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

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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"- these 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.
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(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.

	Total No. of deaths.	Proportion per 1,000 deaths from all causes.
Measles	3,288	7
Whooping cough	2,512	5
Diphtheria	2,673	5
All tuberculosis	35,818	73

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 frequently a sequel of measles and whooping
cough." Ker (1929) and Goodall (1928) subscribe to a
similar opinion. Osler and McCrae (1926) 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. <u>TUBERCULOSIS IN CHILDREN.</u>

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 distri-
bution 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 over-
whelming 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 demon-
strated 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 nor imply immunity.   Also by
analogy with the pseudo-Schick reaction, the more
marked the response the more recent has been infection.

(3).   <u>Primary tubercle infection in children.</u>

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 infiltrat-
ion", or " epituberculosis" ÷ an example of Ranke's
epithelioid tissue reaction in the lung parenchyma.

As Stewart (1932) has shown, it is this "benign
                                        FORM a
infiltration" which later regresses to ør 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 rate 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 1%.

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 pathognomic, 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
Opie (1917).   This is at variance with/the 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:-

Age	Mortality	
0-1 year	78%.	Hempelman (1917).
	56%	McLean and Jeidell (1922).
	53%	Reuben and Smith (1924).
	63.7%	Söderström (1928).
	80%	Nonrad (1930).
Average	66%	

Age		
1-2 years	57%	Hempelman (1917).
	37%	McLean and Jeidell (1922).
	57.6%	Söderström (1928).
	35%	Nonrad (1930).
Average	45%	

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 <u>the</u> 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.

Tuberculin tests.

I. 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 <u>into</u>
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

found 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 excoriation of the epidermis until the pink cutis vera is exposed, before rubbing in the tuberculin.   This comes near to the method of inject-ing 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 interpret-ation.

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 scarif-
ication 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 of 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 carbolic 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 "   ⎬ 1.5% in distilled
Sodium chloride   99 " ⎭   water.

(Glenny 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 phlyctenular 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 differenti-ate 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 with-
out 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 of the infiltrated area.

(iii) In a severe reaction there is actual vesicul-
ation, usually on the 3rd day, sometimes with haemorr-
hage 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 1/10000
dilution produces a reaction as large as 0.1 cc of 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 circul-
ation.   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 O.T. itself.
With 1/1000 dilutions of this control I obtained no
reactions.

IV.   MEASLES

in relation to tuberculosis.

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 niso cito idoneis succaratur remediis, in
phthisin et hecticam fit transitus."

It must be remembered that prior to Koch's discov-
ery of the bacillus and the subsequent eludidation 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 of "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
rife and dissemmination 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 tubercul-
osis 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 (Dow and Lloyd: 1932).
                              earlier
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 activ-
ation 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 Preisich, 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
Tessier 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 anergy.

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 persist-
ing 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 Liege (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 unneccessary 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 O.T.
persists for 48 hours, often with a definite infil-
tration, 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
of interpretation the method was discontinued in favour
of repeating the 1-1000 test, knowing that the stimul-
ation 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 i
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 intra-
dermal test in the standard dilutions of 1-1000 O.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.

	Positive	Negative	Total
No. tested in first week only	6	114	120
" " önly in 3rd week or later	1	30	31
" " both in 1st and 2nd week	11	249	260
" " both in 1st week and 3rd week or later	32	457	489
	50	850	900

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; 2.4% reacted in eruptive period
while 8.25% were found positive in the third week or
later.   This would suggest that about 75% of tubero-
ulin sensitive subjects lose their reaction during
measles.

Table II.

	Eruptive period.	3rd week or later.
Total number tested.	831	520
No. found positive.	21	43
Percentage "	2.40%	8.25%

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
exactly when sensitivity returned/with a large number
but
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.

Day of disease.

	1	2	3	4	5	6	7	8	9	10	11
Positive reactions:	2	6	2	2	4	4	2	2	1	2	2
Negative reactions.	3	2	6	4	4	1	-	-	-	1	-
Percentage negative.	60	25	75	66	50	20	-	-	-	-	-
Combined positive reactions.	2	8	10	12	16	20	22	24	25	27	29
Combined negative reactions.	19	16	15	9	5	2	-	-	-	1	-
Expected percentage negative.	90.4	66.6	60.4	42.8	23.8	9.0	-	-	-	-	-

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.

DAY OF RASH.
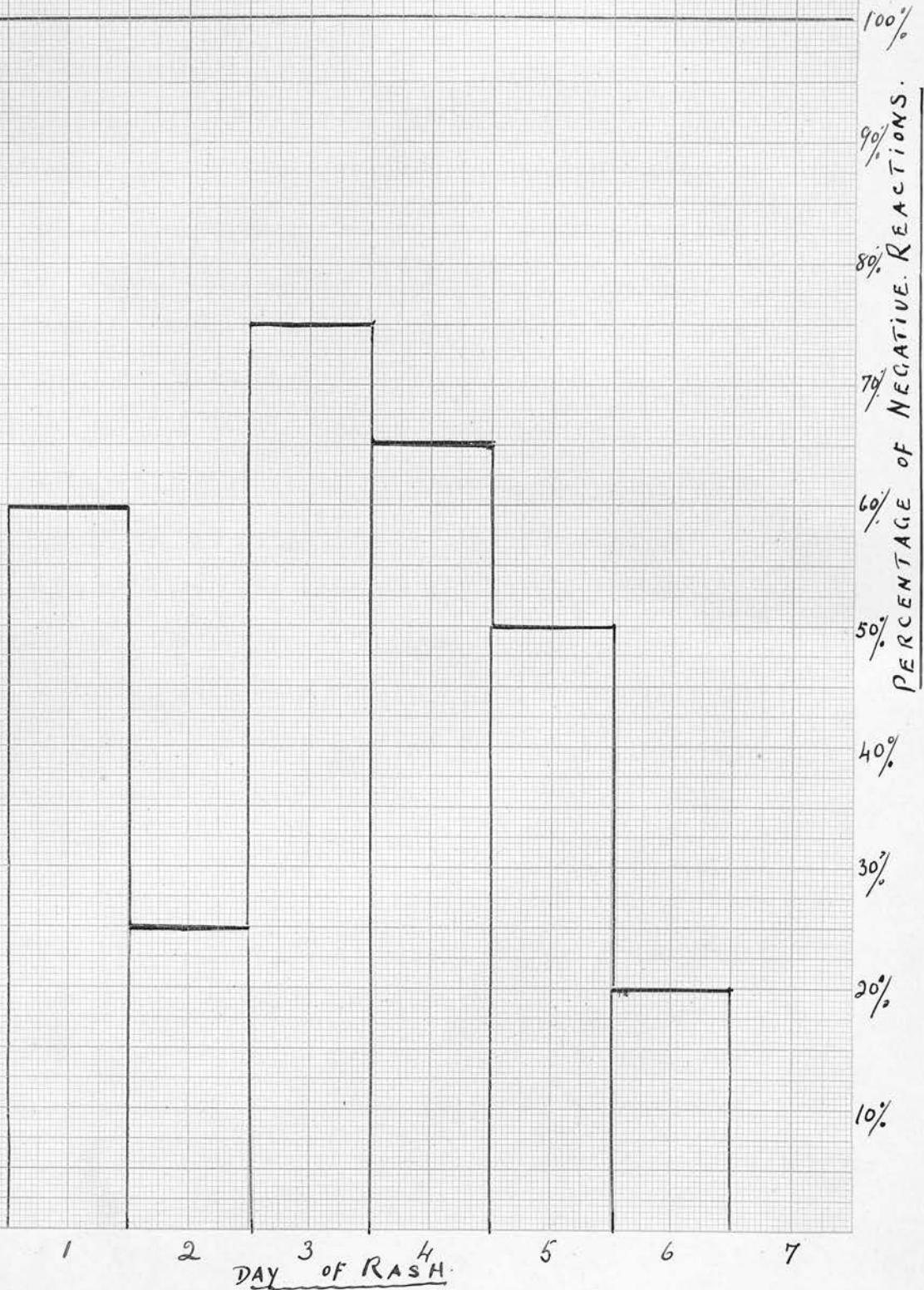
the second week.   This effect appears to be at its
maximum not with the appearance of the rash but when
the eruption is fully developed and suppresses the
reaction at least temporarily in about 60% to 75% of
cases.

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.

	Mild No.	%	Moderate No.	%	Intense No.	%
Positive reactions.	9	56.26	8	34.78	1	25
Delayed positive reactions.	1	6.24	5	21.75	-	-
Negative reactions.	6	37.50	10	45.47	3	75

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. - 48 -
CLASSIFIED ACCORDING TO THE TYPE OF RASH.
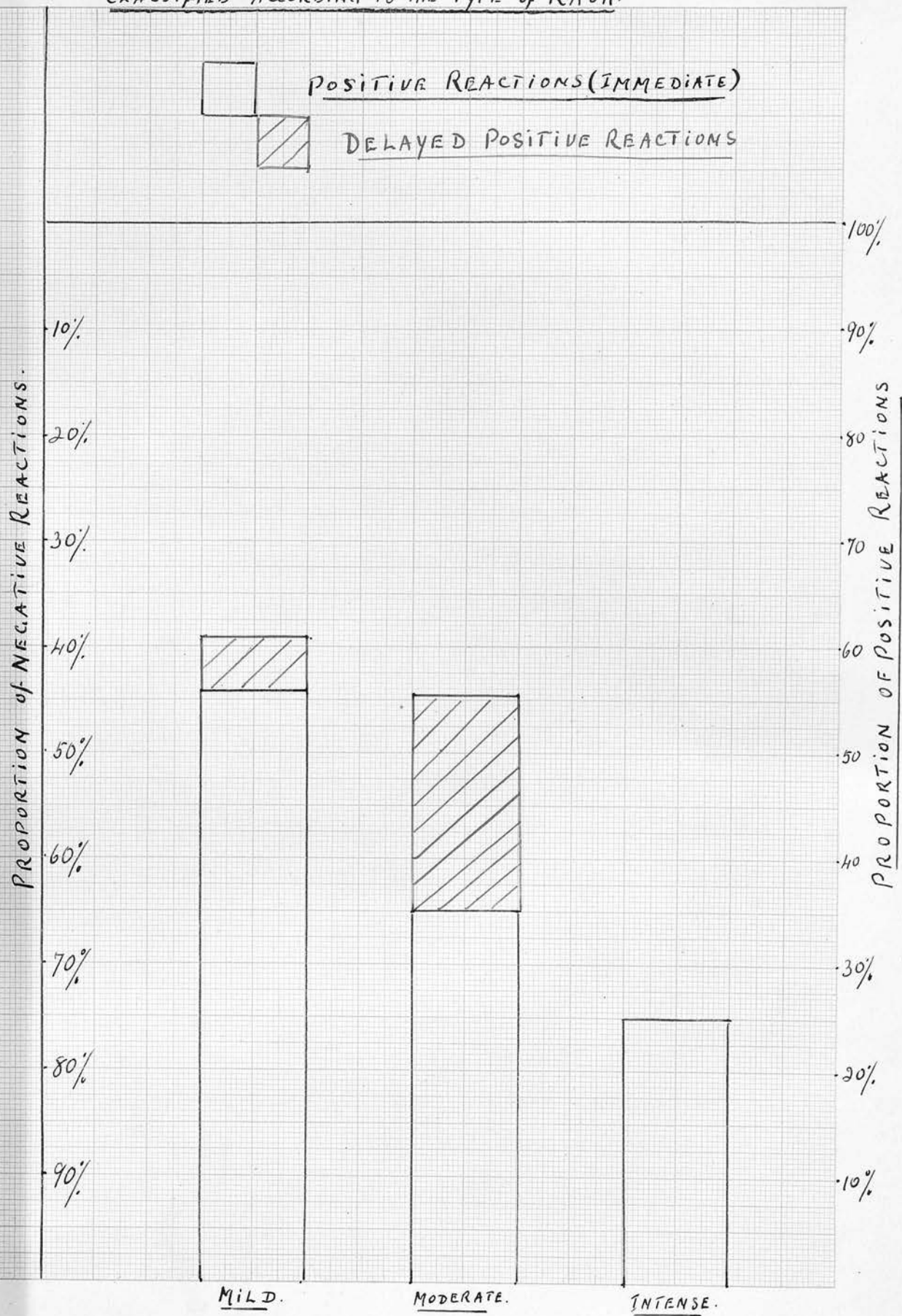
Effect of the Degree of Allergy.

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 con- valescence. 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 reac- tion 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 inci- dence 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.

	DEGREE OF ALLERGY.							
	No.	%	No.	%	No.	%	No.	%
	+		+ +		+ + +		+ + + +	
Negative Result	3	60	6	46.16	6	33.33	1	25%
Delayed Positive "	0	-	3	23.08	3	16.67	1	25%
Immediate "	2	40%	4	30.76	9	50%	2	50%
Totals	5	100%	13	100	18	100	4	100

CASES POSITIVE THROUGHOUT THE
COURSE OF MEASLES.

Of the 50 cases observed 17 gave a positive res-
ponse 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.

PROPORTION OF POSITIVE REACTIONS.

DEGREE OF ALLERGY.

+   + +   + + +   + + + +
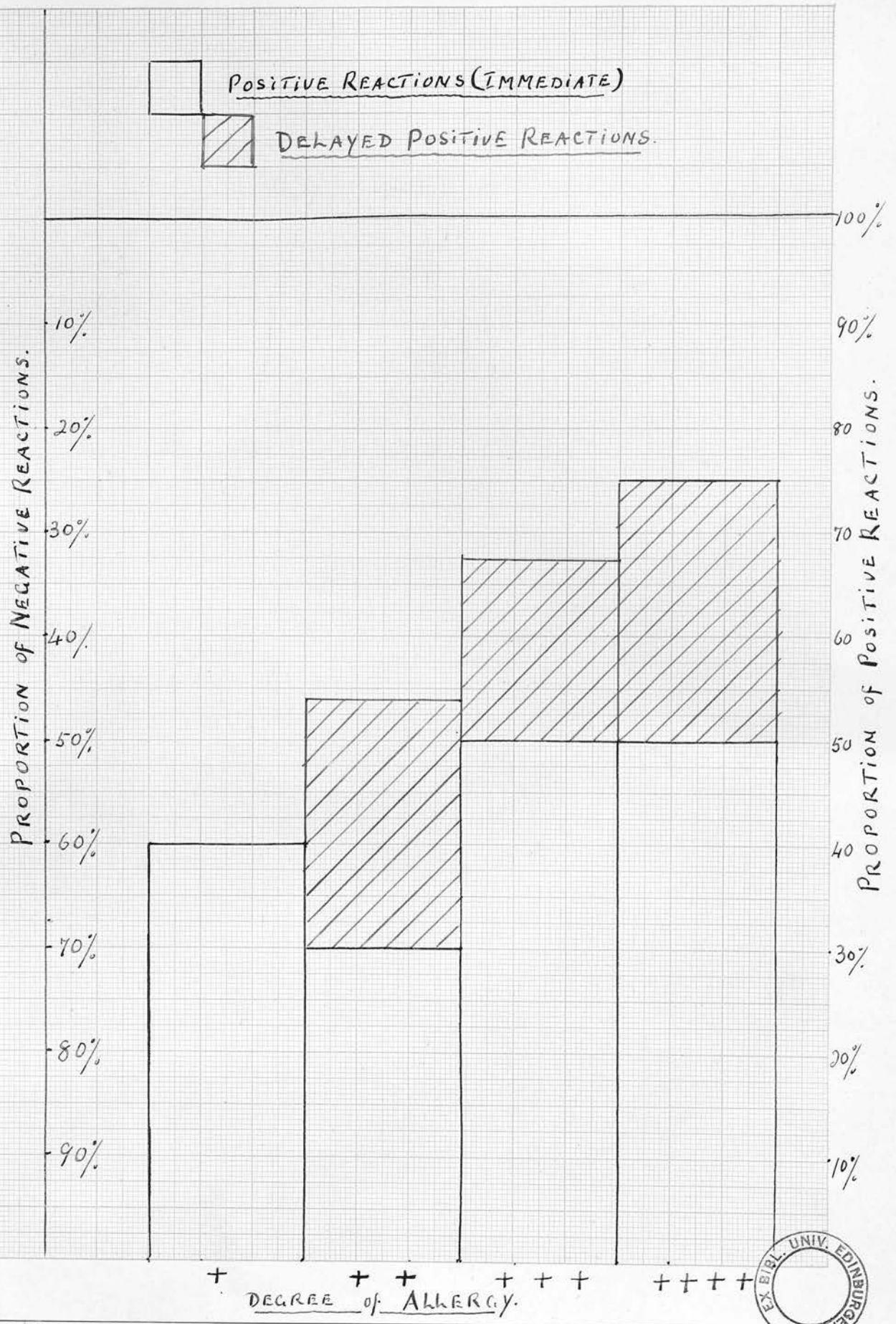
TABLE VI.

CASES FOUND POSITIVE IN THE ACUTE STAGE OF MEASLES

		1st test in acute stage	Maximum test in convalescence.	
Case No.	Day of Rash	Reaction	Day of Rash	Reaction.
3	8	+++10mm. E 25	16	+++: 25 mm. E10
28	2	++15mm	17	+++20 mm. E15
31	2	++15mm	17	+++15mm
33	5	++10mm	19	++++18 mm E20
34	2	+15mm	11	+++20 mm E20
✱35	2	+10mm	5	+15 mm
39	5	+10mm	18	++15
40	4	+10mm	19	+++16
49	1	+15mm	18	++++23 E17
✱50	1	+13mm	4	+18 mm
27	7	+++20mm)		
29	5	+++12)		
32	6	+12)		
43	6	++20)	Not tested in convalescence	
44	3	+++15)		
46	6	+++10:E10)		
48	6	+++17:E23)		

✱ 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 reac-

tion in the test made in convalescence. It is known

that in normal subjects allergy is enhanced by re-

peated tests at short intervals so that a difference

must be marked to indicate that there was some tem-

porary 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 "

<u>Size</u> In 8 cases - 1 case showed no change in size

7 others all showed an increase in size

<u>Surrounding Erythema</u> - as is to be expected the ery-
thema 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.

	Reaction before measles		Reaction during measles.		Reaction in convalescence	
Case	Days before Rash	Reaction	Day of Rash	Reaction	D.of Rash	Reaction
18	13	+12	1	Neg	12	(+)5
49	22	+++20	1	+15	18	+++18E17
50	2	++20	1	+13 $\left(\frac{1}{10,000}\right)$	4	+++18$\left(\frac{1}{10,000}\right)$
17	12	+16	1	Delayed +12	15	+12
25	48	+12	1	+15	20	++16 E14
19	6	++20mmE5	2	Neg	7	++15

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

"   "   50   a reaction as intense with a

$\frac{1}{10,000}$ dilution on the last test as compared with

the $\frac{1}{1,000}$ dil on initial test.

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

Table VIII.

Case	Days before	Reaction	Rash appears ↓	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	Pre-measles test						Day of Rash										
18	13	+12		Test	-	-	-	-	-	-	-	-	-	-	-	-	-
					T	-	-	-									
										T	-	-					
															T	(+)5	(+)5
19	6	++20 E5	T	(+)13	(+)10	(+)10	-	-	-	(+)?5	-	-	-	-			
				T	neg.	-	-	-	-	(+)?5	-	-	-	-			
					T	(+)6	(+)6	(+)?5	-	-							
							T	++15	++15								
17	12	+16	T	-	-	(+)10	+12	+10	(+)8	(+)8						
					T	-	+10	+10	(+)8	(+)8							
									T	+12	+12						
25	48	+12	T	+15	-	-	-	-	+15	(+) stn. 15	(+) stn. 15	(+) stn. 10				
						T	i5	++12	+12	(+) stn. 12							
												T	+20	(+)10	20 day 20		
49	22	+++20	T	+20	+10	+10	(+)18								T ++16	
					T	(+)15	(+)15	(+)15								19 day 20	
							T	+++23	+++20	+++20	++17					T +++23	
50	2	++20	T +20	++20	++20											
				T	+12	+13	(+)13										
					T	+++18	++15	+15									

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 perform-
ed the day before the rash appeared was positive al-
though 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 anergy.

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

Day of Rash

0 1 2 3 4 5 6 7 8 9

```
T - - - - - - 4 5 3 mm.
  T - - - - - 3 4 5
    T - - - - - - -
    T - - - - - - -
      T - - 3 3 -
        T 5 8 8 5
          T 5 7 7
            T 6 7
              T 7
```

Day of Rash

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

Also illustrating the maximum period of anergy
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 re-
covered 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. (Day of rash indicated
in brackets).

Case 19 Aet 6 yrs.

Date	Prodromal stage	Intra der-	Pre-ex-
21/2/32	of measles re-cognised by Koplik spots & temp.of 100.5	mal test $\frac{1}{10,00}$	anthem 24 hrs.
22/2/32	Bright measles rash on face, neck, trunk	(+) 13mm.	(see photo-graph)
23/2/32	Rash still bright: now generalised	(+) 10mm.	I.D.test $\frac{1}{10,00}$ (2)
24	Rash beginning to fade on trunk	(+) 10mm. ft.	negative
25	Rash fading generally	Negative	negative	I.D.test $\frac{1}{10,000}$ (4)
26		-	-	(+) 6m. faint
27	Morbilli-form stain-ing moderate	-	-	(+)5mm. 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 5mm erythema only			Intra dermal test $\frac{1}{10,000}$ (7)
29	All these reactivated tests faded again			+ + 15mm
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.

MANToux
(1-10.000)

Case 19.   Photograph on the 9th day of the Rash

Morbilliform 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 appears 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.

MANTOUX
(7ᵗʰ DAY)
+ + 15.

MANTOUX
(24 hrs. BEFORE
RASH)
STAIN.

MANTOUX
(4ᵗʰ DAY)
NEGATIVE.

MANTOUX.
(2ⁿᵈ DAY)
NEGATIVE

Delayed Reactions.

The usual response on the skin to tuberculin is
a reaction appearing in 24 hours usually at its maxi-
mum 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 re-
garded as exceptional and being infrequent its meaning
has been difficult to interpret.

In this investigation I have found delayed reac-
tions not unusual and particularly in Measles .
Furthermore the delay in the appearance of the reac-
tion 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 appear-
ing 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)
                                        (see appendix)
particularly 3.

Table IX.

Day of rash.

	1	2	3	4
Negative	3	2	3	3
Positive	2	7	6	5
Delayed	1	2	2	2
Total	6	11	3	10
% Delayed.	16.6%	18.2%	27.7%	20%

Incidence of Delayed Reactions.

Reference to Table IX shows that the delayed re-
sults were obtained from tests performed during the
period of maximum anergy - the 1st, 2nd, 3rd and 4th
days of the rash. They were most common in the third
day when they recurred 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 ex-
pects that the negative results will be at their maxi-
mum. 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 reac-
tion completely.

Significance of the Delayed Reactions.

The fact that the period of delay does not cor-
respond with the period of anergy determined by the
negative results would not preclude it from indicating
the period of hypo-sensitivity yet the marked immed-
iate 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 maxi-
mum anergy. I am inclined to believe that the delay-
ed response indicates a balance between the two fac-
tors - exanthem and allergic state. When the rash
outweighs the tuberculin sensitivity a negative res-
ponse is obtained; When a mild rash occurs in the
highly allergic individual a straight positive res-
ponse 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 ap-
pears that the cells of the skin sensitized by the
injection of tuberculin in the anergic period res-
pond 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 dur-
ing the anergic 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 re-
sults up to the 20th day.

Debré and Papp (1926) record two cases found posi-
tive prior to the onset of measles but continuing
negative for 4 months after.   They were using the
Von Pirquet test which is more difficult to interpret
and more liable to traume reactions; and cannot im-
agine that this persistent negative result could be
due to the attack of measles.   Lere-Boullet 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 continu-
ing negative for 25 and 30 days after measles.

The results I have given so far concern the re-
actions 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:-

	Result of test 2 to 4 months after attack.		
	Positive	Negative	Total
Cases reacting negative up to 3 weeks from on-set	1	127	128

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 excep-
tional 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 O.T
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) <u>Review</u> When tubercle infection was more wide-
spread it may be that measles deserved its reputa-
tion 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 bronchi-
tis 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 tuber-
cle may succumb to an ordinary broncho-pneumonia
without pre-existing infection necessarily contribut-
ing 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 not-
able; he definitely refutes the idea that there is
a special relation between the two diseases. In Am-
erica Landis (1908) found tuberculosis an infrequent
complication of Measles occurring in only 0.43% of
457 cases. Copeland (1909) similarly found no in-
stance 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 sug-
gestive of the negative view, namely that there is
no direct relation between the two infections.
Noeggerath 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.
&1930
Nobecourt (1929) however maintains that the
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 a

previous tuberculous lesion there was no re-activation after measles

Lereboullet and Baize (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 tuber-
cle whether it be latent or active; those cases
will be referred to as "tuberculous" or "tubercular"
without necessarily implying clinical activity.

850 cases gave negative reactions while 51
tuberculous subjects were observed. It must be ac-
cepted that of the 850 negative patients a propor-
tion of the 120 cases tested only in acute stage may
actually have been tubercular - 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 hos-
pital irrespective of the character of their attack
and therefore these gave a true estimate of the mor-
tality; 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 test-
ed, so that the mortality figure over the whole
series would not be accurate. Also cases complicated
by whooping cough are excluded as this has consider-
able effect on mortality (See Chapter on Whooping
Cough)

CASE MORTALITY, TABLE X.

	No.Died	Case Mortality
500 consecutive negative cases	33	6.6%
51 positive or tuber- cular cases	4	7.8%

The slight increase in mortality in the tubercu-
lar 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

		0 - 2 years		2 years and over		
	Total	No. Died	Case Mort ality.	Total	No. Died	Case mort- ality.
Negative Group	176	25	14.2%	324	8	2.4%
Positive "	11	2	18.2%	40	2	5.0%
" " excluding deaths from Tuberculosis	11	-	-	40	2	5.0%

The number of tubercular cases is rather small
to provide an adequate comparison; age is so impor-
tant, however, in the prognosis that such a classifi-
cation 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 ex-
clude 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 tu-
berculosis so that the mortality from causes simi-
lar to those of the non-tubercular children was nil.
This is rather surprising. The contrary holds in
the tubercular subjects over 2 years; 2 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 es-
caped fatal complications from secondary invaders
and favours Frenkel's opinion that they with-
stand pyogenic infection remarkably well; the

converse is suggested in the older tubercular subject.

If these fatal cases are analysed it is strik-
ing that the deaths in tubercular children are <u>not</u>
from pulmonary complications in contrast to the
negative group.

<u>Total deaths in control group</u>   45

  <u>Causes of death</u>   Broncho-pneumonia   36

                    Enteritis   4

                    Acute Septicaemia   1

                    Bronchiectasis   2

                    Diphtheritic Croup   2

<u>Total deaths in 51 tubercular children</u> = <u>4</u>

  <u>Causes of Death</u>

Acute streptococcal septicaemia   1

   "   "   "   and pneumococcal
                                      meningitis   1

Tubercular Enteritis - miliary spread compli-
      cated by Whooping Cough   1

Tubercular Meningitis   1

It is rather striking that although broncho-
pneumonia is by far the commonest cause of death
in measles not one of the tubercular children suc-
cumbed to this complication although 6 actually had
this complication.

SUMMARY of 4 FATAL CASES IN TUBERCULAR GROUP

(See Appendix)

Case Age Sex

51. 2yrs. f. This child died within 48 hours of
the onset of measles - an unusually
rapid illness. At autopsy she was
found to have extensive glandular tu-
berculosis 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 intes-
tines. The actual cause of death was
an acute septicaemia a haemolytic strep-
tococcus being isolated from the spleen
post-mortem; there was also an early
acute inflammation in the lung from
which a predominating growth of strep-
tococci were obtained.

35 17 " M. This boy had no clinical evidence
of tuberculosis prior to measles, al-
though he had been suspect. He devel-
oped a pneumococcal meningitis (Type IV
infection) on the 11th day of measles
which was further complicated by an

otitis media in the third week from
which arose a streptococcal septicaemia
(blood culture - **pure** growth of haemo-
lytic 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 calci-
fication. There was no trace of a fo-
cus in the lungs and no evidence of any
recent acitivty 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 ac-
tivity 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 iso-
lated and kept under onservation.
She continued fairly well for 3 months
and then died of tubercular meningitis.

Discussion. Under two years the fatal cases succumb
ed to tuberculosis; in one whooping cough was an
added complication and the measles was very mild hav-
ing 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 con-
sidering 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
septicaemia. 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 diffi-
cult not to conceive some relation between the
rapid success of the haemolytic streptococcus and
the extensive lymphatic tuberculosis found at autop-
sy. This case is similar to those fatal "malignant"
cases of scarlet fever described by Millian 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 streptoccal infection
superimposed on the low-grade pneumococcal meningi-
tis 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.

COMPLICATIONS.

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.

	Tuberculin Negative				Tuberculin Positive			
	0-2 yrs.		2 yrs. & over		0-2 yrs.		2yrs. & over	
	No	%	No	%	No	%	No	%
Total	398		502		11 9		40	
Broncho-pneumonia	60	15.1%	44	8.8%	1	9.1%	5	12.2%
Lobar Pneumonia	6	1.5%	5	1%	-	-	-	-
Enteritis	20	5.1%	3	0.6%	3	27.2%	-	-
Otitis Media	52	129%	47	9.4%	3	27.2%	6	14.6%
Adenitis; Abscesses	10	2.5%	9	1.8%	-	-	1	2.4%
Furunculo- sis, Impeti- go.etc.	3	6.7%	1	1.4%	2	18.1%	-	-

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-

plications 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 sim-
                stage
ply 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 endea-

vour has been made to follow out the cases after their

leaving the hospital; this has not been done so com-

pletely 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-atten-

dance. 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 tuber-

culosis 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 at-

tack; the majority were re-tested with tuberculin to

confirm the previous result.

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

No. of cases personally re-examined and negative test
                            confirmed by re-test 115
  "   "   ".   "   " but not re-tested   30
  "   "   " attending East London Children's Hos.
                and found tubercular negative 3-6
                months after attack   13
                                                    ____
                            Total   158
                                                    ____

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 XIII - TUBERCULAR CASES TRACED SUBSEQUENT TO
LEAVING HOSPITAL.

Case No.	Age	Period of Observation.	Case No.	Age	Period of Observation.
1	5 yrs.	14 months	26	2 yrs	8 mths.
3	20	6 " mths	27	2 "	14 "
6	4 yrs	11 "	29	4 "	4 "
7	3 "	14 "	30	16 "	14 "
8	4 "	2 "	31	6 "	14 "
10	2 "	7 "	36	10 mths.	6 "
11	3 "	12 "	37	6 yrs.	12 "
13	6 "	4 "	38	3 "	8 "
14	3 "	7 "	39	5 "	12 "
15	6 "	8 "	41	1½ "	11 "
16	7 "	8 "	42	6 mths.	6 "
17	7 "	4 "	43	15 "	5 "
19	6 "	10 "	45	15 "	5 "
20	4 "	11 "			
21	3 "	7 "			
22	6 "	6 "			
23	2 "	6 "			
24	3 "	8 "			

It will be seen that 6 of the cases were under 2
years, an age at which an active tubercular manifes-
tation would be expected. Yet all were alive and well
5 - 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
precedure I adopted was to explain to the parents
that the child had been in contact with tuberculosis
at some time prior to the attack os 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 nega-
tive 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 òn 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

gain this lesion requires X-ray confirmation.

The only reliable comparative figure would be
he incidence of tuberculin reactions but even that
aries a great deal with class and age grouping.
 quote the following statistics of various authors
ithout attempting to compare them. My own results
or London indicate the incidence of fatal tuberculo-
s in measles among patients of the "hospital" class.

INCIDENCE OF TUBERCULOSIS.

	Total Cases	Tub.Test positive	Incidence of Tuberculosis	Case Mortality from intraculosis
Rilliet & Barthez (1854)	314	-	7%	-
Tiessinger (1894	650	-	2.3%	1.7%
Landis (1909)	457	-	0.43%	0.43%
Copeland "	75	-	-	-
Mobecourt (1930)	459	7.18%	3.59%	1.5%
Lereboullet & Baize (1931)	75	16.%	4.0%	
Klein (1927) (over 5yrs.)	172	-	-	
Bushnell (1918)	5.943	adults -	2.9%	
Choffé (1929)	137	-	1.4%	
Park Hosp. 1930-32	901	5.0%	-	0.2%

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 tuber-
culosis 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 frequent intervals.

Relation of tubercle infection to measles.

The incidence of fatal tuberculosis in measles
does not suggest any increased susceptibility follow-
ing 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.

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 anergy
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 com-
plication - 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 (O.T.) 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 in-
fluence 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 intra-
dermal tests, came to a similar conclusion, but while
Nobecourt 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 scar-
ification test gave a positive test with the intra-
dermal method.   The intra-dermal 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 4 to become negative
both to the von Pirquet and intra-dermal tests; of
these he cites one which developed tubercular menin-
gitis 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 there-
after 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.

Cases tested on one occasion only.

	Negative	Positive	Total	Percentage positive.
Tested in first week.	22	5	27	18.5%
" after first week.	80	19	99	19.0%

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 diff-
erence 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.

	Tested in first week.	Tested in second week or later.
No. tested once only.	27	99
No. tested twice or oftener.	79	181
Total	106	280
Total positive	9	27
Percentage positive	8.47%	9.6%

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 III.

Case.	INITIAL TEST.		SECOND TEST.	
	Week of disease	Result.	Week of disease.	Result.
10	1st	+ 18	-	-
11	"	++ 18	-	-
12	"	++ 15	4th	+++20 E 15
14	"	+++10E10	-	-
27	"	+++20 E5	5th	++++20 E10
29	"	+10(delayed)	4th	+++20 E 25
32	"	+ 20 E 5	4th	+++15 E 15
5	2nd	Negative	5th	++ 20
6	"	++ 12	5th	+++20 E 20
7	"	++ 20	6th	+++20 E 10
8	"	+++ 20	-	-
9	"	+++++ 20	-	-
17	"	+ 15	-	-
19	"	++ 15	4th	+++20
20	"	++++20E20	-	-
21	"	+++17 E 23	-	-
24	"	++++ 15	-	-
25	"	+ 15	4th	+++ 15 E 5
26	"	Negative	7th	++ 12 E 18
30	"	+++ 20 E 5	-	-
34	"	+ 15	-	-
1	3rd	++ 15	-	-
2	"	+++20 E18	6th	+++ 20 E20
4	"	+++ 18	-	-
31	"	+ 20	-	-
33	"	+++20 E15	-	-
35	"	++ 11 E25	-	-
22	4th	Negative	6th	+++20 E 45
36	"	++++16 E10	-	-
3	5th	Negative	7th	++ 12 E 23
15	"	++ 20	-	-
28	"	+++ 20 E10	-	-
13	6th	+++ 18	-	-
18	"	++ 10	-	-
23	"	(+) 4	-	-
16	9th	+++++ 20	-	-

Only 4 cases where 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 of 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 of the
previous injection of tuberculin.

Table IV.

Results of cases tested on two or more occasions.

Number of cases.	Week of first test.	Usual week of last test.	No. of positive reactions who were negative on first test.
79	1st	6th week	-
61	2nd	6th "	2
55	3rd	7th "	-
65	4th week or	10th "	2
260			4

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 sensitiv-
ity 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 depress-
ed 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.

<u>Four cases which gave an initial negative
response.</u>

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.
<u>On admission</u> 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.

28/12/31   "   "   (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 stimul-
ation 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 accom-
panied 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 conjunctiv-
itis 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., aet 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.

<u>On admission</u> there were no signs of consolidation, there

being numerous fine crepitations with vesicular breath-

ing at each base indicative of a resolving broncho-

pneumonia.   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
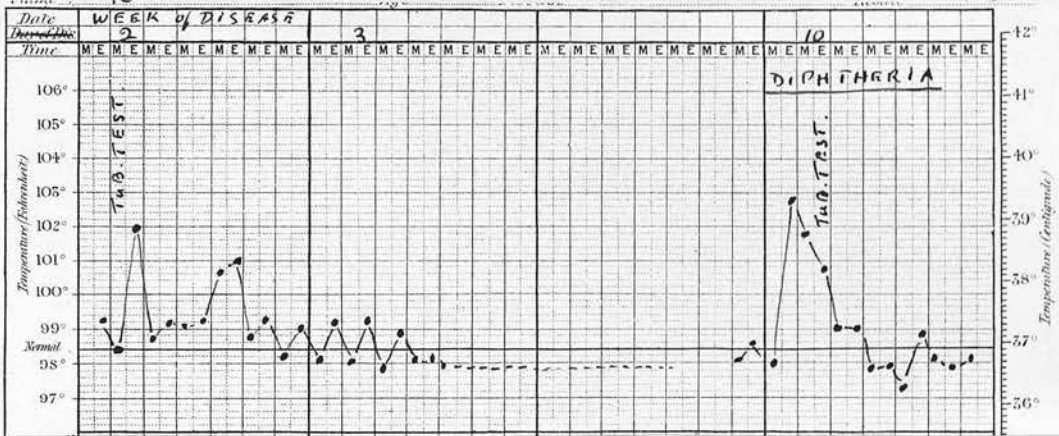
18/6/32 <u>Tuberculin test</u> (2nd week) - was <u>negative</u>.

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 <u>Tuberculin test</u> (7th week) was <u>positive</u>.

++ 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 was
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-muscularily.

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

102° 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 pertussic
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 faded
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.

	Week of primary tuberculin test.			
	1	2	3	4th et seq.
Number of cases	8	12	6	6
Average degree of tuberculin allergy.	2+	2.5+	2.3+	2.4+

The average response in the first week is somewhat lower than that or 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 Möller (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
                     measles
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 of latent tubercle infection in children
of school age.

Mousset (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 3 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. Dumans (1932) in 14 children under
2 years found no effect from the pertussis: 10
gave a positive tuberculin test but had no evidence
of focal activity; they/did well; 4 others had def-
inite hilar and/or lung changes; one died 6 months
after.

: Only one death in 14 children under
2 years with positive tuberculin reactions is really
a favourable result and Dumans 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 mor-
tality 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 of 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 strik-
ing 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 dur-
ation 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 ill-
ness 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 broncho-
pneumonia 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.

	Negative Tuberculin test.				Positive Tuberculin test.			
	0-2 yrs. No.	%	Over 2 yrs. No.	%	0-2 yrs. No.	%	Over 2 yrs. No.	%
Acute enteritis	23	16	3	1.4	-	-	-	-
Broncho-pneumonia	19	13.2	14	6.7	-	-	1	3.4
Lobar pneumonia	2	1.3	1	0.4	-	-	-	-
Bronchiectasis	-	-	3	1.4	-	-	-	-
Bronchitis	6	4.1	4	1.9	-	-	2	6.9
"Convulsions"	8	5.6	-	-	-	-	1	3.4
Adenitis, abscesses	1	0.7	4	1.9	-	-	1	3.4
Otitis media	13	9.0	13	6.2	2	28.5	2	6.9
Ophthalmia	2	1.3	1	0.4	1	14.1	1	3.4
Furunculosis, impetigo	11	7.6	6	2.9	-	-	1	3.4
Total cases	143		204		7		29	

The cases of bronchitis classed as complications
are only those which wer 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 VII.

Case Mortality.

	Total	Deaths	Case mortality
i. Cases with a negative tuberculin reaction (Dec.1931 to Mar.1932 only)	100	6	6%
ii. Cases with a positive tuberculin reaction	36	4	11.11%
iii. Cases with a negative tuberculin reaction complicated by measles	41	5	12.19%

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 tuber-
culosis.   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 mor-
tality 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:-

0.84%	Monraisse	(1901)
1.76%	Boulade	(1907)
1.23%	Deschamps	(1904)
2.46%	Lehlemmes	(1914)
2.17%	D'Espine	(1914)
2.38%	Wall	(1921)

To these may be added the following:-

1%   Koenigsberger and Fuerst
0.2%   Meyer and Burghard
0.74% Park Hospital, 1931-32.

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 (1925), 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 un-
complicated   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 consider-
able 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.

Age	0-1 yr.	1-2 yrs.	2-3	3-4	4-5	5 & over
Total No.	-	7	6	9	6	8
Deaths from Tb.	-	3	-	-	-	-
Deaths from other causes.	-	-	-	1	-	-

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 tuberculosis
in the form of tubercular enteritis (faeces Tb + ;

palpable abdomial glands) but no clinical evidence of
a focus in the lungs; measles ensued in the 7th week
and she died of <u>miliary tuberculosis</u> 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 25. 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 $3\frac{1}{2}$ 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 when examined 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 - $3\frac{1}{2}$ 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:-

Case No.	Age.	Period of observation.			
1	6 yrs.	5 months.			
3	4 "	13 "			
8	2 "	8 "			
9	3 "	14 "			
10	5 "	5 "			
11	4 "	9 "			
12	3 "	12 "			
15	3 "	6 "			
16	$1\frac{1}{2}$ "	6 "			
17	4 "	10 "			
19	3 "	8 "	(Complicated by measles).
21	$2\frac{1}{2}$ "	9 "		"	"	"
36	3 "	8 "		"	"	"
26	5 "	9 "				

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, interpret-
ation 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 ill-
ness 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.

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 Barthez, 1854).   The probable explanation
is that scarlet fever,
       , is not a disease of infancy but of later child-
hood, 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 convales-
cence.   Moltschanoff (1910) also using the scarific-
ation 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 febrile
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 of 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-

ised by an exanthem and fever accompanied by the
symptoms of headache, nausea, and commonly vomiting.
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 compar-
ison with that of measles. It is only the most
intense scarlet rashes that leave a faint yellow stain-
ing, 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
discute 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.

	Negative	Positive	Total
No.tested both in acute stage (1st seven days) and in convalescence (2nd week or later)	185	19	204
No.tested in acute stage only	29	4	33
" " " convalescent stage only	70	11	81
	284	34	318

As a crude indication of some effect on the tubercu-
ulin response, one can calculate the percentage of
positive reactors in the acute period and in convales-
cence; 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.

	Acute period.	Convalescence
Total No. tested.	214	255
No. of positive reactions.	14	30
Percentage " "	6.5%	11.7%

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.

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

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.

Moderate or intense rash.				Mild rash.			
Case No.	Initial test	Allergy	Day of test	Case No.	Initial test	Allergy	Day of test
1	-	+++	25	2	++	+++	21
3	-	+++	27	11	+	+++	
4	-	++	28	12	+++	?	
5	-	++	19	13	-	+	27
6	-	+	12	14	(+)	++	6
7	-	+	13	16	+	++	5
8	+	?		17	++	?	
10	(+)	++	10	23	-	+	37
15	+15	+++	9				
18	(+)	?					
20	-	+	65				
22	+	++	12				

Table VI.

	Moderate or intense rash.				Mild rash	
	No.	%	Allergy.	No.	%	Allergy.
Total	12	100%	1.9+	8	100%	1.8+
Negative	7	58.3%	1.8+	2	25%	1+
Positive	5	41.7%	2.33+	6	75%	2.33+

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 estimat-
ed 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 compar-
able 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. aet. 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 intra-

    dermal 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	Mant.. (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 of
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. Chorré (1929), in a study of 178 cases,
has found among 68, 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 epididym-
itis $2\frac{1}{2}$ 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.

Chorré also noted 8 patients with definite tuberc-
ular lesions prior to the onset; in 4 the lesions were
active.   In no instance was any effect noticed follow-
ing the streptococcal infection.   These results are
therefore equivocal.

Some recent work on the continent, however, has
indicated a relation between the hyper-toxic or malig-
nant 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 observ-
ations.   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-renals 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 complicat-
ions 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.

Complication	Non-tubercular group		Tubercular group.	
	No.	%	No.	%
Total	255	100	34	100
Cervical Adenitis & abscess	22	7.26	4	11.76
Otitis media	38	13.15	3	8.82
Mastoiditis	2	0.69	2	5.88
Albuminuria	46	2.07	-	-
Nephritis	46	2.07	-	-
Rhinitis	6	2.07	6	17.82
Skin sepsis (impetigo furuncles; onychia	3	1.3	4	11.76

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 onychias 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 impress-
ion 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.

Vll. DIPHTHERIA.

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 five retested in
convalescence were positive. The two cases positive
only in convalescence Rolly accepted as illustrative
of the effect of the diphtheria infection. Moltschan-
off (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; Moltschanoff
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:-

Table I.

	Negative	Positive	Total
Number tested in first 2 weeks and also in convalescence (4th, 5th, or 6th week).	104	18	122
Number tested in first 2 weeks only	57	9	66
Number tested in convalescence only	27	3	30
Total	188	30	218

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.

	Acute period	Convalescence
Total number of cases tested	188	152
Number of positive reactions	27	21
Percentage of positive reactions	14.3%	13.8%

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 demon-
strate 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 subsequent-
ly, but the second test was performed 25 days after,
so that the delayed response cannot be ascribed to
this rash as Case 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 know-
ledge of his having been in contact either just pre-
ceding 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 diphtheria - 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 exunating the nares; there was no
faucial inflammation; the submaxillary glands
were slightly enlarged. There was no toxaemia,
the boy being quite comfortable and bright, with-
out 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

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 convales-
cence. 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.

Case	Day of disease	Response
21	3	+++ 20 mm
17	3	++ 20 E 30
18	5	+ 15
23	7	+ 15 E 30
24	6	+++ 18 E 35
27	7	+++ 20
29	7	++ 20 mm.

Cases tested only after the acute stage

Case	Day of disease	Response
7	47	+++ 18 E 17
12	9	+++ 20 E 20
13	9	++ 15
14	18	+ 15
21	32	+ 10
22	32	++ 15 E 25
26	35	+++ 15 E 35
28	14	+++ 18 mm. E 22

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 IV.

Allergy	+	++	+++
Numbers in "acute" group	2	2	3
" " "convalescent" group	2	2	4

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.

	Initial test in acute stage.		Test in convalescence.	
Case No.	Day of disease.	Response.	Day of dis.	Response.
1	7	+ 15	21	++15 E 30
2	3	+++15 E 7	20	+++20 E 10
3	1	++ 15	30	+++17 E 18
5	1	+ 15	12	+15 E 10
8	3	+++20 E 10	46	+++20 E 10
9	3	++ 16	25	+++16
10	3	++ 17	34	+++20 E 10
11	4	+ 12	72	++16 E 14
15	6	++ 20	49	++20
16	3	++ 15	20	++ 18 E 12
19	4	++ 18 E 17	32	+++20 E 25
20	3	+ 17	32	+++15 E 45
26	5	+10(delay- ed 19 days)	25	++ 18 E 27
30	5	+ 14	58	+++ 14
31	5	+ 12	8	+ 10
32	6	+ 15	33	+ 10
33	4	+ 15	27	++ 13 E 17

Case 31 was one of tubercular meningitis com-

plicated 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 faucial diphtheria in the
third week just following an acute cervical abscess.

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

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
               faucial pillars extending on to the soft
               palate; a culture of the throat was posi-
               tive. Presuming that the diphtheria in-
               fection 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 ")
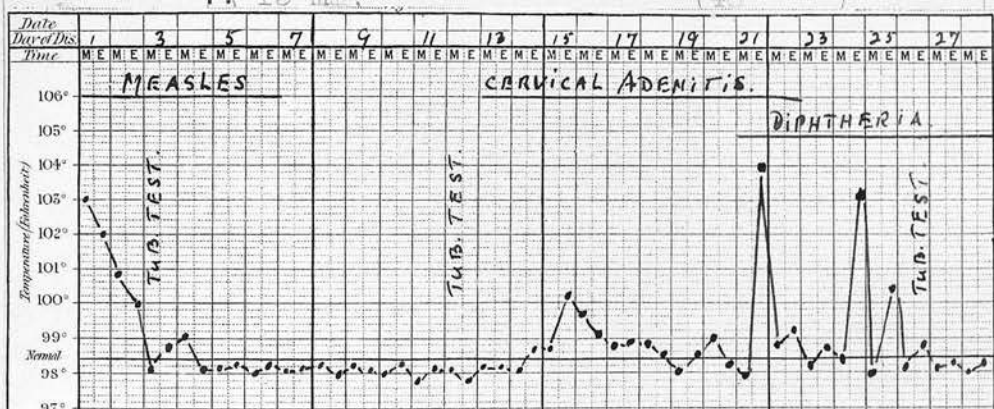
The unusual feature in this case is that the ex-
pected increase in the response to the test made on
3/2/32 did not occur; the reaction was identical with
the previous one. The test was made on the 4th day of
a severe attack of faucial diphtheria. A subsequent
test made three weeks later showed an increase 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 com-
plicated 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

   ++12mm; erythema 18 mm.   (24 hrs.)
   ++12mm.   (48 ")

18/8/32 he complained of sore throat; his tempera-
ture was 102°; the tonsils and fauces 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)   Temp.102°

    + 20 mm. (24 hrs.)   " 98

    ++ 20 mm. (48 hrs.)   " 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 diph-
theria 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 in-
tensity 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 sensitivi-
ty 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 un-
likely 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 criti-
cal 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 Moltschanoff
were examples of what I regard as subjects whose tuber-
culin allergy has diminished and fallen below the re-
action 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 33.

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

++ 13mm; erythema 30 mm. (24 hrs.)   nil

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 con-
trol.

Tuberculin test	right thigh:	right arm	Control (left arm)
4 hrs. after	nil	+ 15mm.	nil
6/5/32 Traces of (+) urticarial erythema (24 hrs.)	10mm.	+ 20mm.	"
7/5/32 Rash gone (48 hrs.)	+ 11mm.	++ 15mm.	"
17/5/32 Tuberculin test	right thigh (same site) + 16mm. erythmia 4 mm. (24 hrs.)		

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 bila-
teral. 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.

	Negative cases		Positive cases.	
	No.	%	No.	%
Total	188	-	32	-
Otitis Media	15	7.9%	3	9.4%
Late adenitis	5	2.6%	-	-

Although it is suggested that tubercle infection
can play a part in the production of the toxic fea-

features of scarlet fever (Millian, 1932) there is no
evidence that the tubercular child is more suscepti-
ble to the toxin of diphtheria. I obtained no im-
pression 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 nega-
tive;   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 appre-
ciable difference between infected and non-infected
children.

CHAPTER VIII.

GENERAL CONCLUSIONS AND SUMMARY.

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 includ-
ing the few exceptions over that age in measles and
whooping cough.

I.   TUBERCULIN ALLERGY IN ACUTE INFECTIOUS
DISEASES.

In addition to the four diseases I have investi-
gated some effect on tuberculin sensitivity has been
recorded in most of the acute infections including
typhoid fever, lobar and broncho-pneumonia (McNeil,
1909; Paisseau and Tixier, 1909, Rolly, 1910; Gavet,
1912; Jousset, 1926); erysepelas (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 re-
action to tuberculin it is a feature of the acute
stage only not persisting long enough to constitute a
serious fallacy.

MEASLES: 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 a temporary depression of allergy during the erup-
tive 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 30 cases of diphtheris sensitive to
tuberculin I was unable to demonstrate an effect on
allergy sufficient to suppress the reaction complete-
ly. 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 ap-
preciable effect on tuberculin allergy. I was unable
to observe the effect on a child whose degree of sen-
sitivity was already known but in 32 cases tested
among their attack there was no evidence of any
effect analysing 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 observ-
ed 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 techni-
que may fail.

MECHANISM OF THE TEMPORARY ANERGY.

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 ap-
peared 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 fac-
tors - 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 recognosed 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. Debre (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 - 1.1000 rather than a
stronger solution thus avoiding the chance of a
pseudo-reaction. (See Chapter III.)

2. TUBERCULOSIS IN RELATION TO ACUTE INFECTIOUS DISEASES

The original intention in starting this investigation was to determine the duration of the anergic 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

		CASE MORTALITY.			
		All ages		0 - 2 yrs.	
	Total	All causes	T.B. only	All causes	T.B. only
All cases	901	6%	0.2%	-	-
Positive reactions	51	8%	4.0%	18.18%	18.18%

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 18.18% 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 cse 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 vases 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 Millian (1932) and Dumitrescu-Baldwin
(1922) in scarlet fever.

WHOOPING COUGH.

| | | CASE MORTALITY | | | |
| | | All ages | | 0 - 2 years. | |
	Total	All causes	T.B.only	All causes	T.B.only
All cases	386	6%	0.74	-	-
Positive reactors.	36	11%	9.0%	42.8%	42.8%

The case mortality from tuberculosis was 0.74%
a figure comparable to the results in the larger ser-
ies of Koenigsberger and Fuerst and Meyer and Burg-
herd. 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
70% 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 suscepti-
bility 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 fre-
quent complication.

The minor complications such as rhinitis impeti-
go; etc. were more frequent in tubercular children

In diphtheria I found no evidence of any rela-
tion between the two infected.

DISCUSSION.   The belief in the specific relation
of tuberculosis to measles and whooping cough ap-
pears to have arisen in the period when tuberculo-
sis was a clinical syndrome - "phthisis" - a pro-
longed 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 diag-
nosed 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 manifes-
tation 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 a exacerbation of tubercle
infection would be to show that the active manifes-
tations increase after an epidemic of measles and

whooping cough.

Analysing the incidence of tubercular menin-
gitis it has been found to bear no relation to
epidemics of measles (Beisken 1925) nor does
tubercular meningitis precede measles and whooping
couhg in such frequency to suggest a specific rela-
tion between the infections. (Noeggerath and Eck-
stein - 1924; Cremieu-Alcan, 1926)

The sum of the evidence is in favour of the
view that measles is not really "la maladie tuber-
culissante"; it is to be realised that the disease
is the commonest of acute infections; very few
children escape it and it attacks the child usual-
ly in the first 3 years the period when tubercle in-
fection 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 ex-
hausting illness appears to have an unfavourable
effect.

P O L I C Y.

It was originally thought that one might sel-
ect positive reactors as suitable cases for con-
valescent treatment to obviate the tendency to ac-
tivation of the latent T.B. infection but the
investigation has shown rather surprisingly that
the majority of cases make straightforward recov-
eries even when returning to home surroundings
straight from the hospital. Such cases as did
develop active tuberculosis were cases to be sus-
pect of activity either by age or clinical evidence
and the result was what might be expected even with-
out the added complications of an acute infection.

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

The ultimate hope is that tuberculin tests
will rank with the Schick and Dick tests as a routine
prodecure 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

III. SUMMARY.

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 intra-dermal tuberculin test be fallacious in acute infectious diseases?

The intra-dermal tuberculin test in the standard dilution of 1-1,000 O.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 the test under 2 years will be of value in diagnosis and prognosis particularly in whooping cough when a fatal 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 tubercle.

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.

F I N I S.

A P P E N D I X . 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, of moderate intensity.

Day of
rash

4	Tuberculin test (rash at site of injection).	
5-20	nil.	
21	- positive response. 15 mm+ (17th day after test)	Tuberculin test
22	14 mm+ (18th day after test).	- - -
23	photographed	++ 20 mm.
24	stain of 12 mm.	+++ 20 mm. Erythema 15 mm.
25		++ 20 mm.

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 obtain-
ed from the second test on the 23rd day of the rash.

MANTOUX.
(19th DAY)
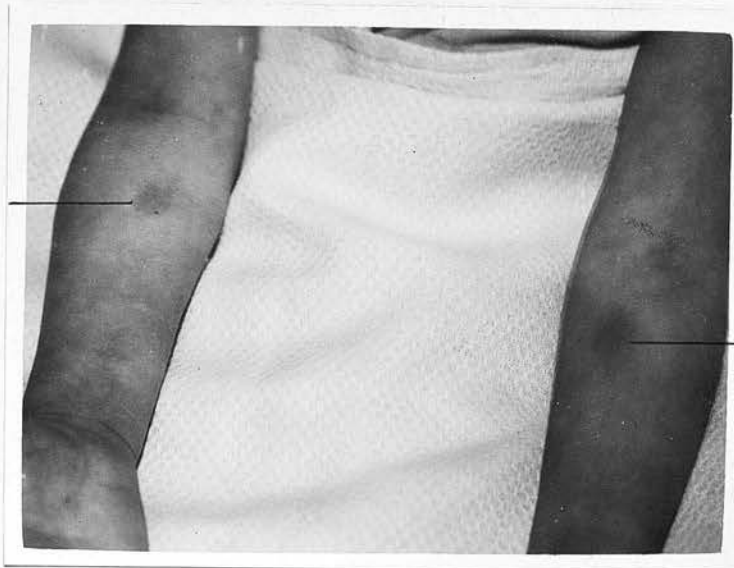
MANTOUX
(24 HRS.)

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   <u>Tuberculin test</u> -
   rash at site.

4   Erythema only - 7 mm.(+)

5   Faint erythema just ...... <u>Tuberculin test</u>
   visible. 7 mm (+)   staining present
                         Temp. normal et
                         seq.

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

7   nil. ------------------- <u>11 mm. ++</u>

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

11   14 mm. ++ - a 24 ------ 11 mm.+ --- <u>Tuberculin test</u>
   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. <u>Looks</u>
                             <u>oldest test.</u>

25   7 mm. purple stain. 8 mm.scal- 10 mm. scal-
                            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

```
 3  Tuberculin test (rash at site). Temp. 102°
 4-12   . nil.  .      Temp. normal on 9th day.
13     15 mm + (red)---------  Tuberculin test
                                (1/1000 dilution)
14     15 mm. (fading purplish).----  ++ 20 mm.
15     no change  --------------- -      "
16     dull red stain ----------    " (photograph)
18     fading stain .--------- Still a red papule = +
```

In this case the initial test was delayed <u>10 days</u>.
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.

IMMEDIATE
RESPONSE

DELAYED
RESPONSE

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.B. Content = definite contact with human tubercle
                infection.

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

Adenopathy: any appreciable changes in the lymphatic
glands clinically, whether it be the typical micro-
adenitis of tubercle the glands being small, rounded
and "shotty" oe a more gross enlargement not neces-
sarily 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 uncluding 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. Contaat. 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 sequela.

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 25mm.
(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. erythema 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. Nol.

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

                   28th "   --- 15mm. (24 hrs.)

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

              33rd "   --- 18 mm. (48 hrs.)

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 manifesta-

  tion.

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: sequela - 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 modi-

fied by the exanthem of scarlet fever.)

Clinical Summary.   Severe attack with intense con

fluent 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 6/12 years.

P. H.   Nil.

T. B. Contact: No.

Clinical T. B. - cervical adenopathy (left side)

Tuberculin tests: 5th day. Negative.

18th " --- 17 mm. erythema 8mm
(48hrs.)

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.

___

No. 12. J. T. Male: 1 5/12 years.

P. H.   bilateral otitis media 3 months ago.

T. B. Contact   No.

Clinical T.B.   Cervical adenopathy (left)

Tuberculin Test. 1st day - negative

10th " -- 10 mm. erythema 10mm.
(24 hrs.)

Clinical Summary : Moderate attack; febrile 5 days; No complication: recovery.

No. 13. J. T. Male, 6 years

P. H.   Nil.

T. B. Contact: No.

Clinical T.B. Nil.

Tuberculin tests: 5th   negative

                    19th   "

                    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.

No. 14. F. A. female, 3 years.

P. 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. G 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 26" - 15 mm. (48 hrs.)

26th " " " 48" -- 13 mm; erythema 17mm.
                                      (24 hrs)

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.

Clinital T.B. Nil.

Tuberculin tests: 3rd day negative.

                    4th " $(\frac{1}{100})$ - 20 mm. (48 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.B. 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.)

                   15th " - 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) R.R. male

3 years.

P.H.   Tonsillitis.

T.B. Contact: No.

Clinical T.B. Cervical adenopathy (bilateral)

Tuberculin tests: 6 days before onset - + 10 mm.
                                          (48 hrs.)

           1st, 3rd and 7th negative.

           12th (+) 5 m.m.)48 hrs.)

           23rd (+) 5 m.m. (48 hrs.)

Clinical Summary: (admitted to hospital with scar-

let fever 50 days before;) No complications;

recovery.

Case 19. J. A. female - 6 years.

P. 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 $\overline{(1000)}^{1}$ ++ 2 Omm.
E: 5 m.m. (24hrs.)

24 hrs. before onset of rash
$\overline{(10,000)}^{1}$ (+) 13m.m. (24 hrs.)

2nd day of rash $\overline{10,000}^{1}$ - negative

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

7th " " "   ++ 15mm. "

Clinical Summary: (Admitted to hospital with scar-
let 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 per-
sistent 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 7days
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 oc-
curred; there was no recurrence of the haematuri
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 tuber-
cle 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-activitated;

(6th day after)

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

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

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.

P.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 - 11mm.
(8 days)

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

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

Clinical Summary: acute stage of measles not observ-
ed; 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 manifesta-
tions.

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 15mm (48hrs.)

             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-

cent serum; febrile 2 days; no complication; re-
covery.

No. 26. B. A. female; 2 yrs.

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 8 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. Para-tubercular 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 com-
plications; 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 -- 15mm. (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 moder-
ate 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: 18 months lat-
er pneumonia: suspected of tuberculosis then but in-
vestigation proved negative.

R. B. Age 16 yr. Disease Result

BRONCHITIS — TUB. TEST — TUB. TEST

second week;   although his appearance was suggestive

MEASLES. BRONCHITIS — MANTOUX — MANTOUX — MANTOUX

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.
                                                    (48hrs.)
                    22nd   "   -- 12mm;   "   28mm.
                                                    (48 hrs.)
                    27th   " --- 16mm.   "   19mm.
                                                    (24 hrs.)

Clinical Summary: A moderate attack with a severe r
rash was followed by a bro"chitis persisting into the
second week;   although his appearance was suggestive
of tuberculosis - a sallow pale complexion with com
emaceation 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. VF 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 charac-ter; some sputum of mucoid character but the physi-cal 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.

P.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.

P.H. broncho-pneumonia (3 yrs.) scarlet fever (3yrs.)

T. B. Contact: No.

Clinical T. B. cervical micro adenopathy (bilateral)

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

19th " ---- 18 mm., erythema 22mm
(48hrs.)

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)
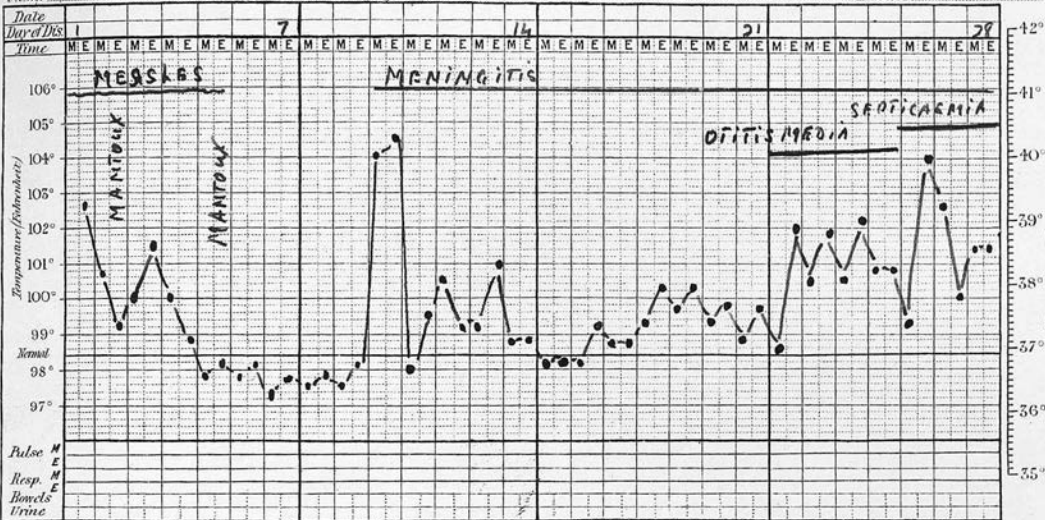   5th day   - 12mm. (48 hrs.)

Clinical Summary: a moderate attack fever of er-
ruptive phase, lasting 4 days:

Complications: pneumococcal meningitis (11th day)

Otitis Media (left) on 22nd day, followed by a
haemolytic (streptococcal pyaemia) (26th day); died
38th day.

Clinical temperature chart

Name: R M   Age: Disease: Result:

Day of Dis: 1 — 7 — 14 — 21 — 28

MEASLES   MENINGITIS

MANTOUX   MANTOUX

OTITIS MEDIA   SEPTICAEMIA

Temperature (Fahrenheit): 106° 105° 104° 103° 102° 101° 100° 99° Normal 98° 97°

Temperature (Centigrade): 42° 41° 40° 39° 38° 37° 36° 35°

Pulse
Resp.
Bowels
Urine

(COPYRIGHT)   Printed & Published by H.K. Lewis & Co., Ltd., 136, Gower St., London, W.C.   (LEWIS'S CLINICAL CHART)

Autopsy:

Autopsy: famileal meningitis (pneumococcal); ulcer-
ative endocarditis; multiple abscesses (streptoco-
ccal); 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 cervi-
cal glands especially on right side probably from
impetigo on the scalp).

Tuberculin test: 2nd day delayed - 10mm. (7 day)
                 10th "   -- 15mm. (48 hrs.)

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

After history: 9 months from onset on enquiry re-
ported 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 " -- 18mm. (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. Marasmus at 9 months; bronchitis at 18 months

T.B. Contact. No.

Clinical T.B. discrete cervical adenopathy (bilateral)

Tuberculin test: 7th day ----- 18 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. (48hrs.)
(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
noersum (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:

(confirmed by subsequent X-ray)

Tuberculin tests: 4th day Maximum reaction at 5th

day - 10 mm. (5mm. erythema only at 48 hrs.)

19th day --- 16mm. (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 -- 20mm. (24 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.

P.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 repponse.

on 7th day - 10mm.

25th   "   -- 17 mm. (24 hrs.)

Clinical Summary: Moderate attack with mild rash
(modified by convalescent measles serum); irregular
slight fever continued for 3 weeks after; complicat-
tions: signs of bronchitis from onset persiting
for 6 weeks; bilateral otitis media (15th day);
papular tubercular erruption (39th day); signs of
infiltration of left apex persisted unchanged.

Name. A.L   Age   Disease   Result

<u>After History:</u> 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.

<u>P.H.</u>   Nil.

<u>T.E. Contact:</u>   Yes.

<u>Clinical,T.B.</u> Discute enlarge cervical glands

<u>Tuberculin tests:</u> 6th day - 20mm. 24 hrs.

<u>Clinical Summary</u>. 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 otorrhoea;   otherwise fit and well;   no
evidence of active tuberculer infection.

Case 44. E. S. male;   1 7/12 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 resj:
Febrile 3 days;   Complication: acute enteritis
(16th day);   Taken home on 26th 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: 64th 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.H.   Bronchitis.

T.B. Contact: No.

Clinical T.B.   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, 49 & 50. (see Whooping cough Nos. 13, 21, 18, 11 respectively.

No. 51. L. P. female. 2 yrs.

P.H.   Quite well until last 2 or 3 weeks when the child "went off her legs" ; became listless, developed a cough.

T.B. Contact: No.

Clinical T.B.   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 5 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 streptococcal septicaemia
complicating measles in a child with extensive
primary lymphatic tuberculosis.

APPENDIX III.

Summary.

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. Nil.

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. Nil.

Tuberculin test; 2nd day; negative.

Clinical summary; moderate attack; complications,
broncho-pneumonia from onset, complicated by croup on

6th day;   signs of consolidation developed with
increasing dullness, especially at right base;   bilater-
al otitis media on 14th day;   died on 21st day.

Autopsy;   lungs, copious muco-pus in bronchioles;
consolidation of whole of 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
muco 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;   muco-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 7/12 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 38th 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;
copious amount of pus in the bronchioles; viscera showed
fatty degeneration; no endocarditis; no pyaemic abscesses.

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   of the alveolar
walls having disappeared, and the cellular exudate
composed of degenerating cells suggesting early abscess
formation. The right lung showed acute congestion and
hypostasis, 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 fibrino-
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;   1 2/12 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 filled 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.

A P P E N D I X IV.

Summary of 36 cases of Whooping Cough
with positive tuberculin reaction.

No. 1.   G.C. male; 8 years.

P.H.   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.   O. M. Male; 3 years.

P.H.   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.H.   Measles complicated by pneumonia at 10
months; scarlet fever at 2 yrs.

T.B. Contact: No.

Tub. Tests: 5th week. Negative.

7th "   ++ 12 mm; erythema 23 mm.

Clinical T.B. Nil.

Summary: Moderate attack: initial bronchitis;
recovery.

Duration of cough: 7 weeks; spasms 8; and whoop;

After History: alive and well, 13 months from
onset.

N.B. Tuberculin tests repeated 11 months after.

23/11/32 Test (Human O.T. only $\frac{1}{1000}$) Negative.

30/11/32 "   (s̄ā Human & bovine O. T. $\frac{1}{1000}$) + 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.

Durationof 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: ertyeham 20mm. (48hrs)

Clinical T.B. Nil.

Summary: Mild afebrile attack: mo complications: recovery

Duration of cough: 4 weeks; spasms 3; no whoop.

No. 7. R. H. female, 4 years.

P.H. measles at 2 years. Diphtheria at 3 years

T.B. Contact: Yes; father died of phthisis 2 years after.

Tub. Tests: 2nd week ++ 20mm. 48 hrs.

          6th   "   +++ 20mm. erytheme 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. R. 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 ++++ (vesiculation) 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 - + 18 mm. (48 hrs.)

Clinical T.B. 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. F. 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 (48hs.)

            (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 infec-
tion.

Case. 13   J. B.   female: 1 10/12 yrs.

T.B. Contact: Yes.

Tub: Tests: 6th week +++ 18 mm. 24 hrs.)

Clinical T.B.   tubercular enteritis: (faeces-Tuber-
cule 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-pneu-
monia at 18 months.

T.B. Contact: Yes.

Tub: Tests: 5th week ++ 15 mm. erythema 10mm.
(48 hrs.)

Clinical T.B. Nil.

Summary: Moderate attack: afebrile; 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. ?

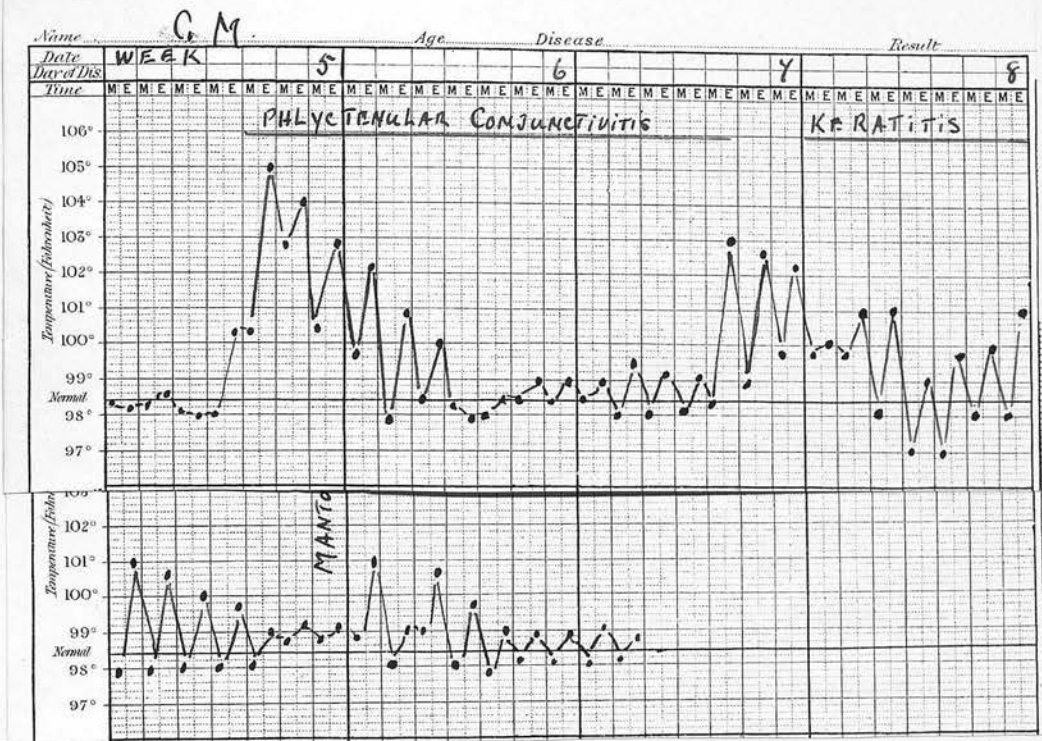T. B. Contact: ?

Tub: Tests: 9th week +++++ (Nrcrosis) temp.99°

Clinical T.B. discute cervical adenopathy (Bilateral)
Para-tubercular manifestation - phlyctenular conjunc-
tivitis.

Summary: Moderate attack: complicated by acute
febrile exacerbations of phlyctenular conjunctivi-
tis 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 tub-

ercular 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. P. 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 bronchi-
tis, otitis media, modified measles, milliary
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

Durationof Cough: 8 weeks. Spasms 8 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, ++++ 28 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.H. 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 tuber
culosis.

Case. 22; E.B. male, 5 yrs.

P.H. Tubercular arthritis.

T.B. Contact: No.

Tub. Tests: 4th week negative: 6th week +++ 20mm.
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 clini-
cal 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, 6 yrs.

T.B. Contact: ?

Tub: Tests: 2nd week + 15 mm. (delayed 12 days)
           4th " +++ 15 mm. (24 hrs.)

Clinical T.B. Nil.

Summary: Mild attack. No complications. Recovery

Duration of Cough: 5 weeks. spasms 8 with whoop.

Case 26. B.B. 5 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. (48hrs.)

Clinical T.B. Nil.

Summary: Severe attack complicated by broncho-
pneumonia 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.

C.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. (48hrs.)

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. Hilar glands enlarged (X-ray'

Summary: Mild attack, complication, initial

bronchitis, rhinits, 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 afebrile attack, uncomplicated
Recovery.

Duration of cough: 4 wks. spasms 6, and whoop.

Case 32. G. A. Male, 1 year.

P.H. Meales 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,
afebrile, 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,
afebrile, Recovery.

Duration of Cough: 9 weeks, spasms 3, 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 lym-
phatic 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, chicken
pox at onset, afebrile 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 consolid-
ation mostly in rught 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; 1 5/12 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 consolid-
ation 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 phosis
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 progress-
ed 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 $\frac{1}{2}$ 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; bronchiectasis.

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.

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