6 years.

P.H. Whooping cough.

T.B. Contact No.

Clinical T.B. Nil.

Tuberculin tests: 48 days prior to measles (4th day of diphtheria) -- 12 mm. (48 hrs.)

1st day delayed -- 15 mm. (6 days: activated)

5th " --- 12 mm; erythema 16 mm (48 hrs.)

10th " ++ 20 mm (right)

20th " ++ 16 mm. erythema 14 mm (48 hrs.)

Clinical Summary: mild attack with slight rash; in convalescence of diphtheria. Modified by convales-

P.H. Nil.

T.B. Contact: ?

Clinical T.B. Nil.

Tuberculin tests: 3rd day, delayed 10 days - 15mm.

13th " -- 20mm. (48 hrs.)

Clinical Summary: Moderate attack in convalescence of chicken pox, febrile 2 days; complicated by bronchitis; recovery.

After History: 8 months after reported alive and well with no tubercular manifestation.

Case 27. I. S. female, 2½ yrs.

P.H. phlyctenular conjunctivitis.

T. B. Contact: Yes; father and mother both suffering from phthisis and under sanatorium treatment.

Clinical T.B. Paratubercular manifestation; phlyctenular conjunctivitis indicative of high degree of tubercular sensitivity; Cervical adenopathy.

Tuberculin test: 7th day - +++ 20mm.

Clinical Summary: Mild attack with moderate rash; (modified by adult serum), febrile 2 days; no complications; recovery.

After History: On enquiry 14 months later alive
and well living with mother at Papworth Settlement.

Case 28. L. M. Male: 3 years;
T.B. Contact: Yes.
Clinical T.B. Nil.
Tuberculin test: 2nd day -- 15 mm. (24 hrs.)
17th day --- 20 mm. erythema 15
   (48 hrs.)
Clinical Summary: Mild attack; febrile 3 days, no complications; recovery.
After History: 14 months after on enquiry alive and well with no tubercular manifestations.

No. 29 D. B. female, 4 years.
P.H: Whooping cough (10 months)
T.B. Contact: No.
Clinical T.B. Abdomen: small shotty glands easily palpable in mesentery.
Tuberculin test: 5th day -- 12 m.m. (48 hrs.)
Clinical Summary: Mild attack with rash of moderate intensity; febrile 3 days; no complications; recovery.
After History: On enquiry 4 months later alive and well.

No. 30. R. B. male: 16 years.
P.H. at 8 years had whooping cough: 16 months later pneumonia: suspected of tuberculosis then but investigation proved negative.
second week; although his appearance was suggestive

Sputum was negative even on an inoculation test; recovery

After History: Re-examined 3 months from onset there was no evidence of tuberculosis; he had gained 14 lbs. in weight during the 6 week previous; on enquiry 14 months after reported alive and well.

Case 31. J. P. female, 7 years.

P.H. Whooping cough (2 years) Pneumonia (5 yrs.)
T.B. Contact: No; father suffers from "chronic catarrh" a suspicious history.

Clinical T.B. Nil.

Tuberculin tests: 15th day - 10mm; erythema 10mm. (48 hrs.)
22nd " -- 12mm; " 29mm. (46 hrs.)
27th " -- 16mm. " 19mm. (24 hrs.)

Clinical Summary: A moderate attack with a severe rash was followed by a bronchitis persisting into the second week; although his appearance was suggestive of tuberculosis - a sallow pale complexion with emaciation and a tendency to excessive sweating - there were no physical signs of any focal lesion.

Sputum was negative even on an inoculation test; recovery

After History: Re-examined 3 months from onset there was no evidence of tuberculosis; he had gained 14 lbs. in weight during the 6 week previous; on enquiry 14 months after reported alive and well.

Case 31. J. P. female, 7 years.

P.H. Whooping cough (2 years) Pneumonia (5 yrs.)
T.B. Contact: Yes.
Clinical T.B. Abdomen: discrete mesenteric glands just palpable.

Tuberculin tests:
- 2nd day -- 15 mm. (48 hrs.)
- 17th " -- 15 mm. ( " )
- 6 months after -- 20mm.
  erythema 20mm. (48)

Clinical Summary: Mild attack: febrile for 3 days; no complications: recovery.

After History:
- 3 months later re-examined: loose cough, more in the morning; not spasmodic; no sputum; appetite good; on physical examination signs over the left lung suggestive of infiltration or bronchial obstruction: impaired note; faint vesicular breathing; no accompaniments; diminished expansion: V.R. W.F. not altered; D'Espine's sign positive.

6 months from onset the child was alive and well but still had a cough of sharp barking character; some sputum of mucoid character but the physical signs on the left lung had gone.

10 months from the attack of measles the child was in fairly good health; on clinical examination there was no evidence of tubercle infection; X-ray examination of the thorax (Guy's Hosp.) revealed increased hilar shadows suggestive of tubercular...
tracheo-bronchial glands.

At 11 months the child was quite well with no symptoms, putting on weight and no signs of tubercle clinically.

Case 32. W. H. Male, 5 years.
F.H. Bronchitis at 3 years.
T.B. Contact: ? (father has "chronic bronchitis" since discharge from Army in 1920.)
Clinical T.B. cervical adenopathy (left supra-clavicular)

Tuberculin test: 6th day - 12 mm. (24 hrs.)
Clinical Summary: Moderate attack; febrile 4 days no complications. recovery.
After History: 7 months later on enquiry reported alive and well.

Case 33: E. H. female; 4 years.
F.H. broncho-pneumonia (3 yrs.) scarlet fever (3 yrs.)
T.B. Contact: No.
Clinical T.B. cervical micr. adenopathy (bilateral)

Tuberculin test: 5th day - 10 mm. (48 hrs.

19th " - - - 13 mm., erythema 22 mm.

Clinical Summary: A severe attack with a moderate rash: the child was toxic and drowsy with dyspnoea and cyanosis; no localising signs in the lungs. febrile 4 days, recovery.
No. 34: A. R., male, 8 years.
P.H. Bronchitis (6 months); Chicken pox (3 yrs.)
pneumonia (5 years) submax-adenitis (8 years)
T.B. Contact: No.
Clinical T.B. Nil.
Tuberculin test: 2nd day = 15mm. (24 hrs.)
11th " --- 20mm; erythema 20mm. (48hrs.)
Clinical Summary: A mild attack with a moderate rash; febrile 2 days; no complications; recovery.
After History: 1 year after on enquiry reported alive and well.

No. 35. R. M. male, 17 years.
P.H. Scarlet fever at 5 years; acute bronchitis at 12 years; suspected of T.B. then and for 3 months under observation at Sanatorium; discharged as non-
tubercular.
T.B. Contact: No.
Clinical T.B. Nil.
Tuberculin test: 2nd day delayed = 10mm. (3rd day)
5th day = 12mm. (48 hrs.)
Clinical Summary: a moderate attack fever of eruptive phase, lasting 4 days:
Complications: pneumococcal meningitis (11th day)
Otitis Media (left) on 22nd day, followed by a haemolytic (streptococcal pyemia) (26th day); died 38th day.
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**Bowel**

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Autopsy: familial meningitis (pneumococcal); ulcerative endocarditis; multiple abscesses (streptococcal); quiescent calcareous tubercular glands at root of lungs

No. 36. D. F. female; 10/12 year.

P.H. Whooping cough at 1 month; impetigo of scalp complicated by erysipelas.

T.B. Contact: ? mother 26 years old had a cervical abscess when 15 years; has had 3 peri-anal abscesses in the last 4 years; had pneumonia with pleurisy 3 years ago.

Clinical T.B. (Marked disease enlargement of cervical glands especially on right side probably from impetigo on the scalp).

Tuberculin test: 2nd day delayed - 10mm. (7 day) 10th " -- 10mm. (48 hrs.)

Clinical Summary: Mild attack with moderate rash; febrile 2 days; no complications.

After history: 9 months from onset on enquiry reported alive and well.
No. 37: F. W. female; 6 years.
P.H. Whooping cough at 4 years.

T.B. Contact: ?; father "always has a cough through the winter."

Clinical T.B. Nil.

Tuberculin tests: 4th day, delayed 11 days - 12mm.
                        16th " -- 16mm. (48 hrs.)

Clinical Summary: Mild attack: febrile 3 days;
Complications: Otitis Media (right) on 17th day;
recovery.

After History: On enquiry 6 months later reported
alive and well.

      On "" 1 year later still alive
and well.

No. 38: J. C. female; 3 2/12 years.
P.H. Mereamus at 9 months; bronchitis at 16 months
T.B. Contact: No.

Clinical T.B. discrete cervical adenopathy (bilateral)

Tuberculin test: 7th day — 16 mm. (48 hrs.)

Clinical Summary: Mild attack of Measles in 4th week
of whooping Cough; complications: diphtheritic
rhinitis (16th day) conjuctivitis (30th day) right
Otitis Media (33rd day); recovery.

After History: Re-examined 8 months after found fit
and well with no active tubercular manifestations;
cervical glands discretely enlarged.
No. 39.  G. V. female, 5 6/12 years.
P.H. Nil.
T.B. Contact: No.
Clinical T.B. A few small discrete cervical glands palpable.
Tuberculin Tests: 5th day - 10 mm. (48 hrs.)
(chicken pox rash on 6th day; no reaction at site of injection) 18th day -- 15 mm. (48 hrs.)
Clinical Summary: Severe attack with moderate rash;
Complicated by Chicken pox (4th day); erythema
necrosurn (18th day) developed scarlet fever 28 days
after complicated by Otitis Media bright).
After History: acquired whooping cough 3 months after
measles: complicated by a broncho-pneumonia.
When re-examined 7 months from onset of measles found
fit and well with no tubercular manifestation.
Examined again a year after her illness and found
well without symptoms and no clinical evidence of
tubercle infection.

No. 40. S.C. female, 6 months old.
P.H. pneumonia at 3 months.
T.B. Contact: Mother suffering from acute phthisis
child in contact for first 4 months.
Clinical T.B. Cervical micro-adenopathy
Lungs: signs of primary infiltration of right lung.
diminished movement, faint vesic sounds: impaired
note:
Tuberculin tests: 4th day - Maximum reaction at 5th day - 10 mm. (5mm. erythema only at 48 hrs.)

19th day --- 16 mm. (48 hrs.)

Clinical Summary: Moderate attack: febrile 2 days; Complication: Otitis Media (right) on 21st day; signs of infiltration in lungs persisted; papula tuberculosis 2 months after; died of tubercular meningitis 3 months after measles (autopsy not held)

No. 41 P.W. male, 1 7/12 yrs.

P.H. Nil.

T.B. Contact: Yes; contact for 7 months prior to measles.

Clinical T.B. Typical shotty glands palpable in the neck.

Tuberculin Tests: 14th day -- 20 mm. (48 hrs.)

Clinical Summary: Acute phase not observed; admitted on 2nd week with an acute bronchitis which subsided after a fortnight; complication - Furuncle on buttock in 3rd week; recovery
After History: re-examined 6 months later and found sound and well without evidence of active tuberculosis.

11 months from the attack he was reported till in good health.

No. 42. A. L. male, 6 months old.
F.H. Bronchitis when 1 month old.
Suspected of tuberculosis; in hospital 1 month prior to measles.

T.B. Contact: Yes.

Clinical T.B. Lungs: signs of primary infection (or epituberculosis) at left apex persistent broncho-vesicular breathing with impaired note. no accompaniments.

Tuberculin test: 2nd day: maximum reponse.
on 7th day - 10mm.
28th " - 17 mm. (24 hrs.)

Clinical Summary: Moderate attack with mild rash (modified by convalescent measles serum); irregular slight fever continued for 3 weeks after; complications: signs of bronchitis from onset persisting for 6 weeks; bilateral otitis media (15th day); papular tubercular eruption (39th day); signs of infiltration of left apex persisted unchanged.
After History: re-examined 6 months after and found fit and well: no cough: rather pale; fed on cow's milk (pasteurised) and take well; clinically no evidence of tubercular infection; signs in lungs gone.

No. 43. K. F., female, 1 3/12 years.

P.H. Nil.

T.B. Contact: Yes.

Clinical, T.B. Discute enlarge cervical glands

Tuberculin tests: 6th day - 20mm. 24 hrs.

Clinical Summery. Moderate attack, febrile 3 days.

Complication: bi-lateral Otitis Media (8th day);
Sub-maxillary adenitis without suppuration (15th day);
Acute apical lobar pneumonia; (28th day) - Case
Crisis on 7th day; residual bronchitis persisted
for week following.

After history: 5 months later re-examined; still bilateral otitis media; otherwise fit and well; no evidence of active tubercular infection.

Case 44. E. S. male; 1 7/18 years.

P.H. Bronchitis at 6 months.

T.B. Contact: Yes; for 1st year.

Clinical T.B. Palpably enlarged mesenteric glands.

Tuberculin Test: 3rd day --- 15 mm. (3rd day)

Clinical Summary: Moderate attack and mild rash; febrile 3 days; complication: acute enteritis (16th day); Taken home on 36th day against advice still febrile with mild diarrhoea.

No. 45. J. C. Male, 1 3/12 yrs.

P.H. Bronchitis at 9 months.

T.B. Contact: Yes; Mother suffering from phthisis Child in contact until 5 months ago.

Clinical T.B. Large glands palpable in mesentery.

Tuberculin Tests: 36th day --- 20 mm. (48 hrs.)

Clinical Summary: Moderate attack complicated by broncho-pneumonia with initial cough on 6th day; successfully recovered from the pneumonia after acute febrile period of 3 weeks followed by uninterrupted convalescence.
After History: 5 months later on enquiry this child was reported alive and well.

No. 46  R. R. male, 2 11/12.
P.E.  Bronchitis.
T.E.  Contact:  No.
Clinical T.E.  Cervical adenopathy
Tuberculin Tests:  6th day --- 10mm. erythema 10mm. 48 hrs.

Clinical Summary: Mild attack; febrile 2 days; complication: diphtheric rhinitis in 4th week.

Nos. 47, 48, 46 & 50. (see Whooping cough Nos. 13, 21, 13, 11 respectively.
No. 51.  L. P. female, 2 yrs.
P.E.  Quite well until last 2 or 3 weeks when the child "went off her legs"; became listless, developed a cough.
T.E.  Contact:  No.
Clinical T.E.  Nil.
Tuberculin test:  15 days before onset of measles
-- 15 mm; erythema 25 mm. (48 hrs.)

Clinical Summary: Admitted with Chicken pox; exposed to measles on 9/4/32 and given 10cc. of Adult serum; 12 days later developed measles and died suddenly within 48 hrs. of onset; the measles rash
appeared on 21/4/32; it was discute generalised; catarrh was mild; at 3 a.m. on the 23rd coffee-ground vomiting occurred and child died an hour later.

Autopsy: There was massive tubercular infection of the lymphatic system; in the abdomen the glands at the root of the mesentery were enlarged; caseous and matted together; the hilar glands showed free but not so extensive; no macroscopic tubercular lesions in the except for sub-peritoneal tubercules at the lower end of the ileum; lungs showed early acute inflammation in left upper lobe but no consolidation; spleen culture gave a pure growth of haemolytic streptococci.

Cause of death: Acute streptococcæl septicaemia complicating measles in a child with extensive primary lymphatic tuberculosis.
12 fatal cases of measles in which the tuberculin test was negative; at autopsy no evidence of tubercular infection was found.
No. 1. E.L. female; 2 years.

P.H. bronchitis.

Tuberculin test 2nd day (1/100 dilution) - negative.

Clinical summary; moderate attack; complications, broncho-pneumonia from onset; corneal ulcer (L) on 9th day; died on 12th day.

Autopsy: lungs showed scattered areas of consolidation, broncho-pneumonia.

No. 2. S.K. male; 7 months.

P.H. Mil.

Tuberculin test; 3rd day; negative.

Clinical summary; severe attack with confluent rash; complications, acute enteritis on 6th day; broncho-pneumonia on 18th day; died on 28th day.

Autopsy; advanced broncho-pneumonia; numerous areas of consolidation, particularly in lower lobes; catarrhal congestion of small intestine; no ulcers; viscera showed fatty degeneration.

No. 3. R.S. male; 9 months.

P.H. Mil.

Tuberculin test; 2nd day; negative.

Clinical summary; moderate attack; complications, broncho-pneumonia from onset, complicated by croup on
5th day; signs of consolidation developed with increasing dullness, especially at right base; bilateral otitis media on 14th day; died on 21st day.  

Autopsy: Lungs, copious mucus-pus in bronchioles; consolidation of whole or right lower lobe; early bronchiectatic cavities; similar but less marked changes in left lower lobe; delayed resolution into early bronchiectasis; pus in both middle ears.

No. 4. L.M. male; 4 years.  

P.H. Nil.  

Tuberculin test; 48 hours before rash - negative.  

Clinical summary; intense rash (confluent) with severe symptoms; complications, broncho-pneumonia on 8th day (signs of consolidation (bilateral)); otitis media (right) on 12th day; died on 15th day.  

Autopsy; Lungs, diffuse areas of consolidation with mucus-pus in air passages; pus in right middle ear.

No. 5. W.K. male; 1 year.  

P.H. Nil.  

Tuberculin test; 1st day - negative.  

Clinical summary; moderate attack; broncho-pneumonia from onset; no signs of consolidation developed; died on 11th day.  

Autopsy; Lungs, areas of consolidation in all lobes but especially at left base; mucus-pus in bronchioles; catarrhal congestion of intestines.
No. 6. A.B. male; 10 months.

P.H. Broncho-pneumonia.

Tuberculin test; 4 days before rash - negative.

Clinical summary: severe attack with broncho-pneumonia from onset; died 7th day.

Autopsy: Lungs, scattered areas of consolidation, particularly at bases; some catarrhal congestion in ileum.

No. 7. P.B. female; 3 11/12 years.

P.H. Whooping cough; bronchitis.

Tuberculin test; 2nd day; negative.

Clinical summary; moderate attack; complications, broncho-pneumonia from onset; bilateral otitis media (6th day); on 15th day developed croup, which did not respond to diphtheria anti-toxin, therefore apparently streptococcal; faucial ulceration, with perforation of the palate followed in the 5th week; sputum became purulent; died on 36th day.

Autopsy: cause of croup found to be a collection of pus lying submucosal below the vocal cords; the cords themselves not affected; no retro-pharyngeal abscess; necrotic ulceration of fauces and palate on right side; lungs showed extensive consolidation in lower lobes with multiple small abscesses but no actual cavitation; viscera copious amount of pus in the bronchioles; showed fatty degeneration; no endocarditis; no pyaemic abscess.
No.8. E.H. Female; 1 4/12 years.

P.H. Nil.

Tuberculin test; 5th day negative; 14th day negative.

Clinical summary: moderate attack; whooping cough intercurrent; broncho-pneumonia ensued on 32nd day; died 35th day.

Autopsy; Fibrinous pleurisy on left side; no effusion; lungs, scattered areas of consolidation on left side in lower lobe; lung tissue soft and necrotic. In the anterior part of the left lower lobe were two very small pin-head abscesses; in microscopic section they showed marked consolidation, the walls having disappeared, and the cellular exudate composed of degenerating cells suggesting early abscess formation. The right lung showed acute congestion and hydropsis, but no consolidation.

Hilar glands were enlarged, with dark purple congestion, and soft in the centre typical of whooping cough.

No.9. R.S. Male; 1 9/12 years.

P.H. Nil.

Tuberculin test; 4th day - negative.

Clinical summary; moderate attack complicated by broncho-pneumonia from the onset; died 6th day.

Autopsy; Left pleura - a few streaks of fibrinous-purulent matter over parietal and diaphragmatic
surfaces; left lung, lower lobe showed complete consolidation; scattered areas in upper lobe; similar changes in right lung with intense congestion characteristic of fibrinous type of broncho-pneumonia.

No. 10. C.B. male; 12/12 years.

P.H. Pneumonia.

Tuberculin tests.  5th day - negative;
7th "    "    
30th " (1/100) - negative.

Clinical summary; moderate attack; broncho-pneumonia from onset; increasing signs of consolidation at left base, with continuous fever and increasing dyspnoea and exhaustion; died on 34th day.

Autopsy; lungs showed early bronchiectasis; the left lower lobe was airless and completely solid; it cut like liver tissue; on section, bronchiectatic cavities revealed rilled with purulent debris lined by necrotic tissue and surrounding fibrosis; the right lung showed no consolidation; a septic capillary bronchitis was especially marked in the left upper lobe. The viscera showed toxic changes.

No. 11. A.B. male;

P.H. Pneumonia.

Tuberculin test; 5th day (1/100) - negative.
14th " (1/1000) - "

Clinical summary; moderate attack; broncho-pneumonia ensued on 6th day; died on 22nd day.
Autopsy; lungs - scattered areas of consolidation on both sides; fibrinous type of broncho-pneumonia; fibrinous adhesions in both pleurae; no effusion.

No. 12. J.S. female; 9 months.

P.H. Nil.

Tuberculin test; 4th day negative; 13th day negative.

Clinical summary; moderate attack; complications, lobar pneumonia on 4th day (affecting left lower lobe); temperature fell by lysis in second week; acute enteritis on 13th day; bilateral otitis media on 19th day; died on 22nd day of acute enteritis.

Autopsy; lungs - hypostasis and, in left lower lobe, evidence of consolidation resolving; stomach and intestines, particularly the ileum; showed acute inflammation; no ulceration.
APPENDIX IV.

Summary of 36 cases of Whooping Cough with positive tuberculin reaction.
No. 1. C. C. male; 6 years.
P.E. Measles, chicken pox.
T.B. Contact. Yes.
Tub. Test: 3rd week -- 15 mm. (48 hrs.)
Clinical T.B. Typical shotty glands palpable in the
neck.
Summary: Mild attack; afebrile; no complications;
recovery.
Duration of Cough: 4 weeks; spasms - 3 with whoop.
After history: alive and well 5 months from visit.

No. 2. C. M. Male; 3 years.
P.E. Measles.
T.B. Contact: No.
Tub. Tests: 4th week: --- 20mm; erythema 18mm. (48 hrs.)
7th " --- 20mm; " 20mm. (48 hrs.)
Clinical T.B. Nil.
Summary: Mild attack; complications; chicken
pox, (4th week) recovery.
Duration of Cough: 3 weeks; spasms 3, no whoop

No. 3. R. F. female; 4 years.
P.E. Measles complicated by pneumonia at 10
months; scarlet fever at 2 yrs.
T.B. Contact: No.
7th " ++ 12 mm; erythema 23 mm.

Clinical T.B. Nil.

Summary: Moderate attack: initial bronchitis; recovery.

Duration of cough: 7 weeks; spasms 6; and whoop;

After History: alive and well, 13 months from onset.

N.B. Tuberculin tests repeated 11 months after.
23/11/32 Test (Human C.T. only 1/1000) Negative.
30/11/32 " (HUMAN & BOVINE C. T. 1/1000) + 12 mm. (48 hrs.)

No. 4. A. H. male, 2 years.

P.H. Tubercular arthritis

T.B. Contact: ?

Tub. Test: 3rd week -- 18 mm. (48 hrs.)

Clinical T.B.: tubercular arthritis of left hip.

Summary: Mild attack: afebrile: No complication
No effect on tubercular lesion, recovery.

Duration of Cough: 6 weeks: spasms 5: no whoop.
No. 5. R. W. Male, 10 years.
T.B. Contact?
Tub. Test: 2nd week - negative
5th " ++ 20mm. (48 hrs.)
Clinical T.B. - enlarged mesenteric glands.
Summary: Mild afebrile attack: no complications
recovery
Duration of cough: 6 weeks; spasms, 7; with whoop

No. 6. K. D. Female, 6 years.
T.B. Contact: ?
Tub. Test: 2nd week ++ 12 (48 hrs.)
6th " ++ 20: erythema 20mm. (48hrs)
Clinical T.B. Nil.
Summary: Mild afebrile attack: no complications:
recovery
Duration of cough: 4 weeks; spasms 3; no whoop.

No. 7. R. H. Female, 4 years.
P.H. measles at 2 yrs. Diphtheria at 3 years
T.B. Contact: Yes; father died of phthisis 2
years after.
Tub. Tests: 2nd week ++ 20mm. 46 hrs.
6th " +++ 20mm. erythema 10mm. (48hrs.)
Clinical T.B. cervical adenopathy (left side)
Summary: Initial bronchitis: mild attack: recovery.
Duration of cough: 6 weeks: spasms 19 with whoop

No. 8. H. P. Male, 2 years. (case 49 measles series)
P.H. Nil.
T.B. Contact: Yes.
Tub. Tests: 2nd week: +++ 20mm. 48 hrs.)
6th week ++++ 20mm. erythema 20mm. (24 hrs.)
Clinical T.B. extensive hilar gland enlargement and infiltration of right middle lobe.

Summary: Complications: initial bronchitis: left Otitis media, Measles in 5th week: recovery after severe attack.
Duration of Cough: 7 weeks: spasms 14 with whoop.
After History: alive and well 8 months from onset; hilar gland enlargement unchanged.

No. 9. C. R. male, 3 years.
P.H. Nil.
T.B. Contact: ?
Tub. Tests: 3rd week +++ (vesication) 23 mm. (48hrs.)
Clinical T.B. Cervical micro-adenopathy (left)

Summary: Mild attack: afebrile: no complications
Recovery.
Duration of Cough: 6 weeks; spasms 6 with whoop.
After History: alive and well 14 months from onset
Case 10.

P.H. Measles at 3 years, chicken pox at 3 years.

T.B. Contact: Yes.

Tub. Tests: 1st week - + 16 mm. (48 hrs.)

Clinical T.E. Cervical micro-adenopathy (left)

Summary: Moderate attack: minor complications
(blepharitis, furuncle): recovery.

Duration of cough: 8 weeks; spasms 4 14 with whoop.

After History: alive and well 5 months after.

No. 11. T. B. Male, 4 years. (No. 50 in measles series)

P.H. Scarlet fever at 14 months.

T.B. Contact: Yes: for 2 months one year ago.

Tub. Tests: 1st week ++ 18 mm. (48 hrs.)

4th week ++ 20 mm. erythema 20 (48 hrs.)

(measles rash present)

Clinical T.B. Cervical adenopathy.

Summary: Mild attack: complications: bronchitis
(Measles and later enteritis: recovery.

Duration of Cough: 5 weeks, spasms; 7 with whoop.

After History: Alive and well 9 months after.

Case 12 R.B. Male: 3 10/12 yrs.

P.H. Measles complicated by broncho-pneumonia at
1 9/12; Adenitis: Nephritis 1 month ago.

T. B. Contact: No:
Tub: Tests: 1st week: ++ 15 mm. (48 hrs.)

4th " +++ 20 mm. erythema 15mm. (48 hrs.)

Clinical T.B. Nil.

Summary: Mild attack: no complications.

Duration of Cough: 6 weeks; spasms 6 with whoop.

After History: re-examined and found fit and well a year later with no evidence of tubercular infection.

Case 13 J. E. female: 1 10/12 yrs.

T.B. Contact: Yes.

Tub: Tests: 6th week +++ 18 mm. 24 hrs.)

Clinical T.B. tubercular enteritis: (faeces-Tubercule bacilli + )

Summary: Moderate attack: Complications: bronchi- tis.

Modified measles; Miliary tuberculosis - died.

Case 14: G. H. female. 1 year.

T.B. Contact: ?

Tub. Tests: 1st week +++ 10 m.m. erythema 10mm. (48 hrs)

Clinical T.B. Nil.

Summary: Moderate attack: no complications: afebrile.

Duration of Cough: 6 weeks; spasms 7 with whoop.
Case 13. J. C. Male, 3½ yrs.
P.H. Measles 4 week before: had broncho-pneumonia at 1½ months.
T.B. Contact: Yes.
Tub: Tests: 5th week ++ 15 mm. erythema 10 mm. (48 hrs.)
Clinical T.B. Nil.
Summary: Moderate attack: febrile; no complications
Duration of Cough: 8 weeks, spasms 10 with whoop
After History: Alive and well 6 months later

Case 16. G. M. female, 1 9/12 years.
P.H. ?
T. B. Contact: ?
Tub: Tests: 9th week +++++ (Necrosis) temp. 99°
Clinical T.B. discrete cervical adenopathy (Bilateral)
Pare-tubercular manifestation - phlyctenular conjunctivitis.
Summary: Moderate attack: complicated by acute febrile exacerbations of phlyctenular conjunctivitis with keratitis and hypopyon of right eye; recovery.
Duration of cough: 9 weeks; spasm 8 with whoop.
After History: alive and well 6 months later; no active tuberculosis
Case 17.  D.P. female: 4 years.

P.H.  Tuberculosis of right hip.

T.B. Contact:  ?

Tub: Tests:  2nd week - 15 mm. (48 hrs.)

Clinical T.B.  tubercular arthritis of right hip.

Summary:  Mild attack: no complications: except initial bronchitis.  No effect on pre-existing tubercular lesion: recovery

Duration of cough:  4 weeks, spasms 5 no whoop

After History:  alive and well 10 months later; still under treatment for tubercular arthritis.
Case 18: M. F. female 1 3/12 years.
P.H. Bronchitis
T.B. Contact: No.
Tub. Tests: 6th week ++ 10mm. 48 hrs.

+++ 17mm. 48 "

Clinical T.B. Nil

Summary: Moderate attack; complications bronchitis, otitis media, modified measles, milliery tuberculosis. Died.

Case 19: L. S. Female, 3 yrs.
P.H. Nil:
T.B. Contact: No.
Tub. Tests: 2nd week: (12th day of measles)

+++ 15 mm. 48 hrs.

4th weekl. (23rd day of measles)

+++ 20 mm. erythema 10 24 hrs

Clinical T.B. A FEW MESENTERIC GLANDS PALPABLE.

SUMMARY: Severe attack complicated at onset by measles. Papular tuberculide (8th week) Recovery

Duration of Cough: 8 weeks. Spasms S with whoop.

After History: Alive and well 8 months from onset

Case 20: S. R. Male 6 yrs.
T. B. Contact: ?
Tub. Tests: 2nd week, +++ 29 mm. erythema 20mm. 48 hrs.
Clinical T.B. A few palpable omental glands.

Summary: Moderate Attack: No complications.

Duration of Cough: 7 weeks. spasms 6 & whoop.

After History: Alive and well 9 months later.

Case 21: E.M. male, 2½ yrs.

P.H. Mastoiditis at 6 months.

T.B. Contact: No.

Tub. Tests: 2nd week (6th day of measles) +++ 17mm.

Erythema 23 mm. (48 hrs.)

Clinical T.B. Nil.

Summary: Mild attack associated with measles.

Complications: Phlyctenular conjunctivitis and a papular tuberculide recovery.

Duration of Cough: 5 weeks: spasms 3 no whoop.

After History: 9 months later examined and found alive and well, with no clinical evidence of tuberculosis.

Case 22: E.B. male, 5 yrs.

P.H. Tubercular arthritis.

T.B. Contact: No.


Erythema 45 mm. (48 hrs.) (see section on negative results.

Clinical T.B. History of tubercular arthritis right
knee three years previously, at present no clinical T.B.

Duration of Cough: 10 weeks, spasms 5, whoop.
Summary: Moderate attack, complications otitis media. Recovery.

Case 23: P.J. female.
T.B. Contact: History of tuberculosis on maternal side.
Tub: Tests: 6th week, (+) 4 mm. (faint) (48 hrs.)
Clinical T.B. Nil.
Summary: Severe attack.
Died from tubercular meningitis in 6th week.

Case 24, E.F. female. 11/12ths.
T.B. Contact: Yes.
Tests: 2nd week ++++ (vesicles on 3rd day)
Clinical T.B. Nil.
Summary: Severe attack, no complications. Recovery.
Duration of Cough: 14 weeks, spasms 10 & whoop.

Case 25: H. M. male, 5 yrs.
T.B. Contact: ?
Tub: Tests: 2nd week + 15 mm. (delayed 13 days)
4th " +++ 15 mm. (24 hrs.)
Clinical T.B. Nil.

Summary: Mild attack. No complications. Recovery
Duration of Cough: 5 weeks. spasms & with whoop.

Case 26. B.E. 3 yrs. (No. 34 in diphtheria series)
P.H. Nil.
T.B. Contact: No
Tub: Tests: 2nd week negative
7th " ++ 12 mm. erythema 18mm. (24hrs.)
10th " ++ 20 mm. 

Clinical T.B. Nil.

Summary: Severe attack complicated by bronchopneumonia at onset. Later faucial diphtheria.
Recovery.
Duration of Cough: 11 weeks. spasms 11 & whoop.
After History. Alive and well, 6 mos. from onset.
Re-examined at 9 months and found well with no clinical evidence of tuberculosis.

No. 27. D. de. S. female, 4 yrs.
P.H. Measles.
T.B. Contact ?
Tub: Tests: 1st week +++ 20 mm. erythema 5 mm. (48 hrs.)
5th week +++ 20 mm. (vesicles) 
erythema 10 mm. 48 hrs.
Clinical T.B. Slight enlargement of mesenteric glands.
Summary: Mild attack, no complications.
Duration of Cough: 8 weeks, spasm 7 and whoop.

No. 28 C.D. female. 2 8/12 yrs
T.B. Contact: ?
Tub Tests: 5th week +++ 20 mm. erythema 10mm.
Clinical T.B.: Nil
Summary: Moderate attack bronchitis, in 5th week.
Recovery.
Duration of Cough: 12 weeks: Spasms 4, no whoop.

Case 29. D. S. female 3½ yrs.
T.B. Contact: ?
Tests: 1st week, + 10mm. (delayed 3 days)
4th " +++ 20mm. Erythema 25mm. (48 hrs.)
Clinical T.B.: A few mesenteric glands palpable.
Summary: Mild attack no complications:
Recovery.
Duration of Cough: 7 weeks, spasms 3 and whoop.

Case 30. W.J. Female. 3 yrs.
P.H. " Consumptive bowels"
T.B. Contact:  Yes.
Tub Tests: 2nd week. --- 20mm. erythema 5mm.
(48 hrs.)
Clinical T.B.: Hilir glands enlarged (X-ray)
Summary: Mild attack, complication, initial bronchitis, rhinitis, recovery.
Duration of Cough: 7 weeks, spasms 4, with whoop.
Case 31. E. W. female, 4 yrs.

P.H. Measles 9 months ago. Nephritis, 1 month ago.

T. B. Contact No.

Tub. Test: 3rd week + 20mm. 48 hrs.

Clinical T.B. Nil.

Summary: Mild afibrile attack, uncomplicated Recovery.

Duration of cough: 4 wks. spasms 6, and whoop.

Case 32. C. A. Male, 1 year.

P.H. Measles 7 months ago, bronchitis, since 3 months old.

T.B. Contact: Yes:

Tub. Tests: 1st week: + 20mm. erythema 5 mm. (48hrs.)

4th week +++ 15mm. " 15 mm. (24"

Clinical T.B. Lymphatic infiltration of upper lobe of left lung ("epituberculosis")

Summary: Severe attack persistent bronchitis, afibrile, Recovery.

Duration of cough 10 weeks spasms 10 and whoop.

Case 33. A. W. female, 2 yrs.

P.H. Measles 1 yr.

T.B. Contact: Yes.

Tub. Test: 3rd week +++ 30mm. erythema 15 mm.

(48hrs.)

Clinical T.B. Nil.

Summary: Moderate attack, no complications, afibrile, Recovery.
Duration of Cough: 9 weeks, spasms 5, no whoop.

Case 34. A.W. 3½ yrs.

P.H. Measles:

T.B. Contact: Yes:

Tub. Test: 2nd week + 15 mm.

Clinical T.B. Nil

Summary: Severe attack complications bronchitis convulsions, died. Autopsy: small cervical lymphatic focus of tubercle not contributing to cause of death.

Case 35. M.F. female, 10 yrs.

P.H. Measles and bronchitis.

T.B. Contact?

Tub. Test: 3rd week ++ 10mm. erythema 25 mm.

Clinical T.B. Nil.

Summary: Mild attack complications, chickenpox at onset, febrile recovery.

Duration of cough 6 weeks, spasms 5 and whoop.

Case 36. J. C. female, 3 2/12th years.

T.B. Contact: Yes:

Tub. Test: 5 week ---- (vesicles) 16mm. (48 hrs.)

Clinical T.B. Cervical glands discretely enlarged

Summary: Moderate attack, complications measles (4th week) bronchitis, rhinitis, conjunctivitis, right otitis media, recovery.

Duration of cough: 8 weeks, spasms 10 and whoop.

After History: alive and well 8 months onset.
APPENDIX V.

Whooping Cough.

Summary of 7 fatal cases of whooping cough with negative tuberculin reaction; no evidence of tubercle infection found at autopsy.
Case No.1. P.C. female; 7/12 yr.
Tuberculin test; 1st week - negative.
Clinical summary; a marasmic baby; severe attack; developed broncho-pneumonia in 2nd week; died on 15th day.

Autopsy; acute broncho-pneumonia; patches of consolidation mostly in right lung; hilum glands congested.
Cause of death; broncho-pneumonia.

Case No. 2. M.D. male; 3 yrs.
Tuberculin test; 1st week - negative.
Clinical summary; moderate attack; initial bronchitis complicated by measles on 18th day; died 22nd day.

Autopsy; acute broncho-pneumonia; scattered patches of consolidation in both lungs; hilar glands congested.
Cause of death; broncho-pneumonia.

Case No.3. J.E. male; 15/12 yrs.
Tuberculin test; 1st week - negative.
Clinical summary; moderate attack complicated by measles on 18th day, followed by broncho-pneumonia; died on 31st day.

Autopsy; acute broncho-pneumonia; area of consolidation in lower lobes; intense haemorrhagic congestion of hilar glands typical of pertussis.
Cause of death; broncho-pneumonia.
Case No. 4. P.B. male; 11/12 yr.
Tuberculin test; 1st week - negative.

Clinical summary; wasted child, pre-existing bilateral otitis media; severe spasms; acute broncho-pneumonia in first week; died in 2nd week, following convulsions.

Autopsy; the lungs showed extensive consolidation; the right lower lobe showed "grey hepatization"; areas of less advanced consolidation in the middle and upper lobes on the right side and at the left base. The hilar glands showed intense congestion.

The cervical glands suspiciously small, hard and "shotty" in microscopic section showed simple phasis without evidence of tubercle infection, probably a result of the chronic otitis media.

Cause of death; broncho-pneumonia.

Case No. 5. F.M. 3 2/12 years.

Tuberculin test; 6th week, negative; 10th week, negative.

Clinical summary; severe spasms; initial bronchitis and mucopurulent sputum in first week quickly progressed to a broncho-pneumonia, with signs of bronchiectasis developing in the 5th week; complicated by bilateral otitis media; continued fever with progressive emaciation terminated in death in the 10th week.

Autopsy; lungs; in the lower lobes were large bronchiectatic cavities varying from ½ to 1 inch in diameter; the left lung was collapsed and airless
evidently from an exploration of the left pleural
cavity made during life; extensive adhesions and thick-
ening of the pleura on the left side; a few fine
adhesions on the right side; no effusion.
Cause of death; bronchectasis.

Case No. 6. A.R. male; 3/12 yr.
Tuberculin test; 1st week - negative.
Clinical summary; moderate attack; acute enteritis in 2nd week; died 15th day.
Autopsy; acute catarrhal inflammation of small intestine, both jejunum and ileum; no pulmonary inflammation; no evidence of tubercle infection.
Cause of death; acute enteritis.

No. 7. O.C. female; 3/12 yr.
Tuberculin test; 2nd week - negative.
Clinical summary; severe attack complicated by broncho-pneumonia in 2nd week; convulsions ensued and child died on 16th day.
Autopsy; Brain, extensive subarachnoid haemorrhage over left hemisphere; bleeding from vein just behind Rolandic fissure close to the sagittal sinus; no inflammatory changes in meninges; Lungs, extensive capillary bronchitis and early consolidation in lower lobe on right side; hypostasis at left base.
Hilar glands acutely congested.
Cause of death; cerebral haemorrhage.
BIBLIOGRAPHY.

Annual Reports of Metropolitan Asylums Board (Infectious Diseases Section); 1926-7; 1927-8; 1928-9.


CHOTTE, P.R. Thèse de Paris, 1929. (No. 168).


COZZOLINO, C. La Riforma Medica, 1913: 44. p. 1203.


HART, P. D'A. Medical Research Council; Special Report Series, No. 164. 1932.


KÄR, - - "Infectious Diseases", 1929. 3rd. edit., Oxford Medical Publications.


" " Münch. med. Wochenschr., 1908: 34. p. 1297.


SCHLEMMER, A. Thèse de Paris, 1914.


SCOTT, M.H. Medical Research Council; Special Report Series, No. 149. 1930.

SENNERT, D. De febribus libri IV, 1641. p. 178. Venice.


